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Editorial

Climate-Related Nephropathies: Emerging Pathways, Global Burden and Future Directions

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Abstract

Rising global temperatures and more frequent extreme heat events are increasingly threatening kidney health. Ambient heat has been consistently associated with different kidney diseases, but most evidence concerns acute kidney injury during hot weather. In dialysis p-atients, extreme heat has been associated with more hospital admissions and deaths, and hurricanes, floods and wildfires have already interrupted dialysis services.

We use "climate-related nephropathy" as a broad label covering a broad spectrum of kidney manifestations. Experimental data link recurrent dehydration, polyol-fructokinase pathway, vasopressin and hyperuricaemia, but cause of chronic kidney disease of unknown aetiology in agricultural communities is not yet fully understood. The most exposed workers in hot regions, especially in lower socio-demographic regions, are underrepresented in routine data, and evidence is mainly limited to observational study on rest, shade and hydration programmes which seems to be associated with improved kidney outcomes. Early detection and kidney-protective therapy may prevent or delay kidney failure, though their environmental value has not been measured.

Indeed, dialysis is itself resource intensive. The 2025 KDIGO Controversies Conference reviewed these de–mands and carbon-footprint studies have quantified emissions for both renal replacement modalities. Haemodialysis uses large volumes of water and elec-tricity, whereas peritoneal dialysis generates plastic waste and depends on regular deliveries.

Nephrology must integrate workplace prevention, heat-health and dialysis continuity planning, and sustainab-le practice to make long-term viable use the scarce resources we have in our planet.

The kidney as a climate-sensitive organ

Ambient heat has been consistently associated with kidney morbidity in epidemiological studies, while global temperatures and the frequency of extreme heat events continue to rise [1,2]. Although plausible physiological mechanisms link heat stress to kidney injury, the renal consequences of heat and of other atmospheric exposures have attracted attention only recently. Acute morbidity during hot weather accounts for most of the epidemiological evidence. The effect of years of repeated exposure on the incidence and progression of chronic kidney disease (CKD) has been examined far less [2], and preventive measures have been tested in a handful of studies, few of them in people with established kidney disease or in workers who face heat every working day.

Climate-related nephropathy is used here as a broad label, under which fall acute kidney injury (AKI) during heatwaves and the chronic tubulointerstitial disease described among agricultural workers in hot regions, together with the renal complications of vector-borne and water-borne infections, whose transmission may shift with temperature and rainfall, and the indirect effects of drought and food insecurity on people who already have kidney disease [2-4].

Emerging pathways

Rodents subjected to recurrent heat-induced dehydration develop proximal tubular injury, renal inflammation and fibrosis In these models the polyol pathway is activated in the kidney and endogenous fructose is metabolised through fructokinase, which is one of the proposed routes of injury [5]. Vasopressin, hyperuricaemia and urate crystalluria have been implicated as well [6], but how much each contributes to chronic injury in people is unknown. Clinical or subclinical rhabdomyolysis

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during heavy physical work may add a further mechanism of acute tubular injury.

Among working-age agricultural and other manual workers in Central America, Sri Lanka and parts of India, there were selected CKD cases with predominant tubulointerstitial injury, with little or no proteinuria and without traditional causes sufficient to explain it [6]. Regional terminology includes Mesoamerican nephropathy, CKD of non-traditional or unknown aetiology, and chronic interstitial nephritis in agricultural communities. Heat and physical workload are among the leading candidates, while agrochemical exposure, metals and other environmental contaminants, infections and genetic susceptibility have also been proposed. Here, although several factors may interact, no single cause has been established [6]. Case definitions remain heterogeneous and are likely to evolve as surveillance and aetiological understanding improve.

Leptospirosis, dengue, malaria and hantavirus infection can all affect the kidney, and climate change can alter their geographic suitability and transmission patterns [4]. The size of these effects differs among pathogens and ecological settings. Flooding can increase contact with contaminated water and with water-borne infections that involve the kidney. Observational studies, pooled in a recent meta-analysis, have associated long-term exposure to ambient fine particulate matter with incident CKD [7]. However, the heterogeneity among studies is high and causality remains uncertain. Nowadays, wildfire smoke contributes as an episodic source of particulate exposure that is growing in importance.

Global burden

Large population-based studies have associated high ambient temperatures with increased AKI and kidney-related health-care utilization [8,9]. These data come mostly from high-income settings with reliable administrative records, and heat-exposed occupational populations in tropical and subtropical regions, where manual labour is common and nephrology services are scarce and underrepresented. The natural history of heat nephropathy adds a further difficulty, since the disease may present as kidney failure years after the relevant exposure.

Many of the populations most vulnerable to the heat-related kidney burden of a warming climate have contributed relatively little to cumulative greenhouse-gas emissions, and they may also have limited access to adequate shade, rest and hydration at work. Agricultural workers in hot regions who develop progressive tubulointerstitial disease often have few therapeutic options, and in many health systems kidney replacement therapy is hard to obtain. The burden of CKD is already concentrated in settings with a lower Socio-demographic Index [10], and heat-related kidney injury in a warming climate appears to be reinforcing that pattern.

For patients on dialysis the risk takes another form. Extreme heat has been associated with more hospital admissions and more deaths in this population [11-13], with a harder volume management in hot weather, and a storm or flood that cuts transport, electricity or water that can be fatal to someone who needs treatment three times a week. Hurricanes, floods and wildfires have already interrupted dialysis services, and what was learned from those episodes has been put into practice unevenly.

The dialysis paradox

Few treatments in medicine consume as much as dialysis, i.e. in-centre haemodialysis session uses large volumes of water and electricity, disposable circuits and dialysers, and a return journey for the patient, while peritoneal dialysis replaces most of that with regular deliveries of fluid bags and the plastic waste they leave behind. The 2025 KDIGO Controversies Conference on green dialysis reviewed these demands in detail [14]. Carbon-footprint studies have put numbers on the greenhouse-gas emissions of both modalities [15,16], while haemodialysis also draws heavily on water [14].

Some of this can be reasonably cut within existing practice: reverse-osmosis reject water can be reclaimed for non-clinical uses, and dialysate flow can be lowered where the clinical situation allows [14]. Home treatment spares the patient's journey to the unit, though part of the saving is taken back by consumables, deliveries and electricity at home, and certainly, the sum works out differs from one setting to another. Transplantation and conservative kidney management, for the patients who are suitable and who want them, use resources differently over the years, and any comparison between modalities depends on the health system and on how its electricity is generated. Further upstream, early detection and guideline-directed kidney-protective therapy may delay or avert kidney failure reducing the need for replacement therapy, bur the environmental value of that has not been measured.

Future directions

Prospective studies of heat exposure and renal injury have to reach the populations at greatest risk and linking kidney function data from occupational health programmes, primary care and community screening to the meteorological and occupational exposure data offers one way to do so. Cross-shift urinary markers of tubular stress and injury offer a way of detecting acute kidney stress during heat-exposed work [17]. How transient biomarker elevations relate to later CKD is

still unclear, and that link is what their use as end–points for workplace prevention programmes would depend on.

Intervention evidence comes mainly from observa–tional and quasi-experimental studies, in which water, rest and shade programmes have been associated with improved kidney outcomes [18]. In a large Nicaraguan cohort of 1044 sugarcane workers that contributed to 1938 person-harvests, an incident kidney injury, clini–cally diagnosed AKI and inflammatory markers decli–ned among burned cane cutters as the rest, shade, hydration and hygiene programme was progressively strengthened, although the study was not randomised [19]. Controlled evaluation of a comparable program–mme would give an estimate of effect size that an observational design cannot.

In people with established kidney disease, heat-health planning rests on individualised advice on hydration and on medication review, temporary adjustment of diuretics, renin-angiotensin system inhibitors and other kidney-protective medications during heatwaves but there is little evidence to guide it [2]. Dialysis services also require continuity plans for disruption of electri–city, water supplies and transport during extreme events with regular rehearsal and update as part of di–saster preparedness.

The relative contributions of heat, dehydration, uric acid, fructose metabolism and toxic co-exposures to chronic tubulointerstitial injury remain uncertain. Allopurinol attenuates injury in experimental heat stress nephropathy [20], and the fructokinase depen–dence of dehydration-induced injury in mice [5] points in the same direction. At present, no human clinical trial data currently supports pharmacological prevention. Susceptibility factors that modify individual risk in exposed populations are another target for genetic studies.

Climate-related kidney risk extends beyond clinical practice through occupational conditions, water secu–rity, urban environments and energy systems [21,22]. International nephrology initiatives have increasingly called for advocacy, climate-resilient kidney care and environmentally sustainable practice. In addition, much of what would protect heat-exposed workers lies in la–bour regulation and workplace practice. The adap–tation of kidney services to extreme weather falls to health-system emergency planning, and the environ–mental footprint of dialysis is set by procurement, wa–ter and energy policy as much as by clinical choices.

Conclusions

Ambient heat has been consistently linked to AKI in settings with reliable records, but how far repeated exposure contributes to chronic tubulointerstitial di–sease is still unresolved. The people most exposed, outdoor workers in hot regions, are the ones routine data see least, and often the ones with limited access to shade, rest and water during the working day. Patients on dialysis are exposed in a different way, to the heat itself and to anything that interrupts thrice-weekly treatment. Nephrology needs to plan for a hotter and less stable climate, from workplace prevention to heat-health and continuity planning for people with estab–lished kidney disease, and at the same time reduce what its own treatments, dialysis above all, cost the environment. Early detection opens the way to guideline-directed kidney-protective therapy, which delays kidney failure in eligible patients and hence, the need for replacement therapy, while the environmental value of that has still to be measured.

Conflict of interest statement. None declared.

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Review

Supplementation Across the Chronic Kidney Disease Journey: From Early Disease to Dialysis and Kidney Transplantation - An Evidence-Based Approach

Mateja Muric Begic[1], Nikolina Basic-Jukic[2,3], Ingrid Prkacin[3,4] and Vesna Herceg-Cavrak[5]

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Abstract

Chronic kidney disease (CKD) represents a progressive systemic disorder characterized by complex metabolic, inflammatory and nutritional abnormalities that evolve throughout the course of disease. Beyond declining kidney function, CKD is associated with protein-energy wasting (PEW), sarcopenia, chronic inflammation, oxidative stress, anaemia, CKD-mineral and bone disorder (CKD-MBD), metabolic acidosis and multiple micronutrient disturbances. These abnormalities significantly contribute to frailty, cardiovascular complications, impaired quality of life and increased mortality.

Nutritional supplementation has therefore become an important component of comprehensive CKD management. However, contemporary evidence no longer supports empirical supplementation but emphasizes individualized interventions based on CKD stage, nutritional status, dietary intake, dialysis modality, biochemical parameters, functional capacity and transplant status. During early CKD, supplementation strategies focus primarily on correction of documented deficiencies, particularly vitamin D deficiency, while maintaining adequate nutritional intake and preventing malnutrition. In advanced CKD and dialysis, the prevention and treatment of PEW become central therapeutic goals, with oral nutritional supplements (ONS), adequate protein intake, iron therapy and correction of metabolic acidosis representing the interventions with the strongest evidence. Emerging approaches targeting inflammation, oxidative stress and the gut-kidney axis, including omega-3 fatty acids, probiotics, prebiotics, magnesium, vitamin K, β-hydroxy-β-methylbutyrate (HMB), coenzyme Q10 and other nutraceuticals, remain areas of active investigation.

Following kidney transplantation, nutritional priorities shift toward prevention of obesity, metabolic syndrome, post-transplant diabetes mellitus and cardiovascular disease while maintaining adequate micronutrient status and avoiding potentially harmful supplement-drug interactions.

This review summarizes current evidence regarding nutritional supplementation throughout the CKD continuum, distinguishing interventions supported by clinical evidence from those that remain promising but insufficiently validated.

Keywords: chronic kidney disease, medical nutrition therapy, protein-energy wasting, CKD-mineral and bone disorder, dialysis, kidney transplantation

Introduction

The changing nutritional phenotype throughout CKD

Chronic kidney disease (CKD) is not only a disorder of filtration but a systemic metabolic condition associated with profound alterations in protein metabolism, inflammation, hormonal regulation, and body composition. As kidney function declines, patients may develop a range of metabolic and nutritional disturbances, including reduced appetite, metabolic acidosis, increased oxidative stress, and chronic inflammatory activation [1].

One of the most important consequences of these abnormalities is protein-energy wasting (PEW), characterized by loss of body protein mass and energy reserves, reduced muscle mass, and inadequate protein and energy intake [2]. PEW is associated with increased morbidity and mortality, particularly among patients with advanced CKD and those receiving dialysis therapy.

The nutritional challenges of CKD change throughout the disease trajectory. In early stages, the main objective is preservation of kidney function while preventing nutritional deficiencies. In advanced CKD and dialysis, the focus shifts toward preventing catabolism and maintaining muscle mass. After transplantation,

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the nutritional phenotype changes again, with increased risk of obesity, metabolic syndrome, post-transplant diabetes mellitus, and cardiovascular complications.
Therefore, supplementation strategies should follow the concept of a CKD journey, where the right intervention is selected for the right patient at the right stage of disease.
The KDOQI Clinical Practice Guideline for Nutrition in CKD recommends regular nutritional assessment and individualized nutritional therapy, including supplementation when dietary counselling alone cannot achieve nutritional targets [1].

CKD G1-G5

Prevention of deficiency and preservation of nutritional status

Vitamin D supplementation: correction of deficiency

Vitamin D abnormalities are common in CKD and may occur early in the disease course. Vitamin D deficiency or insufficiency may contribute to disturbances in mineral metabolism and secondary hyperparathyroidism.
Current recommendations support measurement of serum 25-hydroxyvitamin D [25(OH)D] concentrations and correction of documented vitamin D deficiency or insufficiency using treatment strategies recommended for the general population [3]. However, routine vitamin D supplementation has not been shown to improve clinically relevant CKD outcomes. Therefore, nutritional vitamin D should primarily be used to correct documented deficiency or insufficiency rather than as routine nephroprotective therapy [3].
In adults with CKD G3a–G5 not on dialysis, calcitriol and vitamin D analogues should not be routinely used. Their use may be reserved for patients with CKD G4–G5 with severe and progressive secondary hyperparathyroidism [3].

Vitamin D–Vitamin K axis: emerging importance in CKD-MBD and vascular calcification

The interaction between vitamin D and vitamin K has gained increasing attention in the context of CKD-mineral and bone disorder (CKD-MBD), as both nutrients contribute to calcium homeostasis and bone–vascular metabolism. Vitamin D plays a central role in the intestinal calcium absorption, regulation of parathyroid hormone secretion and maintenance of bone mineral metabolism [3].
Vitamin K is required for the γ-carboxylation and activation of vitamin K-dependent proteins, including osteocalcin and matrix Gla protein (MGP). MGP is an important endogenous inhibitor of vascular calcification. Patients with CKD, particularly those receiving dialysis, frequently exhibit impaired vitamin K status, reflected by increased concentrations of inactive dephosphorylated-uncarboxylated MGP (dp-ucMGP), which have been associated with markers of vascular calcification and adverse cardiovascular outcomes [4]. Clinical trials of vitamin K supplementation, particularly vitamin K2 (menaquinone-7), have demonstrated improvements in vitamin K status and reductions in dp-ucMGP concentrations. However, evidence that vitamin K supplementation reduces progression of vascular calcification or improves cardiovascular outcomes remains insufficient [4,5].

Magnesium supplementation and CKD-mineral metabolism

Magnesium has attracted attention as a potential modulator of CKD progression and vascular calcification. Potential mechanisms include inhibition of calcium-phosphate crystal formation and suppression of phosphate-induced vascular calcification. Observational studies have suggested associations between lower magnesium concentrations and increased risk of CKD progression; however, these findings cannot establish causality [6].
The MAGiCAL-CKD randomized clinical trial demonstrated that magnesium supplementation increased plasma magnesium concentrations but did not significantly reduce the progression of coronary artery calcification in patients with predialysis CKD [7].
Current clinical interpretation comprise: the correction of documented hypomagnesemia is appropriate; magnesium supplementation may be considered in selected patients; and the routine magnesium supplementation specifically for prevention of vascular calcification is not currently supported by sufficient clinical evidence.

Progressive CKD (G3b–G5): Prevention of protein-energy wasting

As CKD progresses, metabolic and nutritional disturbances become increasingly pronounced. Patients may develop anorexia, metabolic acidosis, chronic inflammation and impaired anabolic metabolism, contributing to protein-energy wasting (PEW) and progressive loss of skeletal muscle mass [1,2].

Oral nutritional supplements

Oral nutritional supplements (ONS) are an established nutritional intervention for patients with CKD who are unable to meet their nutritional requirements through dietary counselling alone. According to the KDOQI Clinical Practice Guideline for Nutrition in CKD, ONS should be considered in adults with CKD 3-5D who are at risk of or have protein-energy wasting when dietary counselling alone does not achieve sufficient energy and protein intake [1].
Potential clinical indications for ONS include: inadequate dietary intake; protein-energy wasting or risk

of PEW; unintended weight loss or declining nutri–tional status; and a reduced muscle mass or other evidence of nutritional deterioration.
Hence, the renal-specific ONS are often formulated to provide: concentrated energy density; adequate high-quality protein; low or controlled electrolyte content; a formulation adapted to fluid and electrolyte restric–tions in CKD.
Clinical studies suggest that ONS can improve: the total energy and protein intake; body weight and se–lected nutritional parameters; and nutritional status, par–ticularly in patients with PEW or inadequate nutritional intake [1].

Protein restriction, ketoacid supplementation and nutritional preservation in CKD

Protein metabolism undergoes profound alterations during CKD progression. Although dietary protein restriction may reduce nitrogenous waste and poten–tially slow CKD progression, excessive dietary restric–tion may increase the risk of protein-energy wasting (PEW), particularly in patients with reduced appetite or increased nutritional risk.
Current recommendations emphasize individualized pro–tein prescription according to CKD stage, metabolic stability, diabetes status, nutritional status and thera–peutic goals. Adequate energy intake should accom–pany protein restriction to help maintain nutritional status and prevent loss of lean body mass [1].
In metabolically stable adults with non-dialysis CKD G3-G5 without diabetes, KDOQI recommends, under close clinical supervision, either a low-protein diet providing 0.55-0.60 g/kg/day or a very-low-protein diet providing 0.28–0.43 g/kg/day with additional ketoacid/amino acid analogues to meet protein requirements of 0.55–0.60 g/kg/day [1].
Potential benefits of ketoacid/amino acid supplementa–tion include reduction of nitrogenous waste and su–pport of nutritional adequacy while allowing a lower dietary protein intake. However, implementation is li–mited by adherence, availability and the need for ca–reful patient selection and clinical monitoring. There–fore, ketoacid supplementation should be considered as part of structured dietary management under spe–cialist supervision [1].

Leucine-enriched protein, whey protein and β-hydroxy-β-methylbutyrate (HMB)

Loss of skeletal muscle mass and function is strongly associated with adverse outcomes in patients with CKD. Nutritional optimization combined with resis–tance exercise is considered an important component of strategies aimed at preventing and managing sar–copenia in CKD [9].
Leucine and leucine-enriched protein supplements have attracted interest because leucine stimulates muscle protein synthesis through activation of anabolic sig–nalling pathways, including the mTOR pathway. Ho–wever, evidence from randomized clinical trials (RCTs) in older adults remains inconsistent. A systematic re–view and meta-analysis of 17 RCTs found that isolated leucine supplementation did not significantly improve total lean mass or muscle strength, whereas some combined nutritional interventions showed benefits in selected functional outcomes [8].
Thus, potential nutritional strategies include: leucine-enriched protein supplements; whey protein prepara–tions; and essential amino acid mixtures.
β-hydroxy-β-methylbutyrate (HMB), a metabolite of leucine, has also been investigated as a potential stra–tegy to attenuate muscle loss. However, CKD-specific evidence remains limited, and available studies in he–modialysis patients have not demonstrated consistent improvements in body composition or other clinically relevant outcomes [9].
The current clinical approach: prioritize adequate energy and protein intake according to CKD stage, metabolic status and nutritional risk; combine nutritional inter–ventions with resistance exercise whenever feasible; consider amino acid or leucine-enriched protein supp–lementation only in selected patients within indivi–dualized nutritional strategies; HMB supplementation should not be routinely recommended in CKD because of insufficient CKD-specific evidence [9].

Metabolic acidosis and sodium bicarbonate supplementation

Metabolic acidosis is a frequent complication of ad–vanced CKD, resulting from impaired renal acid ex–cretion and reduced capacity for bicarbonate regene–ration. Persistent metabolic acidosis is associated with several metabolic disturbances, including increased protein catabolism, loss of skeletal muscle mass, in–creased bone resorption, insulin resistance and poten–tial acceleration of CKD progression [10,11].
Oral sodium bicarbonate supplementation has been investigated as a therapeutic strategy to correct meta–bolic acidosis and attenuate its adverse metabolic con–sequences. A randomized controlled trial by de Brito-Ashurst *et al*., demonstrated that bicarbonate supp–lementation in patients with CKD and metabolic aci–dosis slowed decline in kidney function and improved nutritional parameters compared with standard care [10].
Subsequent randomized trials and systematic reviews have demonstrated that bicarbonate therapy effectively increases serum bicarbonate concentrations. A syste–matic review and meta-analysis of 15 RCTs found that sodium bicarbonate may slow decline in kidney fun–ction and reduce the risk of kidney failure although, the certainty of evidence was low, and effects on mor–

tality and other clinically relevant outcomes remained uncertain [11].

From a nutritional perspective, correction of metabolic acidosis may help reduce protein catabolism and su–pport preservation of nutritional status. However, the clinical significance of these effects remains uncertain, and sodium bicarbonate should be considered a tar–geted intervention in patients with persistent metabolic acidosis confirmed by biochemical assessment [10,11].

Current clinical considerations: sodium bicarbonate supplementation should be guided by repeated measu–rement of serum bicarbonate concentration; treatment should take into account sodium load, blood pressure and the risk of fluid retention; patients with hyper–tension, edema or heart failure require careful moni–toring; and the correction of metabolic acidosis should be integrated with individualized nutritional manage–ment and strategies aimed at preventing PEW and sarcopenia.

Therefore, sodium bicarbonate may provide benefits beyond correction of serum bicarbonate concentra–tions, including potential effects on nutritional status and kidney function. However, the certainty of evi–dence remains limited, and further adequately powered randomized trials are required to determine its long-term effects on clinically relevant outcomes [10,11].

Iron Supplementation in CKD-Associated Anaemia

Anaemia is one of the most frequent complications of CKD and results from multiple mechanisms, including reduced erythropoietin production, iron deficiency or iron-restricted erythropoiesis, chronic inflammation and increased hepcidin concentrations. Hepcidin decreases intestinal iron absorption and limits iron release from storage sites, contributing to iron-restricted erythropoiesis.

Iron therapy remains a cornerstone of CKD-associated anaemia management. Available strategies include oral and intravenous (i.v.) iron.

Oral iron advantages are simple administration, lower cost and no requirement for i.v. access.

Limitations of oral iron are: impaired gastrointestinal absorption, particularly in the presence of inflammation, gastrointestinal adverse effects and slower increases in haemoglobin and iron indices compared with i.v. iron.

Intravenous iron advantages are: bypasses gastrointes–tinal absorption, more rapid increase in haemoglobin and iron indices and particularly important in patients receiving haemodialysis, in whom KDIGO 2026 su–ggests a proactive i.v. iron strategy when iron therapy is initiated [12].

The choice of iron therapy should be individualized according to the degree of anaemia and iron defi–ciency, haemoglobin, ferritin and transferrin saturation (TSAT), treatment with erythropoiesis-stimulating agents (ESAs) or HIF-PHIs, dialysis status, tolerability, availa–bility, cost and patient preferences [12].

The updated KDIGO 2026 Clinical Practice Guideline emphasizes individualized iron management rather than reliance on a single fixed laboratory threshold. For patients with CKD not receiving haemodialysis or with CKD G5 receiving peritoneal dialysis, KDIGO su–ggests initiating iron when ferritin is <100 ng/ml and TSAT <40%, or when ferritin is 100–<300 ng/ml with TSAT <25% [12]. Routine iron should generally be with–held when ferritin is >700 ng/ml or TSAT ≥40% [12].

Dialysis phase: replacing losses and preventing protein-energy wasting

Patients receiving dialysis are at particularly high risk of nutritional deterioration and PEW due to multiple interacting factors, including dialysis-related losses of amino acids and other nutrients, chronic inflammation, oxidative stress, metabolic acidosis, reduced appetite and increased protein requirements [1].

The goals of nutritional supplementation during dialy–sis include maintaining adequate energy and protein intake, preserving muscle mass, preventing or treating PEW and supporting functional status. Nutritional in–terventions should be individualized according to nut–ritional status, dialysis modality, dietary intake, co–morbidities and metabolic requirements [1].

Oral nutritional supplements and intradialytic nutrition

Patients undergoing maintenance haemodialysis have higher protein requirements than patients with non-dialysis CKD because of amino acid losses during dialysis, chronic inflammatory activation and anabolic resistance. According to the KDOQI Clinical Practice Guideline for Nutrition in CKD, oral ONS should be considered in patients with CKD 3–5D who are at risk of or have protein-energy wasting when dietary coun–selling alone does not achieve sufficient energy and protein intake [1].

Renal-specific ONS may provide concentrated energy and protein while allowing adaptation of electrolyte and fluid content to CKD-related dietary restrictions.

Clinical studies suggest that ONS can improve energy and protein intake and may improve selected nutritional parameters, including serum albumin, particularly in patients with inadequate nutritional intake or PEW [1].

Intradialytic oral nutritional supplementation has emer–ged as a practical strategy for providing nutritional support during haemodialysis. RCTs in malnourished haemodialysis patients have demonstrated improvements in selected nutritional markers with intradialytic ONS com–pared with dietary counselling or usual care [13,14].

Recent evidence also suggests that combining intra–dialytic protein supplementation with neuromuscular electrical stimulation may provide additional benefits

for selected measures of muscle mass and physical function in haemodialysis patients [15].

Water-soluble vitamins during dialysis

Haemodialysis may contribute to losses of several water-soluble vitamins, including thiamine (vitamin B1), vitamin B6, folate, vitamin B12 and vitamin C. In addition to dialysis-related losses, inadequate dietary intake, dietary restrictions, impaired absorption and comorbid illness may contribute to micronutrient deficiencies in patients with CKD [1].

Therefore, in patients receiving dialysis who have sustained inadequate dietary intake, malnutrition or other evidence of micronutrient deficiency, supplementation with multivitamins containing water-soluble vitamins may be considered to prevent or treat deficiencies [1].

However, routine high-dose supplementation should be avoided. Vitamin C requires particular caution because excessive intake may increase serum oxalate concentrations and potentially contribute to calcium oxalate accumulation, particularly in patients with advanced kidney disease [1].

Current clinical practice should therefore favour individualized supplementation rather than routine high-dose administration of individual vitamins. Supplementation should be guided by nutritional assessment, dietary intake, clinical circumstances and, when appropriate, biochemical assessment [1].

Zinc supplementation

Zinc deficiency has been reported in patients with CKD, particularly among those receiving maintenance haemodialysis. Reduced zinc status in CKD may be related to inadequate dietary intake, inflammation, altered metabolism and dialysis-related factors. Low zinc status has been associated with impaired taste perception, reduced appetite and poorer nutritional status in some CKD populations [16].

Several RCTs and meta-analyses have evaluated the effects of zinc supplementation in patients with CKD, including those receiving haemodialysis. Zinc supplementation consistently increases serum zinc concentrations and may improve selected nutritional parameters. A 2026 systematic review and meta-analysis found increases in body weight, serum zinc, serum albumin and dietary energy intake, however, the overall certainty of evidence was low [16]. Earlier evidence in maintenance haemodialysis patients similarly demonstrated increases in serum zinc and dietary protein intake, together with reductions in selected inflammatory and oxidative stress markers [17].

Evidence regarding clinically important outcomes, including hospitalization, cardiovascular events and mortality, remains insufficient. Therefore, current evidence does not support routine zinc supplementation in all patients with CKD.

Zinc replacement may be considered in patients with documented deficiency or a high clinical suspicion of deficiency, particularly those with poor nutritional intake, anorexia, taste disturbances or malnutrition. Supplementation should be individualized and monitored to avoid unnecessary or excessive intake [16,17].

Current clinical approach considers: assess zinc status in selected high-risk patients; correct documented zinc deficiency; consider supplementation in selected patients with poor nutritional intake or clinical features suggestive of deficiency; and avoid universal supplementation because evidence for effects on hard clinical outcomes remains limited [16,17].

Gut–kidney axis: fibre, probiotics and synbiotics

The interaction between intestinal microbiota and kidney disease has become an increasingly investigated area in nephrology. CKD is associated with alterations of the gut-kidney axis, including changes in microbial composition and diversity, impaired intestinal barrier function and increased production of gut-derived uraemic toxins.

Nutritional interventions targeting the gut microbiome include dietary fibre, prebiotics, probiotics and synbiotics.

Dietary fibre and prebiotics

Potential mechanisms include: an increased production of short-chain fatty acids; modulation of microbial composition and diversity; enhancement of intestinal barrier function; and potential reduction in intestinal generation and systemic exposure to uraemic toxins.

Potential sources include resistant starch, inulin, psyllium and other fermentable fibres. Although experimental and small clinical studies suggest favourable effects on microbiome composition and selected metabolic markers, evidence for clinically relevant outcomes remains limited.

Probiotics and synbiotics

Recent systematic review and meta-analysis evidence suggests that probiotic and synbiotic supplementation may reduce blood urea nitrogen (BUN) and C-reactive protein (CRP) concentrations in patients with CKD. However, effects on serum creatinine and eGFR have not been consistently demonstrated, and evidence for effects on uraemic toxins and other clinical outcomes remains limited [18].

Therefore, microbiota-targeted supplementation should currently be considered an emerging supportive strategy rather than standard therapy for all patients with CKD. Larger, adequately powered RCTs are required

to determine whether modulation of the gut micro–biome can translate into meaningful clinical benefits [18].

Emerging nutritional supplements targeting oxidative stress and inflammation

Beyond established nutritional interventions, increasing interest has focused on nutritional supplements targe–ting oxidative stress and chronic inflammation, both of which are important pathophysiological mechanisms in CKD progression and its complications [20].
Several compounds, including polyphenols, curcumin-based preparations, vitamin E and other antioxidant supplements, have demonstrated biological effects in experimental studies and clinical trials. Some studies have reported improvements in selected inflammatory or oxidative stress biomarkers; however, evidence for consistent clinically meaningful renal outcomes re–mains limited [20,21]. Therefore, these supplements should currently be considered emerging or adjunctive interventions rather than established renoprotective therapies, and routine use cannot be recommended on the basis of current evidence [20,21].

Coenzyme Q10 (CoQ10) and alpha-lipoic acid (ALA)

CKD is associated with increased oxidative stress, alterations in mitochondrial function and disturbances in cellular energy metabolism. These processes may contribute to endothelial dysfunction, chronic infla–mmation and progressive tissue injury [19,20].
Coenzyme Q10 is an essential component of the mitochondrial electron transport chain and functions as a lipid-soluble antioxidant. Alpha-lipoic acid acts as a mitochondrial cofactor and redox regulator with anti–oxidant properties.
Potential mechanisms of action include: reduction of reactive oxygen species production, modulation of mi–tochondrial energy metabolism, modulation of infla–mmatory signalling pathways and reduction of oxi–dative damage.
Small clinical studies of antioxidant interventions have reported effects on selected biomarkers of oxidative stress and inflammation in patients with CKD. However, evidence remains insufficient to establish that CoQ10 or alpha-lipoic acid slows CKD progression, improves cardiovascular outcomes or reduces mortality [19,20].
Therefore, we should consider: CoQ10 and ALA re–main biologically plausible but insufficiently validated interventions; their use should currently be considered investigational rather than established CKD nutritional therapy; routine supplementation cannot currently be recommended.
Further adequately powered RCTs are required before these interventions can be incorporated into standard CKD nutritional management [19,20].

Curcumin and other nutraceuticals

Chronic inflammation and oxidative stress are impor–tant pathophysiological features of CKD and may con–tribute to disease progression, endothelial dysfunction and PEW [19,20]. Curcumin, the principal bioactive compound derived from *Curcuma longa* (turmeric), has attracted interest because of its anti-inflammatory and antioxidant properties [21].
Potential mechanisms include modulation of NF-κB signalling, regulation of pro-inflammatory cytokine produc–tion and modulation of oxidative stress pathways [21].
Experimental studies and small clinical trials suggest potential biological and renoprotective effects, however, human evidence in CKD remains limited and hetero–geneous. Important limitations include variable bio–availability, differences between curcumin formula–tions and limited long-term clinical safety data [21].
Therefore, curcumin should currently be considered an investigational nutraceutical rather than an established CKD therapy**,** and routine supplementation cannot currently be recommended.

L-carnitine supplementation

Carnitine plays an important role in mitochondrial fatty acid transport and cellular energy metabolism. In patients undergoing haemodialysis, plasma and tissue carnitine concentrations may decrease because of dia–lysis-associated losses, reduced dietary intake and im–paired endogenous synthesis.
Potential clinical effects of L-carnitine supplementa–tion include: improvement of muscle energy meta–bolism; possible reduction of muscle cramps; potential improvement in erythropoiesis-stimulating agent (ESA)-resistant anaemia.
Several clinical trials and systematic reviews have investigated L-carnitine supplementation in haemodialy–sis patients. Although some studies have suggested po–tential benefits, particularly for muscle symptoms and selected haematological parameters, evidence remains inconsistent, and clinically meaningful effects on ma–jor patient-centred outcomes have not been conclu–sively demonstrated [22].
Current clinical approach comprehense: L-carnitine supplementation is not routinely recommended for all dialysis patients; but it may be considered in selected patients with documented carnitine deficiency and per–sistent symptoms or clinical problems that remain ina–dequately controlled with standard management [22].
Further well-designed RCTs are needed to clarify the clinical role of L-carnitine supplementation in haemo–dialysis patients.

Vitamin D after transplantation

Vitamin D deficiency remains common after kidney transplantation. Several factors may contribute to reduced vitamin D status in transplant recipients, including limited sunlight exposure, corticosteroid therapy, persistent CKD-related mineral and bone abnormalities, and alterations in vitamin D metabolism.
Low vitamin D status after transplantation has been associated with: impaired bone health; increased fracture risk; persistent abnormalities of mineral metabolism; potential effects on immune regulation.
Recent expert consensus recommendations support monitoring and correction of vitamin D deficiency in patients with CKD, including kidney transplant recipients, while avoiding excessive dosing and maintaining appropriate biochemical monitoring. Vitamin D supplementation should therefore be individualized according to serum 25-hydroxyvitamin D concentration and relevant biochemical parameters, including calcium, phosphate and parathyroid hormone levels, rather than prescribed routinely at high doses without an indication [23].
Monitoring should include: serum 25-hydroxyvitamin D [25(OH)D]; serum calcium; serum phosphate; and parathyroid hormone (PTH).
Although low vitamin D status has been associated with several adverse outcomes after kidney transplantation, evidence that vitamin D supplementation improves graft survival or other major transplant outcomes remains insufficient. Further RCTs are required to determine whether correction of vitamin D deficiency translates into clinically meaningful benefits in transplant recipients [23].

Magnesium and calcineurin inhibitors

Hypomagnesemia is a frequent metabolic complication after kidney transplantation, particularly among patients receiving calcineurin inhibitors (CNIs) such as tacrolimus and cyclosporine.
Calcineurin inhibitors can promote renal magnesium wasting through effects on tubular magnesium transport. Tacrolimus has been associated with increased urinary magnesium loss and reduced serum magnesium concentrations due to alterations in renal tubular magnesium handling [24,25].
Low magnesium concentrations after kidney transplantation have been associated with several metabolic and cardiovascular risk factors, including: an increased risk of post-transplant diabetes mellitus (PTDM); adverse metabolic profiles; and cardiovascular risk factors [25,26].
Correction of documented hypomagnesemia is appropriate, particularly in patients with significant biochemical abnormalities or symptoms. However, current evidence remains insufficient to recommend routine magnesium supplementation for all kidney transplant recipients or to demonstrate improvement in graft survival or other major transplant outcomes [25].
Therefore, magnesium management after transplantation should be individualized according to: the immunosuppressive regimen; serum magnesium concentration; kidney function; risk of post-transplant diabetes; and the cardiovascular and metabolic risk profile [25,26].

Avoiding uncontrolled supplementation after transplantation

Kidney transplant recipients require particular caution regarding dietary supplements because of the potential for interactions with immunosuppressive therapy, particularly calcineurin inhibitors such as tacrolimus and cyclosporine.
Potential concerns include: an altered tacrolimus or cyclosporine exposure; the modulation of cytochrome P450 (CYP3A4/CYP3A5) enzymes and drug transport pathways; unpredictable pharmacological effects of herbal products; and variable composition and uncertain pharmacological effects of commercially available herbal and nutraceutical products [27,28].
Particular caution is required with: herbal products; concentrated nutraceutical combinations; and a high-dose antioxidant preparations.
Because immunosuppressive drugs have a narrow therapeutic window, any supplementation strategy after kidney transplantation should be discussed with the transplant care team and accompanied by appropriate monitoring of immunosuppressant drug levels and relevant clinical parameters [27,28].

Evidence-based classification of nutritional interventions across the CKD journey

The evidence-based classification of nutritional interventions according to current clinical evidence is summarized in Table 1.

Table 1. Evidence-based classification of nutritional interventions across the CKD journey

Intervention	Evidence level	Current clinical position
Medical nutrition therapy (MNT)	Strong	Recommended throughout CKD as the foundation of individualized nutritional managemen
Oral nutritional supplements (ONS) in patients at nutritional risk	Low / limited	Recommended as a trial when dietary counselling alone does not achieve adequate energy and protein intake
Protein supplementation in	Moderate / individualized	Individualized according to CKD stage,

PEW/sarcopenia risk		metabolic status and nutritional risk
Iron supplementation	Strong / established	Recommended for CKD-associated anaemia according to haemoglobin, ferritin, TSAT and clinical context
Correction of vitamin D deficiency	Moderate	Recommended when deficiency is documented, with biochemical monitoring
Sodium bicarbonate in metabolic acidosis	Moderate / evolving	May be considered in selected patients with persistent metabolic acidosis; long-term clinical benefit remains uncertain
Exercise combined with nutritional therapy	Increasing evidence	Important adjunctive strategy for prevention and management of sarcopenia and functional decline
Water-soluble vitamin/B-complex supplementation in dialysis	Targeted / deficiency-based	Consider in patients with inadequate intake or documented/suspected deficiency; routine high-dose supplementation is not establishe
Omega-3 fatty acids	Limited–moderate	Not routinely recommended as nephroprotective or cardiovascular preventive therapy in CKD/dialysis
Magnesium supplementation	Emerging	Correction of documented deficiency is appropriate; routine supplementation is not established
Vitamin K2	Emerging	Improves vitamin K status and surrogate markers such as dp-ucMGP; cardiovascular outcome benefits remain unproven
Fibre/prebiotics	Emerging	Promising gut–kidney axis strategy; clinical outcome data remain limited
Probiotics/synbiotics	Emerging	May improve selected uraemic and inflammatory biomarkers; effects on clinical outcomes remain uncertain
HMB	Emerging	Potential role in muscle preservation; insufficient evidence for routine CKD use
L-carnitine	Limited	May be considered in selected dialysis patients; routine supplementation is not recommended
Coenzyme Q10 / alpha-lipoic acid	Experimental	Biological plausibility exists, but clinical evidence is insufficient for routine use
Curcumin/nutraceuticals	Experimental	Investigational; insufficient evidence for routine clinical application
High-dose antioxidant supplementation	Not routinely recommended	No established clinical benefit sufficient to support routine use; potential for inappropriate or excessive supplementation

Abbreviations: CKD, chronic kidney disease; ONS, oral nutritional supplements; PEW, protein-energy wasting; HMB, β-hydroxy-β-methylbutyrate; dp-ucMGP, dephosphorylated-uncarboxylated matrix Gla protein.

Table 2. Supplementation strategies across CKD stages

Supplement/intervention	Early CKD G1–G3	Advanced CKD G3b–G5	Dialysis	Transplantation
Vitamin D	Correct documented deficiency with nutritional vitamin D; monitor CKD-MBD parameters	Consider active vitamin D analogues reserved for selected patients with severe/progressive secondary hyperparathyroidism	Correct deficiency and monitor calcium, phosphate and PTH	Correct deficiency; monitor vitamin D status and bone health
Vitamin K	Investigational; possible role in vascular calcification pathways	Investigational; evidence mainly based on vitamin K status and surrogate markers	Deficiency may occur; clinical benefit of supplementation remains unproven	Consider potential interactions, particularly with vitamin K–antagonist anticoagulants
Magnesium	Correct documented deficiency; monitor according to kidney function	Use cautiously because of reduced renal magnesium excretion	Consider in selected patients with documented deficiency	Monitor frequently because calcineurin inhibitors may promote magnesium wasting
Oral nutritional supplements (ONS)	Consider when dietary intake is	Important in patients at risk of PEW or	Recommended/considered in patients with	Usually not routine; consider according

	inadequate	sarcopenia	malnutrition or inability to meet nutritional targets despite dietary counselling	to nutritional status
Protein supplementation	Individualized according to CKD stage and nutritional risk	Individualized; balance nutritional adequacy with avoidance of excessive protein intake	Increased protein requirements; frequently required in PEW risk	Focus on adequate protein intake, healthy body composition and metabolic control
Ketoacid analogues	Selected patients receiving very-low-protein diets	May be considered within structured dietary programs	Not routinely used	Not standard therapy
Sodium bicarbonate	Consider if metabolic acidosis develops	Evidence-supported in selected patients with persistent low bicarbonate	Individualized; depends on acid-base status.persistent metabolic acidosis	Rarely required unless metabolic acidosis persists
Iron supplementation	According to iron status and anaemia parameters	According to Hb, ferritin, TSAT and clinical context	Frequently requires intravenous iron according to laboratory findings and clinical context	According to anaemia status
B vitamins	Usually adequate intake	Consider in selected patients with poor intake or deficiency risk	Consider in patients with inadequate intake, malnutrition or deficiency risk	Individualized
Omega-3 fatty acids	Cardiovascular/lipid indications; not established as nephroprotective therapy	Selected patients according to cardiovascular risk profile	Consider mainly for cardiovascular/lipid indications	Cardiovascular risk management
Fibre/probiotics	Research area	Promising gut–kidney axis strategy; clinical outcome data remain limited	Adjunctive only; clinical outcomes uncertain	Use cautiously, particularly early after transplantation
HMB/amino acids	Investigational	May be considered in selected patients at risk of sarcopenia	Investigational; insufficient evidence for routine use	Not routinely recommended.
CoQ10/ALA	Experimental	Experimental	Experimental	Consider potential drug interactions; not routinely recommended,
Curcumin/nutraceuticals	Experimental	Experimental	Not routinely recommended	Avoid uncontrolled use because of potential interactions with immunosuppressive therapy

Abbreviations: CKD, chronic kidney disease; PEW, protein-energy wasting; ONS, oral nutritional supplements; CKD-MBD, chronic kidney disease–mineral and bone disorder; PTH, parathyroid hormone; HMB, β-hydroxy-β-methylbutyrate; CoQ10, coenzyme Q10; ALA, alpha-lipoic acid.

Summary table: Supplementation across CKD stages

The recommended supplementation strategies accor–ding to CKD stage are summarized in Table 2.

Conclusions

Nutritional supplementation in CKD has evolved from a generalized supplementation approach toward indi–vidualized and evidence-based nutritional strategies guided by disease stage, nutritional phenotype and specific clinical needs.

The best-established components of nutritional mana–gement currently include: individualized medical nut–rition therapy, oral nutritional supplements in patients at nutritional risk, appropriate protein management according to CKD stage and nutritional status, iron therapy according to CKD-associated anaemia guide–lines, correction of documented vitamin D deficiency, and treatment of metabolic acidosis when present.

Several emerging interventions, including magnesium supplementation, vitamin K strategies, fibre-based the–rapies, probiotics and synbiotics, HMB, amino acid supp–lementation and antioxidant or mitochondrial-targeted strategies such as CoQ10 and alpha-lipoic acid, rep–resent promising areas of investigation. Ho–wever, cu–rrent evidence remains insufficient to support routine im–plementation of these interventions in all CKD patients.

The future of supplementation in CKD is not the pres–cription of more supplements, but the selection of the right intervention for the right patient at the right stage of kidney disease. This approach should be guided by nutritional assessment, biochemical evaluation and cli–nically meaningful outcomes rather than surrogate markers alone.

Conflict of interest statement. None declared.

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Original article

Early Creatine Kinase Elevation and Acute Kidney Injury in Trauma Patients: A Prospective Cohort Study

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Abstract

Introduction. Creatine kinase (CK) reflects muscle injury, but its relationship with the timing of acute kidney injury (AKI) after trauma is unclear. We assessed its association with early AKI and its added predictive value.
Methods. This prospective cohort included 251 adults with normal kidney function admitted to a trauma intensive care unit (ICU). We measured CK on ICU days 1 (CK1) and 2 (CK2). We defined AKI by KDIGO criteria and classified it as early (days 2-4) or late (days 5-14). Firth logistic regression was adjusted for age, diabetes, Injury Severity Score, lactate and vasopressor use. Because early AKI could already be present on day 2, CK2 was also analysed further after excluding patients with AKI on day 2.
Results. Early AKI occurred in 77 patients (30.7%) and late AKI in 50 (19.9%). Median CK was higher in early AKI than in patients without AKI on day 1 (826 vs 316 U/L) and day 2 (1,233 vs 310 U/L; both $p<0.001$), whereas CK in late AKI was similar to that in patients without AKI. Each doubling of CK increased the odds of early AKI (adjusted odds ratio [OR] 1.41 for both days; 95% CI 1.15–1.74 and 1.18-1.71). Among 215 patients without AKI through day 2, CK2 remained associated with AKI on days 3-4 (adjusted OR 1.50, 95% CI 1.18–1.93). This AKI developed in 59% of patients with CK2 >3,000 U/L, compared with 15% of the others. Adding this threshold to the clinical model increased the area under the curve from 0.83 to 0.86 (difference 0.031, 95% CI -0.002 to 0.076).
Conclusions. Higher early CK was associated with an early AKI. CK may support closer renal monitoring, but its incremental predictive value remains uncertain.

Keywords: acute kidney injury, creatine kinase, rhabdomyolysis, trauma, intensive care unit

Introduction

Acute kidney injury (AKI) is a frequent complication in trauma patients admitted to the intensive care unit (ICU) and is associated with increased morbidity and mortality [1,2]. Several factors may contribute, including hemorrhagic shock, impaired renal perfusion, muscle injury, and subsequent complications during the ICU stay [3,4].
Creatine kinase (CK) is an inexpensive and widely available marker of skeletal muscle injury. Muscle damage also releases myoglobin, which can contribute to kidney injury, particularly when accompanied by hypovolaemia and impaired perfusion [5]. CK concentrations above 5,000 U/L have been used in studies of rhabdomyolysis-associated kidney injury, and CK is included in prediction scores for renal replacement therapy or death [6,7].
However, the clinical meaning of CK depends on when it is measured and when AKI develops. Although peak CK has been associated with AKI in trauma cohorts, the peak is often reached only after AKI has developed, which limits its value for early prediction [4]. Admission CK has also shown limited added value over clinical prediction models [8]. Furthermore, combining early and late AKI into a single outcome may obscure differences in their relationship with muscle injury. The value of CK measured during the first two ICU days, and the information it adds beyond routinely available clinical risk factors, therefore warrants further evaluation.
We aimed to describe CK concentrations during the first ICU days and their subsequent course by AKI timing, assess their association with early AKI after adjusting for clinical risk factors, and evaluate exploratory CK thresholds. We also examined whether day-2 CK above 3,000 U/L added predictive information beyond routine clinical factors. ICU mortality was a secondary outcome.

Material and methods

Patients and definitions. We included all trauma pa–tients enrolled consecutively in the trauma ICU of the University Hospital of Trauma, Tirana, in a prospec–tive observational cohort study (May 2024-March 2026). Adults with normal kidney function at admi–ssion (estimated glomerular filtration rate [eGFR] >90 mL/min/1.73 m²) were eligible; patients with pre-existing or obstructive kidney disease, kidney trans–plantation, previous dialysis, direct kidney trauma, death within 48 hours, or a fall in creatinine >0.3 mg/dL within 72 hours were excluded. The study followed the Declaration of Helsinki, was approved by the Ethics Committee of the University of Medicine, Tirana (no. 472/6), and obtained written informed consent from patients or legal representatives. We defined AKI by Kidney Disease: Improving Global Outcomes (KDIGO) creatinine and urine-output criteria [9], using ICU-admission creatinine as baseline, and classified it by the day of first documented onset as early (ICU days 2–4) or late (ICU days 5–14). CK was measured on ICU days 1 (CK1) and 2 (CK2).

Statistical analysis

Data are median (interquartile range, IQR) or n (%). Early AKI was compared with no AKI and with late AKI using the Mann–Whitney U or Fisher's exact test, with Bonferroni correction. CK over ICU days 1–5 was analysed with a linear mixed model of log-CK (day×group interaction, random intercept per patient); measurements after day 2 were at clinicians' discre–tion. Day-1 to day-2 changes were assessed with the Wilcoxon signed-rank test in patients without AKI through day 2.

Associations with AKI were estimated with Firth lo–gistic regression adjusted for age, diabetes, Injury Severity Score (ISS), and first-24-hour lactate and inotrope/vasopressor use, with $\log_2$-CK (odds ratio [OR] per doubling); discrimination was assessed by the area under the receiver operating characteristic curve (AUC). CK1 and CK2 were evaluated for early AKI (days 2-4) and late AKI (days 5-14), based on the first documented AKI episode. Early AKI was com–pared with patients without early AKI (no AKI or late AKI), whereas late AKI was compared with no AKI, excluding early cases. Because CK2 measurement and AKI could occur on the same day, a sensitivity ana–lysis excluded patients with documented AKI on day 2 (n=36); the remaining 215 patients were analysed with AKI on days 3-4 as the outcome. Exploratory thre–sholds (>3,000 and >5,000 U/L) were analysed with the same models, and the added value of CK2 >3,000 U/L over these covariates was assessed by bootstrap difference in AUC (2,000 resamples).

ICU mortality was analysed with Firth regression adjusted for age, ISS, Glasgow Coma Scale (GCS) and day-1 Sequential Organ Failure Assessment (SOFA) score. Tests were two-sided ($p<0.05$). Analyses used Python 3.13 (statsmodels) and a custom Firth implementation [10,11].

Results

Patient characteristics

Out of 251 trauma patients, 124 (49.4%) had no AKI, 77 (30.7%) developed early AKI, and 50 (19.9%) developed late AKI (Table 1). Compared with patients without AKI, those with early AKI were older and more often diabetic, had higher ISS, day-1 SOFA score, and lactate, and more often had extremity/pelvic injury and received inotropes/vasopressors in the first 24 hours (all $p\leq0.04$). Compared with late AKI, early AKI was associated with higher ISS and lactate, more thoracic and extremity/pelvic injury, and more frequent inotrope/vasopressor use. In contrast, patients with late AKI more often had hypertension and head and neck injury (all $p\leq0.02$).

Table 1. Characteristics and outcomes of trauma ICU patients by timing of AKI

Characteristic	All (n=251)	No AKI (n=124)	Early AKI, days 2–4 (n=77)	Late AKI, days 5–14 (n=50)	p, early vs no AKI	p, early vs late AKI
Demographics and Comorbidities						
Age, years	60(42-70)	56(33-66)	62(49-71)	66(52-77)	0.02	0.34
Male sex, n (%)	218(86.9)	105(84.7)	67(87.0)	46(92.0)	1.00	1.00
Hypertension, n (%)	76(30.3)	31(25.0)	20(26.0)	25(50.0)	1.00	0.02
Diabetes mellitus, n (%)	67(26.7)	22(17.7)	30(39.0)	15(30.0)	0.003	0.69
Injury and severity						
ISS	25(25-41)	25(25-38)	30(25-54)	25(25-25)	0.001	<0.001
GCS	8(6-11)	9(6-10)	9(4-12)	7(5-9)	1.00	0.43
SOFA score, day 1	5(4-6)	5(4-6)	6(4-7)	6(5-7)	0.04	1.00

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Head and neck injury, n (%)	215(85.7)	108(87.1)	59(76.6)	48(96.0)	0.16	0.006
Thoracic injury, n (%)	75(29.9)	35(28.2)	33(42.9)	7(14.0)	0.09	0.002
Abdominal injury, n (%)	18(7.2)	9(7.3)	8(10.4)	1(2.0)	0.89	0.17
Extremity/pelvic injury, n (%)	52(20.7)	23(18.5)	26(33.8)	3(6.0)	0.04	<0.001
First 24 hours in ICU						
Lactate, mmol/L	2.9(1.9-4.0)	2.2(1.8-3.2)	3.8(2.9-5.4)	2.5(1.7-3.1)	<0.001	<0.001
Inotropes/vasopressors, n (%)	29(11.6)	1(0.8)	23(29.9)	5(10.0)	<0.001	0.02
Surgery, n (%)	31(12.4)	16(12.9)	10(13.0)	5(10.0)	1.00	1.00
Contrast-enhanced CT, n (%)	11(4.4)	6(4.8)	5(6.5)	0(0.0)	1.00	0.31
Nephrotoxic drugs, n (%)	31(12.4)	20(16.1)	8(10.4)	3(6.0)	0.60	1.00
Outcomes						
Renal replacement therapy, n (%)	12(4.8)	0(0.0)	7(9.1)	5(10.0)	0.002	1.00
ICU death, n (%)	132(52.6)	31(25.0)	55(71.4)	46(92.0)	<0.001	0.01
ICU length of stay, days	12(7-20)	13(8-23)	9(6-16)	13(9-16)	0.02	0.08

Values are median (interquartile range) or n (%). Variables under "First 24 hours in ICU" refer to the first 24 hours after ICU admission. p-values compare early AKI with no AKI (n=201) and early AKI with late AKI (n=127), using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables, with Bonferroni correction for two comparisons.
AKI-acute kidney injury (KDIGO), CT-computed tomography, GCS-Glasgow Coma Scale, ICU-intensive care unit, ISS-Injury Severity Score, SOFA-Sequential Organ Failure Assessment

CK course by timing of AKI

CK concentrations were higher in patients with early AKI than in those without AKI or with late AKI, on both day 1 (median 826 vs 316 and 320 U/L) and day 2 (1,233 vs 310 and 330 U/L; all p<0.001). CK concentrations in patients with late AKI were similar to those in patients without AKI (Table 2).

Table 2. Creatine kinase on ICU days 1 and 2 by timing of AKI in trauma patients

	No AKI (n=124)	**Early AKI, days 2-4 (n=77)**	**Late AKI, days 5-14 (n=50)**
CK day 1, U/L	316(154-836)	826(300-2.167)*	320(114-632)
CK day 2, U/L	310(160-1,200)	1.233(337-3.500)*	330(120-972)
AUC, CK day 1	-	0.69	0.44
AUC, CK day 2	-	0.71	0.46
Adjusted OR, CK day 1 (per doubling)	-	1.41(1.15-1.74)	0.98(0.76-1.25)
Adjusted OR, CK day 2 (per doubling)	-	1.41(1.18-1.71)	1.08(0.86-1.35)

CK values are median (interquartile range). *p<0.001 vs both no AKI and late AKI (Mann–Whitney U test, Bonferroni-corrected for two comparisons). In 36 patients with early AKI, AKI was first documented on day 2, the day CK2 was measured.
AUC for early AKI: early AKI vs all other patients; AUC for late AKI: late AKI vs no AKI (patients with early AKI excluded). Adjusted OR per doubling of CK from Firth penalized logistic regression adjusted for age, diabetes, ISS, lactate and inotrope/vasopressor use in the first 24 hours.
AKI, acute kidney injury (KDIGO); AUC, area under the ROC curve; CK, creatine kinase; ISS, Injury Severity Score; OR, odds ratio.

Across available measurements on ICU days 1-5, model-estimated CK concentrations differed between groups (p<0.001; Figure 1). Estimated concentrations were highest on day 4 in the early-AKI group and on day 2 in patients without AKI, while remaining lower in the late-AKI group. Measurements after day 2 were obtained at clinicians' discretion, limiting interpretation of the later course.

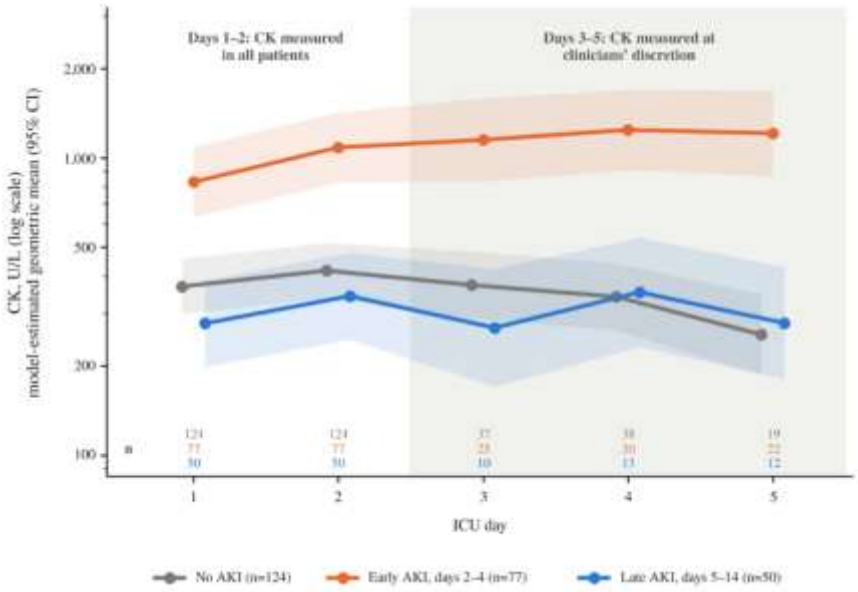

Fig. 1. CK concentrations over the first five ICU days by timing of AKI. Points and bands show model-estimated geometric means and 95% confidence intervals from a linear mixed model of log-CK with a patient-specific random intercept. Groups are no AKI (grey), early AKI on days 2-4 (orange) and late AKI on days 5-14 (blue).
No patient had documented AKI on day 1. CK was available in all patients on days 1–2; later measurements were obtained at clinicians' discretion, with daily sample sizes shown above the x-axis. AKI, acute kidney injury; CK, creatine kinase.

From day 1 to day 2, CK increased slightly in all three groups ($p<0.01$ within each group), but the increase was largest in patients who later developed early AKI. Among the 41 patients whose early AKI was first documented on day 3 or 4, CK rose by a median of 56 U/L (IQR 10 to 1,090) before AKI was documented, compared with 10 U/L (IQR-16 to 201) without AKI and 13 U/L (IQR-15 to 329) with late AKI (early vs no AKI p=0.008; early vs late AKI p=0.02; Figure 2).

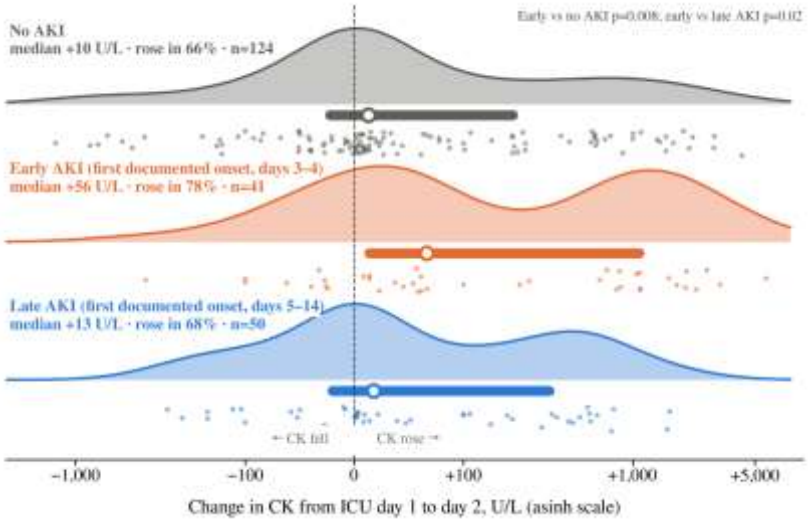

Fig. 2. Change in CK from ICU day 1 to day 2 by AKI timing. Patients with documented day-2 AKI were excluded. Dots represent patients, white circles medians, bars interquartile ranges and shaded curves smoothed distributions. The dashed line indicates no change; the x-axis uses an inverse hyperbolic sine (asinh) scale. Mann–Whitney U p-values are Bonferroni-adjusted for two comparisons. CK, creatine kinase; AKI, acute kidney injury.

CK and risk of early AKI

Both CK1 and CK2 were higher in patients who developed early AKI. Each doubling of CK increased the adjusted odds of early AKI by about 40% (OR 1.41 for both; AUC 0.69 for CK1 and 0.71 for CK2). Neither CK1 nor CK2 was related to late AKI (AUC 0.44 and 0.46; Table 2).
In 36 patients, AKI was first documented on day 2, the same day CK2 was measured. In a sensitivity analysis

excluding these patients, the remaining 215 patients showed a similar result: CK2 was still associated with early AKI on days 3-4 (adjusted OR per doubling 1.50, 95% CI 1.18-1.93; AUC 0.71). Additionally, we examined CK categories of ≤3,000, 3,001–5,000 and >5,000 U/L (Figure 3).

On day 1, early AKI developed in 62 of 230 patients (27%), 9 of 14 (64%) and 6 of 7 (86%), respectively. Overall, 15 of 21 patients (71%) with CK1 >3,000 U/L developed early AKI. Late AKI occurred in only one patient with CK1 >3,000 U/L, in the 3,001-5,000 U/L category (Figure 3A).

On day 2, in the sensitivity analysis (n=215), early AKI (days 3-4) occurred in 28 of 193 patients (15%) with CK2 ≤3,000 U/L, 8 of 13 (62%) with 3,001-5,000 U/L and 5 of 9 (56%) with >5,000 U/L. Overall, 13 of 22 patients (59%) with CK2 >3,000 U/L developed AKI on days 3-4, and only one developed late AKI (Figure 3B).

On both days, CK above 3,000 U/L remained asso–ciated with early AKI after adjustment for age, diabe–tes, injury severity, lactate and vasopressor use (ad–justed OR 5.26 for CK1 and 7.59 for CK2; Table 3).

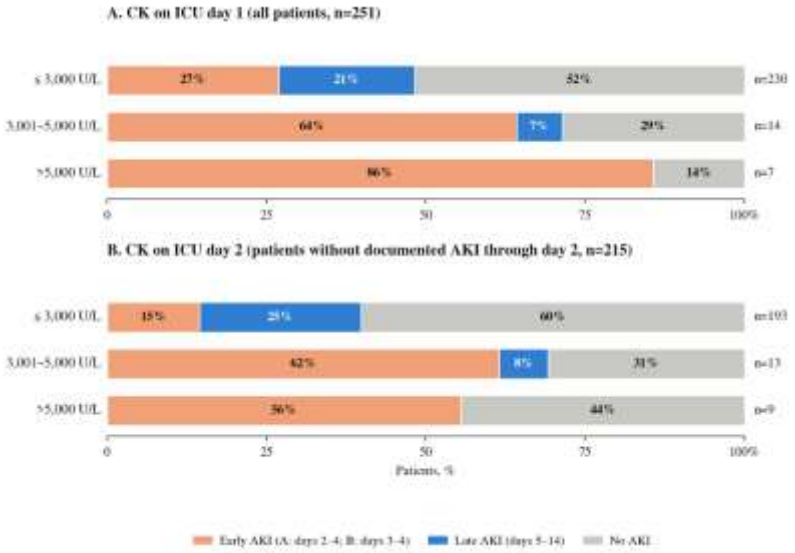

Fig. 3. AKI timing by CK category in trauma ICU patients. (A) Day-1 CK in all patients (n=251); early AKI: days 2–4. (B) Day-2 CK in patients without documented AKI through day 2 (n=215); early AKI: days 3–4. Timing refers to first documented AKI; late AKI: days 5-14. Bars show percentages; right-hand numbers indicate group sizes. Categories >5,000 U/L were small and are descriptive. CK, creatine kinase; AKI, acute kidney injury.

Table 3. Risk of early AKI above CK thresholds

Threshold	Patients above threshold, n	Early AKI above vs At or below threshold, %	Adjusted OR (95% CI)	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Day 1: CK1 and early AKI, days 2–4 (n=251; 77 events)							
CK1 >3,000 U/L	21	71 vs 27	5.26(1.78-17.1)	19	97	71	73
CK1 >5,000 U/L	7	86 vs 29	11.2(1.75-127)	8	99	86	71
Day 2: CK2 and first documented AKI, days 3–4, in patients without documented AKI through day 2 (n=215; 41 events)							
CK2 >3,000 U/L	22	59 vs 15	7.59(2.33-27.1)	32	95	59	85
CK2 >5,000 U/L	9	56 vs 17	8.96 (1.94–48.2)	12	98	56	83

Each threshold was analysed separately, comparing patients above with those at or below the threshold. Adjusted ORs from Firth penalized logistic regression adjusted for age, diabetes, ISS, lactate and inotrope/vasopressor use in the first 24 hours.

Day-2 analysis restricted to patients without documented AKI through day 2. Estimates for >5,000 U/L are exploratory and imprecise because of small numbers.AKI, acute kidney injury (KDIGO); CK1/CK2, creatine kinase on ICU day 1/day 2; ISS, Injury Severity Score; NPV, negative predictive value; OR, odds ratio; PPV, positive predictive value.

We further assessed whether CK2 >3,000 U/L im–proved discrimination beyond a clinical model con–taining age, diabetes, injury severity, lactate, and ino–trope/vasopressor use. The model's AUC was 0.83;

adding the CK2 threshold yielded an AUC of 0.86 (ΔAUC, 0.031; 95% CI, -0.002 to 0.076; p=0.09), a difference that was not statistically significant.

CK and ICU mortality

ICU mortality was 52.6% (132/251): 25.0% without AKI, 71.4% with early AKI and 92.0% with late AKI (early vs no AKI p<0.001; early vs late AKI p=0.01; Table 1). CK showed little discrimination for ICU mortality (AUC 0.48 for CK1 and 0.49 for CK2). CK2 was not significantly associated with ICU death after adjustment for age, ISS, GCS and day-1 SOFA (adjusted OR per doubling 1.13, 95% CI 0.96-1.34). With additional adjustment for any AKI, AKI was strongly associated with ICU death (adjusted OR 10.1, 95% CI 5.1-21.4), whereas CK2 was not (adjusted OR 0.96, 95% CI 0.79-1.16). Among patients with AKI, the association between CK2 >3,000 U/L and mortality was uncertain (70% vs 82%; adjusted OR 0.89, 95% CI 0.29–2.95). Among patients with early AKI, ICU length of stay was shorter in non-survivors than in survivors (median 8 vs 11.5 days).

Discussion

In this prospective cohort of trauma patients in the ICU, CK measured on the first two days was closely linked to the timing of AKI. Patients with early AKI had higher CK concentrations on both days, and later measurements suggested a more prolonged elevation. In contrast, patients with late AKI had lower CK1 and CK2 concentrations, similar to those without AKI. Among patients without documented AKI through day 2, CK2 >3,000 U/L identified a small group in whom 59% developed first documented AKI on days 3–4. However, its added predictive value beyond routine clinical factors remained uncertain, and CK2 was not independently associated with ICU mortality.

The link between CK and early AKI is biologically plausible. CK is released from injured skeletal muscle together with myoglobin, which damages the kidney through direct tubular toxicity, intratubular cast formation, and renal vasoconstriction, especially when hypovolaemia and acidosis are present [5]. In our patients, early AKI occurred in the most severely injured patients, who had more extremity and pelvic injuries, higher lactate, and more frequent need for vasopressors. CK therefore probably reflects the extent of muscle injury in patients who are also in shock. The association remained after adjustment for injury severity, lactate and vasopressor use, suggesting that muscle injury may add to the risk beyond shock alone. Because this is an observational study, however, we cannot conclude that muscle injury directly caused AKI. A multicenter trauma cohort also found peak CK to be associated with AKI after adjustment for injury severity, hemorrhagic shock and prehospital hemodynamics. However, peak CK was not included in the predictive model because it is a late variable [4].

The course of CK over time adds to this picture. In patients without AKI, model-estimated CK was highest on day 2 and then declined, broadly consistent with the peak around 40 hours after admission reported in a Thai trauma cohort [12]. In our early-AKI group, model-estimated concentrations remained elevated until about day 4; selective later sampling limits interpretation. The larger day-1 to day-2 increase before first documented AKI supports the relevance of early serial measurements, as recommended in current trauma consensus [13]. However, it remains unclear whether this change provides information beyond the day-2 CK concentration.

The different CK pattern in late AKI suggests that admission muscle injury may be less informative for renal dysfunction developing later. Patients with late AKI more often had head injury and hypertension and less often extremity injuries. Subsequent complications may contribute, but this analysis did not establish their role. Our findings therefore suggest that the timing of AKI should be considered when interpreting CK; they do not establish why the association differs between early and late AKI.

In our cohort, CK above 3,000 U/L was independently associated with early AKI, after accounting for age, diabetes, injury severity, lactate and vasopressor use. About 70% of patients with CK1 above this value developed early AKI, compared with about 27% of those with lower values. This threshold is lower than the 5,000 U/L commonly used in rhabdomyolysis studies [6], suggesting that in trauma ICU patients' risk is already increased at more moderate CK elevations. Sensitivity was low, as expected, because early AKI after trauma has several causes and marked CK elevation occurred in only a minority of patients. However, the threshold had a high positive predictive value: the patients with CK above 3,000 U/L had a higher risk to develop early AKI (Table 3). CK is therefore best seen not as a general predictor for all trauma patients, but as an early signal of a high-risk subgroup, which supports measuring it on ICU days 1 and 2. Adding CK to age, diabetes, injury severity, lactate and vasopressor use improved discrimination in the whole cohort only slightly, likely because the high-risk subgroup was small. This is consistent with Tarazona *et al.*, who found that admission CK alone discriminated AKI only modestly in severe trauma and added little when combined with clinical variables [8]. Established rhabdomyolysis scores, such as the McMahon score, were developed in patients with CK above 5,000 U/L to predict renal replacement therapy or death [7], and therefore address a different popularion and outcome than early AKI in our trauma ICU cohort.

CK2 was not independently associated with ICU mortality, either before or after additional adjustment for AKI. This is in line with a large multicenter trauma ICU registry, in which severe rhabdomyolysis (CK >5,000 U/L) was not associated with 30-day mortality after propensity score adjustment [14]. Thus, its asso–ciation with early AKI did not translate into a clear association with survival. Mortality was high in pa–tients with AKI, and AKI itself was strongly asso–ciated with death. The shorter ICU stay in early AKI may partly reflect earlier deaths: non-survivors stayed a median of 8 days, compared with 11.5 days among survivors. The association between AKI and mortality is consistent with previous trauma cohorts [3,4].

Our study's strengths include prospective enrolment, using both serum creatinine and urine-output criteria to define AKI, and classifying by the day of first docu–mented AKI, allowing separate analyses of early and late AKI and assessment of CK before subsequent AKI documentation.

There are also limitations. This was a single-center observational study with a moderate number of events, and residual confounding cannot be excluded. Labo–ratory tests were ordered at the clinicians' discretion: CK was available in all patients solely on days 1 and 2, limiting interpretation of its later course, and creati–nine was not measured daily, so some patients in the sensitivity analysis may have had unrecognized AKI on day 2. The 3,000 U/L threshold was selected during analysis and requires external validation. Restricting to patients with preserved admission kidney function and excluding deaths within 48 hours limits generalizabi–lity. Finally, we did not measure myoglobin, and we did not account for fluid management in the analyses.

Conclusion

In conclusion, in trauma ICU patients, higher CK concentrations on ICU days 1 and 2 were independent–tly associated with early, but not late, AKI. Most pa–tients with marked muscle injury (CK above 3,000 U/L) developed early AKI, so measuring CK on the first two ICU days may help recognize this risk and support closer renal monitoring. CK2 above 3,000 U/L added little to the clinical model in the whole cohort, likely because only a minority of patients with early AKI had marked CK elevation. This threshold requires external validation.

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Conflict of interest statement. None declared.

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Original article

Rituximab in Therapy of Glomerular Diseases: Single Center Experience

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Abstract

Introduction. Glomerular diseases remain challenging to treat, particularly in patients with persistent proteinuria and an inadequate response to conventional immunosuppressive therapy. Rituximab has emerged as an important therapeutic option in refractory or relapsing cases. We aimed to evaluate the early clinical response to rituximab in patients with glomerular diseases previously treated with conventional immunosuppressive therapy.

Methods. We conducted a retrospective observational case series at the Department of Nephrology and Renal Replacement Therapy, Clinical Center University of Sarajevo, over a two-year period. Twelve patients with glomerular diseases treated with rituximab were included. Demographic and clinical characteristics, underlying disease, previous immunosuppressive therapy, proteinuria, serum creatinine, and estimated glomerular filtration rate (eGFR) were analyzed. The primary outcome was the change in proteinuria three months after rituximab treatment.

Results. The cohort included 11 men and 1 woman, with a mean age of 47 years (range, 23-68). Membranous nephropathy was the most common diagnosis (58.3%), followed by ANCA-associated vasculitis (16.6%), lupus nephritis, minimal change disease, and thrombotic microangiopathy each accounted for 8.3%. All patients had previously received immunosuppressive therapy, most commonly corticosteroids, cyclophosphamide, and calcineurin inhibitors. In 11 patients, rituximab was administered at 375 mg/m² once weekly for four weeks, while one patient received 1 g twice, 14 days apart. Among six patients with paired measurements, mean proteinuria decreased from 9.53 to 0.86 g/day after three months, representing an approximately 91% reduction. Five patients achieved proteinuria <1 g/day. In membranous nephropathy, mean proteinuria decreased from 7.46 to 0.41 g/day (n=4). In lupus nephritis, proteinuria decreased from 18.12 to 0.74 g/day. Among seven patients with available creatinine measurements, mean serum creatinine decreased from 162 to 149 µmol/L. eGFR remained stable in six patients (41.8 vs. 42.4 mL/min/1.73 m²).

Conclusion. Rituximab was associated with a marked early reduction in proteinuria without deterioration of renal function in this single-center series of previously treated glomerular diseases. The most pronounced response was observed in membranous nephropathy. Larger studies with longer follow-up are needed to confirm these findings.

Keywords: rituximab, glomerular diseases, membranous nephropathy, proteinuria, lupus nephritis, immunosuppressive therapy, renal function

Introduction

Glomerular diseases represent a heterogeneous group of kidney disorders that may lead to significant proteinuria, nephrotic syndrome, progressive deterioration of kidney function and, in a proportion of patients, progression to end-stage kidney disease (ESKD). The treatment of these diseases remains challenging because of their diverse pathophysiological mechanisms, variable clinical course, and heterogeneous response to immunosuppressive therapy. Although conventional therapeutic strategies, including corticosteroids, cyclophosphamide, calcineurin inhibitors, and other immunosuppressive agents, may induce remission and preserve kidney function, a substantial proportion of patients fail to achieve an adequate response, experience disease relapse, or develop treatment-related adverse effects [1].

Increasing evidence indicates an important role of B lymphocytes and their products in the pathogenesis of several immune-mediated glomerular diseases. B cells contribute to disease activity through antibody production, antigen presentation, cytokine release, and interactions with other components of the immune

system. These findings provide a rationale for B-cell–depleting therapies in selected glomerular diseases [1-3].
Rituximab is a chimeric monoclonal antibody directed against the CD20 antigen expressed on the surface of B lymphocytes. By inducing B-cell depletion, rituximab may reduce the production of pathogenic autoantibodies and modulate the immune response. Its use has increasingly been investigated in a variety of glomerular diseases, including membranous nephropathy, lupus nephritis, ANCA-associated vasculitis, and other immune-mediated kidney diseases [1-5].
Rituximab has demonstrated clinically meaningful reductions in proteinuria in patients with membranous nephropathy and has become an important therapeutic option, particularly in patients at risk of disease progression or with an inadequate response to conventional therapy. In the randomized MENTOR trial, rituximab was noninferior to cyclosporine in achieving complete or partial remission of proteinuria at 12 months and was superior in maintaining remission at 24 months [4].
Potential advantages of rituximab include targeted immunological activity, the possibility of reducing corticosteroid exposure, and the potential to achieve sustained remission in selected patients. However, treatment response may vary according to the underlying glomerular disease, disease severity, previous exposure to immunosuppressive therapy, and the degree of chronic kidney damage (CKD) [1,4,5].
In this context, we evaluated the early clinical response to rituximab in patients with glomerular diseases treated at a single nephrology center. The primary objective was to assess the change in proteinuria three months after rituximab administration, while secondary analyses evaluated changes in serum creatinine and estimated glomerular filtration rate (eGFR). Particular attention was given to treatment response according to the underlying glomerular disease, with the aim of presenting our center's experience with rituximab in patients who had not achieved an adequate response to previous conventional immunosuppressive therapy.

Material and methods

A retrospective observational case series was conducted at the Department of Nephrology and Renal Replacement Therapy, Clinical Center University of Sarajevo, over a two-year period. Twelve patients with glomerular diseases who were treated with rituximab were included in the study.
All patients had biopsy-proven kidney disease. The cohort consisted of seven patients with membranous nephropathy, two patients with ANCA-associated vasculitis, and one patient each with minimal change disease, systemic lupus erythematosus (SLE)–associated lupus nephritis, and thrombotic microangiopathy (TMA).
Before rituximab administration, all patients had received previous immunosuppressive treatment and were initiated on rituximab because they had either achieved complete remission followed by relapse, or failed to achieve remission despite previous treatment.
We analyzed demographic and clinical characteristics, underlying glomerular disease, previous immunesuppressive therapy, proteinuria, serum creatinine, and eGFR. The primary outcome was the change in proteinuria three months after rituximab treatment. Secondary outcomes included changes in serum creatinine and eGFR. Treatment response was evaluated according to the underlying glomerular disease.

Results

The cohort consisted of 11 men and one woman, with a mean age of 47 years (range, 23-68 years). Seven patients (58.3%) had membranous nephropathy, two patients (16.6%) had ANCA-associated vasculitis, and one patient each (8.3%) had lupus nephritis, TMA, and minimal change disease.
Eleven patients received rituximab at a dose of 375 mg/m² once weekly for four consecutive weeks, whereas one patient received 1 g twice, 14 days apart.

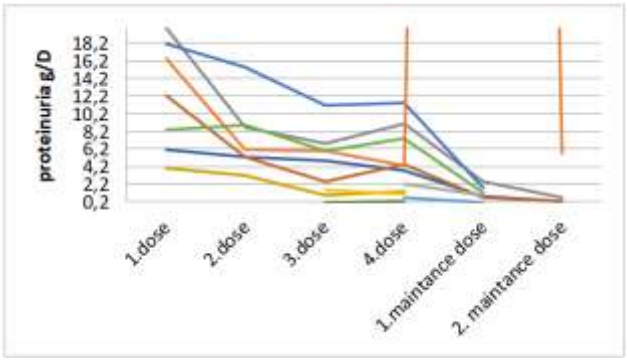

Fig. 1. Changes in proteinuria from baseline to three months after rituximab treatment

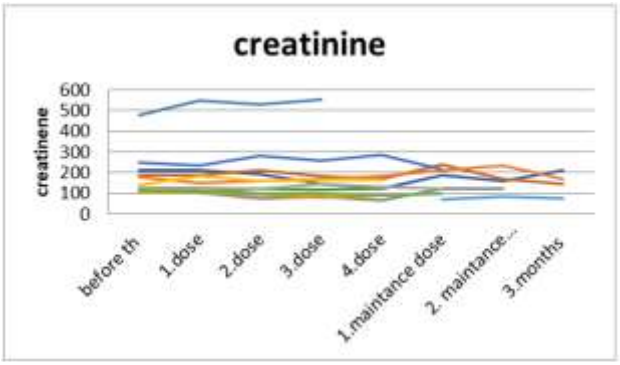

Fig. 2. Changes in serum creatinine before and after rituximab treatment

Among six patients with available paired measurements, mean proteinuria decreased from 9.53 g/day at baseline to 0.86 g/day three months after rituximab administration, representing an approximately 91%

reduction. Proteinuria below 1 g/day was achieved in five patients.

The most pronounced response was observed among patients with membranous nephropathy, in whom mean proteinuria among four patients decreased from 7.46 g/day at baseline to 0.41 g/day three months after rituximab treatment. In the patient with lupus nephritis,proteinuria decreased from 18.12 g/day to 0.74 g/day.

Among seven patients with available serum creatinine measurements, mean serum creatinine decreased from 162 to 149 µmol/L. Eleven patients had some degree of chronic kidney disease, whereas one patient had normal nitrogenous waste parameters.

Among six patients with available paired measure–ments, eGFR remained essentially stable, with mean values of 41.8 and 42.4 mL/min/1.73 m² before and three months after rituximab treatment, respectively.

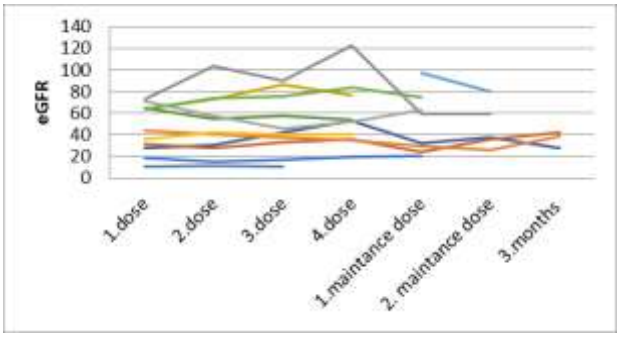

Fig. 3. Changes in estimated glomerular filtration rate (eGFR) from baseline to three months after rituximab treatment

Discussion

The results of our study demonstrated that rituximab treatment was associated with a marked reduction in proteinuria in patients with membranous nephropathy and was also associated with a reduction in proteinuria in patients with ANCA-associated vasculitis and lupus nephritis. Although the number of patients was small, this finding is clinically relevant because proteinuria is an important marker of glomerular injury and an es–tablished prognostic factor for the progression of CKD. Our findings are consistent with previous evidence in–dicating an important role of B lymphocytes and auto–antibody production in the pathogenesis of several immu–ne-mediated glomerular diseases and suggesting that B-cell depletion with rituximab may result in reduced proteinuria and improved renal outcomes [1-5].

The most pronounced reduction in proteinuria in our cohort was observed among patients with membranous nephropathy. This finding is consistent with randomized clinical trials demonstrating the efficacy of rituximab in reducing proteinuria and inducing partial or complete remission in primary membranous nephropathy. In the MENTOR trial, which included 130 patients with membranous nephropathy and proteinuria ≥5 g/day, rituximab was noninferior to cyclosporine in achieving complete or partial remission at 12 months. At 24 months, remission was maintained in 60% of patients treated with rituximab compared with only 20% of those treated with cyclosporine [4].

The evidence for the antiproteinuric effect of rituximab is particularly strong in membranous nephropathy. In the GEMRITUX trial, rituximab was administered in addi–tion to non- immunosuppressive antiproteinuric treat–ment and compared with antiproteinuric treatment alone. Although the difference in remission rates was not statistically significant at six months, extended follow-up demonstrated a significantly higher rate of complete or partial remission in the rituximab group. After a median follow-up of approximately 17 months, remission was achieved in 64.9% of patients treated with rituximab compared with 34.2% of patients re–ceiving supportive therapy alone [6,7].

These findings are particularly relevant to the inter–pretation of our results because they indicate that the clinical effect of rituximab on proteinuria may develop gradually and that the reduction in proteinuria may not occur immediately after treatment. The relatively short three-month follow-up in our study therefore repre–sents an assessment of an early treatment response rather than the final therapeutic effect.

The biological basis for this delayed clinical response is also supported by the relationship between B-cell depletion, anti-phospholipase A2 receptor (PLA2R) antibody levels, and proteinuria. In membranous neph–ropathy, immunological remission, reflected by a re–duction or disappearance of anti-PLA2R antibodies, may precede clinical remission by several months. Con–sequently, patients without a substantial reduction in proteinuria at three months should not necessarily be considered treatment failures, particularly if an immu–nological response has occurred [6,7].

The RI-CYCLO trial provides additional evidence re–garding the time course of response. In this rando–mi–zed trial, complete or partial remission at 12 months was achieved in 62% of patients treated with ritu–ximab, compared with 73% of those receiving cyclic corticosteroid-cyclophosphamide therapy. At 24 months, complete or partial remission was observed in 83% and 82% of patients, respectively. These findings de–monstrate that the clinical response to rituximab may continue to increase during longer-term follow-up [4].

In our cohort, the marked reduction in proteinuria among patients with membranous nephropathy from 7.46 to 0.41 g/day among the four patients with paired measurements appears greater than the average re–duction reported in many clinical studies. However, this observation should be interpreted cautiously be–cause of the very small sample size and the potential influence of spontaneous fluctuations in proteinuria, concomitant antiproteinuric therapy, and differences in baseline disease severity. Nevertheless, the finding is

consistent with the established efficacy of rituximab in membranous nephropathy.

The interpretation of proteinuria reduction in patients with ANCA-associated vasculitis is more complex. The primary therapeutic goals in ANCA-associated vasculitis are induction and maintenance of remission, control of systemic and renal disease activity, and preservation of kidney function. Proteinuria alone is therefore insufficient to define renal response. In the RAVE trial, rituximab was noninferior to cyclophosphamide for induction of remission in severe ANCA-associated vasculitis and was superior in patients with relapsing disease. Rituximab was also effective in patients with major renal disease [4].

Similarly, the RITUXVAS trial evaluated rituximab in patients with ANCA-associated vasculitis and renal involvement. At 12 months, sustained remission was achieved in 91% of patients in both treatment groups, with no significant difference between rituximab and cyclophosphamide-based therapy. Renal function also improved substantially in the rituximab group, with median eGFR increasing from approximately 20 to 39 mL/min/1.73 m² at 12 months [10].

Therefore, the reduction in proteinuria observed in our patients with ANCA-associated vasculitis may represent one component of an early renal response to control of vasculitis activity. However, changes in proteinuria should be interpreted together with serum creatinine, eGFR, urinary sediment, and other indicators of disease activity. It is particularly important to distinguish active glomerular inflammation from residual proteinuria caused by chronic structural kidney damage.

The available evidence for rituximab in lupus nephritis is more heterogeneous. In the LUNAR randomized controlled trial, rituximab was added to mycophenolate mofetil and corticosteroids in patients with active proliferative lupus nephritis. Although the overall renal response rate was numerically higher with rituximab than with placebo (56.9% versus 45.8%), the difference did not reach statistical significance. Nevertheless, rituximab produced profound peripheral B-cell depletion and significant improvements in complement levels and anti-double-stranded DNA antibodies. Greater reductions in anti-dsDNA levels were associated with reductions in proteinuria [11].

Observational data have suggested a more favorable response in patients with refractory lupus nephritis. In the prospective Rituxilup cohort, rituximab combined with mycophenolate mofetil without maintenance oral corticosteroids resulted in complete remission in 52% and partial remission in 34% of patients at 52 weeks [12]. These findings suggest that rituximab may have clinically meaningful activity in lupus nephritis, particularly in selected or refractory patients, despite the neutral results of the LUNAR randomized trial.

In our study, the patient with lupus nephritis demonstrated a marked reduction in proteinuria, from 18.12 to 0.74 g/day after three months. Although this represents a substantial early response, this finding cannot be generalized because it is based on a single patient finding. Furthermore, the patient had previously received immunosuppressive therapy, and the observed improvement may reflect the combined effect of rituximab, previous treatment, supportive therapy, and the natural fluctuation of lupus nephritis activity.

Another important consideration is the stability of kidney function observed in our cohort. Mean serum creatinine decreased from 162 to 149 µmol/L among seven patients with available measurements, while mean eGFR remained essentially unchanged, from 41.8 to 42.4 mL/min/1.73 m². The absence of deterioration in kidney function is clinically relevant, particularly because most patients had pre-existing CKD. However, the short follow-up period and the small number of patients with paired measurements prevent conclusions regarding the long-term renoprotective effect of rituximab.

Our findings should be interpreted in light of several limitations. First, the study included only 12 patients, and paired proteinuria measurements were available in only six patients. Second, the cohort was heterogeneous, comprising several different glomerular diseases with distinct pathophysiological mechanisms. Third, this was a retrospective single-center study without a control group, making it impossible to determine the extent to which the observed changes were attributable specifically to rituximab. Fourth, patients had received different immunosuppressive regimens before rituximab, and concomitant supportive treatment may have influenced proteinuria. Finally, the three-month follow-up may have been too short to capture the full clinical effect of rituximab, particularly in membranous nephropathy.

Despite these limitations, our results provide useful real-world data regarding the early response to rituximab in patients with difficult-to-treat glomerular diseases. The pronounced reduction in proteinuria observed in the membranous nephropathy subgroup is consistent with the evidence from randomized trials supporting rituximab as an effective therapy for primary membranous nephropathy. The findings in ANCA-associated vasculitis and lupus nephritis are more difficult to interpret because proteinuria is only one component of renal disease activity and because the evidence supporting rituximab differs between these diseases.

Overall, our results support the hypothesis that rituximab may induce an early reduction in proteinuria in selected patients with immune-mediated glomerular diseases. The strongest evidence for an antiproteinuric effect exists in membranous nephropathy, whereas data in ANCA-associated vasculitis and lupus nephritis are more heterogeneous. Longer follow-up and larger prospective studies are required to determine whether the early reduction in proteinuria observed in our cohort is sustained and translates into durable renal remission and preservation of kidney function.

Conclusion

In this single-center case series of patients with previously treated glomerular diseases, rituximab treatment was associated with a marked early reduction in proteinuria without deterioration in kidney function. The most pronounced response was observed in patients with membranous nephropathy, with proteinuria below 1 g/day achieved in most patients with available follow-up measurements.

Although these findings support the potential role of rituximab in patients with difficult-to-control glomerular diseases, they should be interpreted cautiously because of the small sample size, heterogeneous disease spectrum, absence of a control group, and short follow-up period. Larger prospective studies with longer follow-up are needed to confirm these findings and to better define the role of rituximab in refractory glomerular diseases.

Conflict of interest statement. None declared.

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Original article

The Role of Direct Immunofluorescence in Diagnosis of the Glomerular Diseases

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Abstract

Introduction. Glomerular diseases are considered the leading cause of morbidity and mortality in renal pathology patients. There are restricted approaches for the morphologic analysis of renal biopsies, such as the pathognomic morphologic changes. Deposition of immu–noglobulin (Ig) and/or complement factors in glomerulus causes injury, which leads to an inflammatory response ending in proliferative glomerulonephritis. Immunofluo–rescence (IF) is crucial in diagnosing glomerular diseases, revealing immune deposits (like IgG, IgA, IgM, com–plement) in kidney biopsies to classify conditions (e.g., IgA nephropathy, lupus nephritis) and under–stand mechanisms, often showing distinct patterns (li–near for Goodpasture's, granular for immune complex diseases) that guide treatment alongside light and electron microscopy.

The aim of this study is to present the importance of the immunofluorescent evaluation of the renal biopsies and to receive fundamental data for diagnosis of the glomerular disease

Methods. All cases of native renal biopsies performed from 2018 to 2025year in our department were re–viewed retrospectively in this study. All biopsies with an adequate biopsy specimen were estimated by light microscopy (LM) and some of them with immunofluores–cent (IF) techniques. Electron microscopy was also used to confirm the diagnosis. Clinical details were documented in a predesigned form. Hence, we could have evaluated 242 out of 493 kidney biopsies re–ceived in this period.

Results. 242 biopsies had sufficient material and were analysed with immunofluoresce. The predominant cli–nical presentation in this study was IgA nephropathy (16,1%), followed by membranous nephropathy (15,2%). The other glomerular diseases were as follows: focal–segmental glomerulosclerosis (8,2%), minimal glomerular abnormalities (7,4%), mesangial glomerulonephritis without IgA immundeposit (7,8%), extracapillar rapid progressive glomerulonephritis (6,6%), membranopro–liferative glomerulonephritis (5,3%), lupus nephritis (5,3%) and amyloidosis (4,9%). diabetic nephropathy (6,1%), glomerulosclerosis (7,1%). Other cases (10%) with several patients each, were: tubulointerstitial neph–ritis, renal lymphoma, myeloma multiplex-light chain GN, fibrillary and immunotactoid nephropaties, con–firmed with electron microscopy.

Conclusion. Direct IF is vital for classifying GN, followed by electron microscopy, which is an essential tool. This article describes a rational evaluation of kid–ney biopsies on LM in a way that guides toward the logical assessment to reach the diagnosis. Light mic–roscopy alone can misdiagnose renal disease. This is especially important in cases of early stage mem–branous nephropathy, IgA nephropathy (IgAN), Lupus nephritis and IgM nephropathy (IgMN), as these enti–ties can only be diagnosed by correlating the micro–scopic, immunofluorescence findings and clinical details.

Keywords: glomerulonephritis, renal biopsy, immunofluorescence

Introduction

Glomerular diseases are considered the leading cause of morbidity and mortality in renal pathology patients [1]. There are restricted approaches for the morpho–logic analysis of renal biopsies, such as the patho–gnomic morphologic changes. Deposition of immu–noglobulin (Ig) and/or complement factors in glome–rulus causes injury, which leads to an inflammatory response ending in proliferative glomerulonephritis [2,3,4]. Proliferative glomerulonephritis is defined by an increase in glomerular cellularity due to infiltration and proliferation of leukocytes within the glomerulus or from the proliferation of mesangial cells and pa–rietal epithelial cells [2,5,6]. In severe forms of diffuse proliferative glomerulonephritis, the crescent is formed by the obliteration of bowman space by epithelial proliferation. Recognizing this pattern on light mic–roscopy (LM) and categorizing it into different disease entities with the help of direct immunofluoresence (DIF) is essential for an accurate diagnosis.[7] Immu–nofluorescence (IF) is crucial in diagnosing glomerular

diseases, revealing immune deposits (like IgG, IgA, IgM, complement) in kidney biopsies to classify con–ditions (e.g., IgA nephropathy, lupus nephritis) and understand mechanisms, often showing distinct pa–tterns (linear for Goodpasture's, granular for immune complex diseases) that guide treatment alongside light and electron microscopy.

The aim of this study is to present the importance of the immunofluorescent evaluation of the renal biopsies to receive fundamental data for diagnosis of the glo–merular disease.

Material and methods

All cases of native renal biopsies performed from 2018 to 2025 year in our department were reviewed retro–spectively in this study. The number of renal biopsies varies and was different for each year. The lower number was seen in the period of corona virus disease pandemy. All biopsies were estimated by LM and but some of them also with IF techniques. The number of immunofluorescent analysis was lower because of technical problems as the tissue sent for DIF was in–adequate. Clinical details were documented in a pre–designed form.

Renal biopsy was done and after that the tissue is embedded in the cryostat embedding medium, frozen and cut at 3 μ thickness at -22°C. Sections were taken on slides and later, the slides were rinsed in phosphate buffer saline at pH 7.2 for 10 min. The sections were treated with optimally diluted antisera (3 drops on each slide) - IgG, IgA, IgM and C3. The slides were incubated in wet chamber for 1 h in dark room, washed with PBS, and mounted with glycerine jelly. The slides were observed of the fluorescence mic–roscope. DIF reporting is done based on the nature and distribution of immune deposits, glomerular localiza–tion, the intensity of staining, and the pattern of immune complex deposits. The intensity of staining was graded subjectively from 0 to 3,0 being negative and 3 maximum intensity (mild +1, moderate +2, and marked + 3) [1,3]. After correlating clinical data with LM and IF findings, the final diagnosis was rendered.

Results

In despite of the histomorfological estimation 242 biopsies were evaluated with direct immunofluores–cence. Biopsies in transplanted patients were not in–cluded in this study. The predominant clinical pre–sentation in this study was IgA nephropathy (16,1%), followed by membranous nephropathy (15,2%) as presented in Table 1. The other glomerular diseases were as follows: focal segmental glomerulosclerosis (8,2%), minimal glomerular abnormalities (7,4%), mesangial glomerulonephritis without IgA deposition (7,8%), extracapillar rapid progressive glomerulonephri–tis (6,6%), membranoproliferative glomerulonephritis (5,3%), lupus nephritis (5,3%) and amyloidosis (4,9%). diabetic nephropathy (6,1%), glomerulosclerosis (7,1%). The rest of the cases (10%) with several patients each, were: tubulointerstitial nephritis, renal lymphoma, myeloma multiplex-light chain GN, fibrillary and immunotactoid nephropathies, confirmed with electron microscopy.

Table 1. Clinical presentation of chronic glomerulonephritis, diagnosed with DIF in this study

Mode of presentation	IgAN	MN	FSGS	MGA	MsG	MPGN	RPGN	SLE	AMD	DN	GSc
Total cases N=242	39	37	20	18	19	13	16	13	12	15	17
(%)	16,1	15,2	8,2	7,4	7,8	5,3	6,6	5,3	4,9	6,1	7,0
Nephrotic syndrom	4	30	18	16	11	10	/	9	12	12	/
Nephritic syndrom	15	/	/	/	/	/	/	/	/	/	/
Proteinuria	/	7	2	2	8	3	10	4	/	3	10
Eritruria	20	/	/	/	/	/	6	/	/	/	7

IgAN-IgA nephropathy, MN-membranous nephropathy, FSGS-focal segmental glomerulosclerosis, MGA-minimal glomerular abnormalities, MsG-mesangial glomerulonephritis without IgAdeposits, MPGN membranoproliferative glomerulonephritis, RPGN-rapidly progressive glomerulonehritis, AMD- amyloidosis, SLE-systemic lupus erithematodes, DN-diabetic nephropathy, GSc- glomerulosclerosis

The dominant deposit on IF in Lupus nephritis (LN) was C3 and IgG, but also several cases were "full house" screen. A high deposit of IgA in IgA nephropathy and IgG deposition along the GBM in membranous neph–ropathy, also deposition of IgG and C3 in membra–noproliferative GN was evaluated.

Discussion

Immunofluorescence studies play an essential role in the evaluation of medical renal biopsies. Particularly, in the study of renal glomerular diseases, where it pro–

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vides fundamental data for the diagnosis, classifica–tion, and etiology of the glomerular pathologies.
We noted different incidences during different periods of time, especially for patients with membranous and IgA nephropathy. The most frequent histological forms in our study were IgA nephropathy (16,1%), as in studies from other Mediterranean countries. The inci–dence of membranous nephropathy is also high (15,2%). A multidisciplinary diagnostic approach remains essen–tial for managing glomerular diseases [8]. However, significant disparities in access to biopsy, nephronpa–thology, and serological testing hamper optimal care in many regions. Investment in diagnostic infrastructure, clinician training, and health policy reforms are critical for improving global kidney health outcomes [9,10].
Glomerular diseases are a significant contributor to chronic kidney disease (CKD) globally, accounting for up to 30% of end-stage kidney disease cases (ESKD). Diagnostic accuracy is crucial for appropriate mana–gement but remains challenging, especially in low-resource settings. Immunofluorescence (IF) is an essen–tial diagnostic tool for glomerulonephritis, because it uses fluorescent antibodies to identify and visualize immune deposits (like antibodies, complement, and antigens) in the kidney tissue. This process helps in accurately diagnosing, classifying, and determining the cause of various types of glomerulonephritis, provi–ding crucial information beyond what might be seen with a light microscope alone [2,11,12].
How immunofluorescence aids in diagnosing glome–rulonephritis? Visualizes immune deposits and detects the presence and location of specific proteins, such as IgA, IgG, IgM, and complement factor (C3), that are deposited in the glomeruli and indicate immune-mediated kidney damage [1,2,10]. Also, it classifies types of glomerulonephritis such as specific pattern and type of immune deposits found are characteristic of different forms of the disease, allowing for precise classification. For example, IgA nephropathy is identi–fied by the presence of IgA deposits, typically in the mesangium. It helps distinguish between primary forms of glomerulonephritis and those caused by other diseases, such as autoimmune disorders or infections.
Correlation with clinical findings is needed. The results from immunofluorescence staining are correlated with clinical symptoms and other laboratory findings, like blood and urine tests, to provide a complete picture of the patient's condition [7,11]. The presence or absence of certain immune deposits can also provide information about the disease's potential course and prognosis.
IF uses fluorescently labeled antibodies to light up specific proteins (antibodies, complement factors like C3, C1q) in kidney tissue. The location and appearance of deposits are important for diagnosis. Granular IgG immune subepithelial deposit along GBM was found in membranous glomerulonephritis (Figure 1).

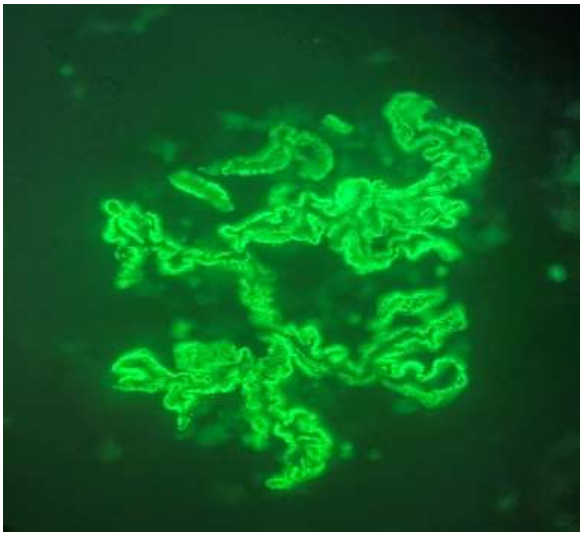

Fig.1. IgG granular subepitelial immun deposits along GBM. IgG-FITC in membranoous GN grade III

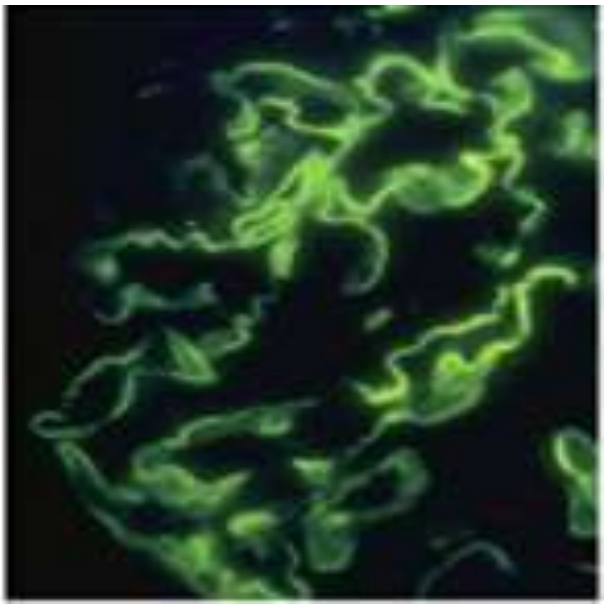

Fig. 2. Linear immun deposit along GBM-IgG-FITC in Goodpasteure syndrome

Linear pattern suggests antibodies directly attacking the glomerular basement membrane, which is common in Goodpasture's Syndrome (anti-GBM disease) (Figure 2).
Granular pattern indicates immune complexes deposited in the glomerulus, typical in lupus nephritis or IgA nephropathy.
Deposits in the mesangium (IgA nephropathy) versus capillary loops (membranous nephropathy) help diffe–rrentiate diseases. Different IgA, IgG, IgM, C3 patterns help diagnose specific diseases like IgA Nephropathy (most common), Membranous Nephro–pathy, or C3 Glomerulopathies (e.g., Dense Deposit Disease).
The diagnostic approach to glomerular diseases by integrating clinical evaluation, laboratory findings, imaging techniques, and histopathological assessments.

Primary glomerulonephritis comprises several renal-limited diseases that can cause haematuria and pro–teinuria, CKD, nephrosis and ESKD. The most common of these are IgA nephropathy (IgAN), primary mem–branous nephropathy (PMN), Focal Segmental Glo–merulosclerosis (FSGS) and Minimal Change Disease (MCD). Although rare, these diseases cause a signi–ficant burden to health care systems, given the high cost of treating ESKD with dialysis or transplantation. Until recently, the pathogenesis of primary glomeru–lonephritis has remained obscure. However, recent advances in understanding of how these diseases evolve has led to the introduction of novel therapeutic agents. Trials are underway or have recently completed that have huge implications for the standard of care for the primary glomerulonephritidies, and should dramatically reduce the number of patients who progress to ESKD. This article reviews according to the international Kidney Disease Improving Global Outcomes (KDIGO) guide–lines for the treatment of glomerular diseases, as well as recent research on pathogenesis and treatment [12].

Conclusion

Direct IF is vital for classifying the type of glomeru–lonephritis, followed by electron microscopy, which is an essential tool. Using the IF technique and compa–ring it with LM and clinical details, we evaluated the patients in our center. Immunofluorescence proved an important diagnostic tool in reaching the exact diag–nosis in various types of GN.

Light microscopy alone can misdiagnose renal disease. This is especially important in cases of early stage membranous nephropathy, IgA nephropathy, Lupus nephritis and IgM nephropathy, as these entities can only be diagnosed by correlating the microscopic, immunofluorescence findings and clinical details.

Conflict of interest statement. None declared.

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Original article

Impact of Anemia on Kidney Transplant Outcome

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Abstract

Introduction. Post-transplant anemia (PTA) is a frequent complication of kidney transplantation (KTx), but it remains unclear whether anemia diagnosed three months after KTx independently predicts deterioration of renal graft function one year after transplantation.

Methods. This retrospective-prospective longitudinal observational single-center study included 95 kidney transplant recipients with complete one-year follow-up. PTA was defined as a hemoglobin (Hb) concentration <110 g/L three months after transplantation, and re–cipients were divided into two groups according to the presence of PTA. Deterioration of graft function was defined as a serum creatinine increase ≥25% or an estimated glomerular filtration rate (eGFR) decline ≥30% at the 12-month compared with the 3-month post-transplant time point.

Results. PTA was present in 27.37% of recipients and was significantly more frequent in women than in men (42.86% vs. 20.90%; p=0.029). Recipients with PTA had significantly lower Hb, hematocrit, and red blood cell counts at all post-transplant time points and significantly lower eGFR at one-year post-transplant compared with recipients without PTA. A serum creati–nine increase ≥25% (23.08% vs. 4.35%; p=0.005) and an eGFR decline ≥30% (19.23% vs. 1.45%; p=0.001) were significantly more frequent in the PTA group. In multivariable regression analyses, PTA independently predicted serum creatinine increase ≥25% (OR 8.485, 95% CI 1.111-64.83) and an eGFR decline ≥30% (OR 27.54, 95% CI 2.28-340.4). Furthermore, deceased-donor transplantation independently predicted a serum creatinine increase ≥25%.

Conclusions. PTA independently predicts deterioration of renal graft function one year after transplantation, and can be helpful in identifying recipients who wa–rrant closer surveillance of the graft function.

Keywords: anemia, graft function, hemoglobin, kidney transplantation, outcome, risk factors

Introduction

Chronic kidney disease (CKD) is estimated to affect 843 million people worldwide and represents a major and growing public health problem, responsible for approximately 1.5 million deaths annually, corresponding to one death every 20 seconds [1]. Kidney transplan–tation (KTx) is the treatment of choice for end-stage kidney disease (ESKD) and, compared with dialysis, is associated with a substantially lower long-term risk of death [2].

Despite continuous advances in surgical technique and immunosuppressive therapy, long-term preservation of graft function remains a major challenge [3], and post-transplant complications contribute substantially to morbidity and mortality in this population [4]. Among hematological complications, post-transplant anemia (PTA) has attracted increasing attention because of its frequency and clinical relevance [4].

PTA has frequently been assessed in the early post-transplant period [5-7], and a hemoglobin (Hb) concen–tration <110 g/L three months after transplantation is an established definition adopted to identify early PTA with potential impact on graft function [5,6]. In a re–cent meta-analysis of studies using various definitions, the median prevalence of PTA was 59.8% within the first three months after transplantation, decreasing to 27.2% between the second and third post-transplant year [8]. PTA typically follows a biphasic pattern: early PTA develops within the first three months after transplantation and is favoured by pre-existing anemia, perioperative blood loss, iron deficiency, and delayed graft function (DGF), whereas late PTA develops thereafter and largely reflects declining graft function and impaired erythropoietin production, with chronic inflammation, infections, and the myelosuppressive

effects of immunosuppressive and other drugs contributing in both periods [4,8].

Pathophysiologically, reduced Hb concentration leads to chronic hypoxia of the renal graft, which may promote interstitial fibrosis, tubular atrophy, and progressive loss of graft function [9,10]. Accordingly, PTA has been associated with deterioration of graft function, graft loss, cardiovascular complications, and increased mortality, although the results of individual studies are not fully consistent [11-13]. Furthermore, the reported prevalence of PTA varies substantially with the definition and timing of assessment [5,8,14], and it has not been fully clarified whether anemia diagnosed three months after transplantation independently predicts deterioration of graft function one year after transplantation. This question is clinically relevant because, unlike most established risk factors for adverse graft outcomes, PTA is readily identifiable and amenable to treatment.

The aim of this study was therefore to evaluate whether anemia diagnosed three months after transplantation independently predicts deterioration of renal graft function one year after KTx.

Material and methods

This retrospective-prospective longitudinal observational study was conducted at the Nephrology Clinic, Clinical Center University of Sarajevo. A total of 116 kidney transplant recipients regularly followed at the outpatient transplant clinic were initially screened, and 17 were excluded because of incomplete follow-up data. Of the 99 recipients included in the study, four died within the first six months after transplantation; the remaining 95 recipients with complete one-year follow-up were included in the analyses of PTA-related outcomes. Baseline characteristics are reported for the entire cohort (99 recipients), whereas all PTA-related comparisons and outcome analyses were performed in these 95 recipients. Inclusion criteria were age over 18 years and performed KTx. Recipients younger than 18 years and those with a diagnosed malignancy were excluded.

For each recipient, sociodemographic data (age, sex) and the following clinical data were collected: pretransplant dialysis modality or pre-emptive transplantation, pretransplant dialysis duration, comorbidities (diabetes mellitus (DM), new-onset diabetes after transplantation (NODAT), hypertension), donor type (living related, living unrelated, or deceased), presence of DGF, and maintenance immunosuppression (tacrolimus or cyclosporine). Laboratory parameters included Hb, hematocrit (Hct), red blood cell count (RBC), serum creatinine, and 24-hour proteinuria, and the eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 equation. Complete blood count was evaluated at four time points (before transplantation, immediately after transplantation, and at 3 and 12 months after transplantation), whereas serum creatinine, proteinuria, and eGFR were assessed immediately after transplantation and at 3-months and 12-month time point. Data were obtained from the electronic health information system and hospital records.

PTA was defined as an Hb concentration <110 g/L three months after transplantation, and recipients were divided into two groups according to the presence of PTA. Deterioration of graft function was defined as a serum creatinine increase ≥25% or an eGFR decline ≥30% at the 12-month compared with the 3-month post-transplant time point. A composite outcome comprising death and/or the need for hemodialysis one year after transplantation was also evaluated.

Statistical analysis was performed using RStudio. Categorical variables are presented as absolute and relative frequencies, and continuous variables as mean ±standard deviation (SD) or as median and interquartile range (IQR). Categorical variables were compared using the chi-square test, with calculation of odds ratios (OR) and 95% confidence intervals (CI), and continuous variables were compared using the Student t-test. Univariable and multivariable binary logistic regression analyses were used to identify predictors of deterioration of renal graft function and to assess the association between PTA and these outcomes. The multivariable models were adjusted for age, sex, DM, hypertension, and donor type. A two-sided p value <0.05 was considered statistically significant.

Results

Baseline characteristics of the initially included cohort (n=99) are summarized in Table 1. Most recipients were male (71.7%), with mean age of 43.55±11.83 years, hemodialysis was the predominant pretransplant dialysis modality (78.6%), most recipients received a graft from a living donor (71.7%), and tacrolimus-based maintenance immunosuppression was used in 91.9% of recipients. All subsequent analyses included the 95 recipients with complete one-year follow-up, among whom PTA was present in 26 (27.37%).

Comparison of clinical characteristics between recipients with and without PTA is presented in Table 2. PTA was significantly more frequent in women than in men (42.86% vs. 20.90%; p=0.029), and male sex was associated with lower odds of PTA (OR 0.352, 95% CI 0.136-0.913). Hypertension was associated with a significantly lower frequency of PTA (p=0.026; OR 0.164, 95% CI 0.028-0.959). No other variables were significantly associated with PTA.

Recipients with PTA had significantly lower Hb, Hct, and RBC at all post-transplant time points (all p<0.001), whereas pretransplant values did not differ significantly between the groups. Serum creatinine was significantly higher in the PTA group immediately after transplantation (162.8±77.86 vs. 134.9±52.08 μmol/L;

p=0.046), and eGFR was significantly lower immediately after transplantation (p=0.012) and at the 12-month time point (50.46±17.26 vs. 63.80±18.82 mL/min/1.73 m²; p=0.002). Proteinuria was significantly higher in

Table 1. Baseline characteristics of kidney transplant recipients[a]

Characteristic	Value
Age (years), mean ± SD	43.55±11.83
Sex	
Male (n, %)	71(71.7)
Female (n, %)	28(28.3)
Pretransplant dialysis modality	
Hemodialysis (n, %)	77(78.6)
Peritoneal dialysis (n, %)	8(8.2)
Both modalities (n, %)	6(6.1)
No dialysis, preemptive transplantation (n, %)	7(7.1)
Pretransplant dialysis duration (months), median (IQR)	
Hemodialysis	36.0(12.0-64.5)
Peritoneal dialysis	8.5(3.0-32.5)
Both modalities	33.5(31.0-36.0)
Hypertension	
Yes (n, %)	93(93.9)
No (n, %)	6(6.1)
DM	
Yes (n, %)	9(9.1)
No (n, %)	90(90.9)
Donor type	
Living related (n, %)	52(52.5)
Living unrelated (n, %)	19(19.2)
Deceased (n, %)	28(28.3)
DGF	
Yes (n, %)	10(10.1)
No (n, %)	89(89.9)
Maintenance immunosuppression	
Tacrolimus (n, %)	91(91.9)
Cyclosporine (n, %)	8(8.1)
PTA[b]	
Yes (n, %)	26(27.37)
No (n, %)	69(72.63)

Abbreviations: IQR, interquartile range; SD, standard deviation; DM, diabetes mellitus; DGF, delayed graft function; PTA, post-transplant anemia. [a]n=99; dialysis modality was unavailable for one recipient, and the corresponding percentages are calculated among the 98 recipients with documented modality. [b]Assessed in 95 recipients with complete follow-up data; defined as hemoglobin <110 g/L.

Table 2. Comparison of clinical characteristics between recipients with and without post-transplant anemia

Characteristic	PTA (n=26)	Without PTA (n=69)	Test statistic	*p*	OR (95% CI)
Sex			*χ^2=4.791*	*0.029**	
Male (n, %)	14 20.90)	53(79.10)			0.352(0.136-0.913)
Female (n, %)	12(42.86)	16(57.14)			
Age (years), mean ±SD	45.42±13.50	42.33±11.28	t=1.127	0.263	
Pretransplant dialysis modality			χ^2=2.216	0.330	
Hemodialysis (n, %)	18(24.66)	55(75.34)			
Peritoneal dialysis (n, %)	3(37.5)	5(62.5)			
Both modalities (n, %)	3(50.0)	3(50.0)			
Donor type			*χ^2=2.586*	*0.108*	
Living (n, %)	22(31.88)	47(68.12)			2.574(0.791-8.375)
Deceased (n, %)	4(15.38)	22(84.62)			
Glucose metabolism			*χ^2=2.251*	*0.324*	
DM (n, %)	4(50.0)	4(50.0)			2.950(0.674-12.91)
No DM (n, %)	20(25.32)	59(74.68)			
NODAT (n, %)	2(25.0)	6(75.0)			
Hypertension			*χ^2=4.976*	*0.026**	
Yes (n, %)	22(24.72)	67(75.28)			0.164(0.028-0.959)
No (n, %)	4(66.67)	2(33.33)			
DGF			*χ^2=0.451*	*0.502*	
Yes (n, %)	3(37.5)	5(62.5)			1.670(0.369-7.547)
No (n, %)	23(26.44)	64(73.56)			

Abbreviations: CI, confidence interval; DM, diabetes mellitus; NODAT, new-onset diabetes after transplantation; DGF, delayed graft function; OR, odds ratio; PTA, post-transplant anemia; SD, standard deviation. Categorical variables were compared using the chi-square test and continuous variables using the Student t-test. Dialysis modality was compared among the 87 recipients with a documented modality; seven recipients underwent

preemptive transplantation and data were unavailable for one. *p<0.05.

Table 3. Hematological and renal function parameters in recipients with and without post-transplant anemia

Parameter	PTA (n=26)	Without PTA (n=69)	*t*	*p*
Hb (g/L)				
Before transplantation	105.2±21.74	116.0±17.30	-1.884	0.066
After transplantation	91.37±12.38	119.9±19.50	-6.929	<0.001*
3 months	100.8±5.912	129.7±15.02	-9.510	<0.001*
12 months	121.5±17.29	145.9±18.31	-5.889	<0.001*
HCT (%)				
Before transplantation	32.70±6.47	35.15±5.833	-1.342	0.186
After transplantation	28.05±3.962	36.94±6.53	-6.488	<0.001*
3 months	34.41±2.913	42.95±5.571	-7.423	<0.001*
12 months	38.10±4.828	44.57±6.119	-4.847	<0.001*
RBC (×10¹²/L)				
Before transplantation	3.632±0.658	3.797±0.681	-0.821	0.416
After transplantation	3.062±0.445	3.933±0.741	-5.615	<0.001*
3 months	3.755±0.445	4.660±0.697	-6.151	<0.001*
12 months	4.365±0.658	5.063±0.676	-4.520	<0.001*
Serum creatinine (µmol/L)				
After transplantation	162.8±77.86	134.9±52.08	2.019	0.046*
3 months	131.8±35.51	129.8±40.73	0.224	0.823
12 months	147.7±50.36	127.8±49.27	1.746	0.084
eGFR (mL/min/1.73 m²)				
After transplantation	49.08±21.04	61.94±21.96	-2.575	0.012*
3 months	55.27±16.04	61.81±18.07	-1.620	0.109
12 months	50.46±17.26	63.80±18.82	-3.147	0.002*
Proteinuria (g/24 h)				
After transplantation	0.721±0.581	0.418±0.515	2.313	0.023*
3 months	0.476±0.750	0.344±0.382	1.107	0.271
12 months	0.325±0.320	0.238±0.269	1.300	0.197

Abbreviations: Hb, hemoglobin; Hct, hematocrit; RBC, red blood cell count; eGFR, estimated glomerular filtration rate; PTA, post-transplant anemia. Data are presented as mean ± standard deviation. Variables were compared using the Student t-test. Pretransplant hematological parameters and proteinuria were not available for all recipients, and these comparisons were therefore performed in the recipients with available measurements. *p<0.05.

the PTA group immediately after transplantation (p=0.023), without significant differences at later time points (Table 3).

Table 4 shows that at one year post-transplant, a serum creatinine increase ≥25% occurred in 23.08% of recipients with PTA compared with 4.35% of those without PTA (OR 6.60, 95% CI 1.51-28.80; p=0.005), and an eGFR decline ≥30% occurred in 19.23% of recipients with PTA compared with 1.45% of those without PTA (OR 16.19, 95% CI 1.79-146.42; p=0.001).

Table 4. Univariable analysis of one-year outcomes in recipients with and without post-transplant anemia

Outcome	PTA (n=26)	Without PTA (n=69)	χ^2	*p*	OR (95% CI)
Serum creatinine increase ≥25% (n, %)	6(23.08)	3(4.35)	7.724	0.005*	6.60 (1.51-28.80)
eGFR decline ≥30% (n, %)	5(19.23)	1(1.45)	10.09	0.001*	16.19 (1.79-146.42)
Hemodialysis at one year (n, %)	0(0.0)	1(1.45)	0.381	0.537	0.862 (0.03-21.82)
Death at one year (n, %)	1(3.85)	1(1.45)	0.526	0.468	2.72 (0.16-45.15)

Abbreviations: CI-confidence interval, eGFR-estimated glomerular filtration rate, OR-odds ratio, PTA-post-transplant anemia. Categorical variables were compared using the chi-square test. *p<0.05.

In univariable logistic regression, PTA was significantly associated with both a serum creatinine increase ≥25% (OR 6.600, 95% CI 1.513-28.80; p=0.012) and an eGFR decline ≥30% (OR 16.19, 95% CI 1.790-146.4; p=0.013). After adjustment for age, sex, DM, hypertension, and donor type, multivariable logistic regression analysis showed that PTA remained an independent predictor of both outcomes, serum creatinine increase ≥25% and an eGFR decline ≥30% (OR 8.485, 95% CI 1.111-64.83; p=0.039, and OR 27.54, 95% CI 2.280-340.4; p=0.010). Deceased-donor transplantation was also an independent predictor of a

serum creatinine increase ≥25% (OR 17.54, 95% CI 1.335-230.38; p=0.029), while hypertension was inversely associated with this outcome (OR 0.003, 95% CI 0.000-0.164; p=0.004) (Table 5).

Table 5. Univariable and multivariable logistic regression analysis of the impact of post-transplant anemia on deterioration of renal graft function one year after transplantation

	Serum creatinine increase ≥25%				
Predictor	***B***	**SE**	**OR**	**95% CI**	***p***
Univariable logistic regression					
PTA	1.887	0.752	6.600	1.513-28.80	0.012*
Multivariable logistic regression					
PTA	2.138	1.038	8.485	1.111-64.83	0.039*
Age (years)	0.024	0.046	1.024	0.936-1.121	0.601
Female sex	-1.892	1.384	0.151	0.010-2.271	0.172
DM	1.966	1.276	7.143	0.586-87.067	0.123
Hypertension	-5.677	1.975	0.003	0.000-0.164	0.004*
Deceased-donor transplantation	2.864	1.314	17.54	1.335-230.38	0.029*
eGFR decline ≥30%					
Univariable logistic regression					
PTA	2.784	1.124	16.19	1.790-146.4	0.013*
Multivariable logistic regression					
PTA	3.316	1.283	27.54	2.28-340.4	0.010*
Age (years)	-0.002	0.048	0.998	0.908-1.096	0.959
Female sex	-2.907	2.123	0.055	0.001-3.504	0.171
DM	0.670	1.268	1.954	0.164-23.45	0.597
Hypertension	-3.011	2.276	0.049	0.001-4.262	0.186
Deceased-donor transplantation	1.236	1.229	3.442	0.310-38.30	0.314

Abbreviations: B-regression coefficient, CI-confidence interval, PTA-post-transplant anemia, DM-diabetes mellitus, eGFR-estimated glomerular filtration rate, OR-odds ratio, SE-standard error.

Discussion

In this single-center cohort of kidney transplant recipients, the prevalence of PTA three months after transplantation was 27.37%. PTA was significantly more frequent in women and less frequent in recipients with hypertension, whereas age, pretransplant dialysis modality, donor type, glucose metabolism disorders, and DGF were not significantly associated with its occurrence. Recipients with PTA had significantly lower Hb, Hct, and RBC at all post-transplant time points, together with significantly lower eGFR immediately after transplantation and at one year. A serum creatinine increase ≥25% and an eGFR decline ≥30% at one year were significantly more frequent in the PTA group, and after adjustment for age, sex, DM, hypertension, and donor type, PTA remained an independent predictor of both outcomes of deterioration of renal graft function, while deceased-donor transplantation independently predicted a serum creatinine increase ≥25%.

The observed prevalence of PTA in our study closely matches the 28.85% reported by Banjeglav and Zibar, who applied the same Hb threshold at three months in a Croatian cohort [5]. On the contrary, a study using the same threshold at a comparable time point reported a considerably lower rate of 13% [6]. Higher figures emerge where the World Health Organization (WHO) criteria are applied: 76.7% and 87% at three months in two prospective cohorts [15,16], and 51.3% six months after transplantation in a retrospective cohort [17]. The influence of the definition is best illustrated by the study of Einollahi *et al.*, in whose cohort the prevalence was 52.7% according to WHO criteria at six months but only 24.4% when PTA was defined as Hb ≤110 g/L [14]. These differences confirm that the choice of the diagnostic threshold and time assessment directly determine the reported prevalence and support the use of a lower Hb cut-off to identify clinically relevant anemia in transplant recipients.

The higher frequency of PTA among women in the present study is consistent with the findings of Banjeglav and Zibar (p=0.025) [5] and with a large cohort in which female sex was significantly associated with PTA [14]. In women whose menses had ceased before transplantation, periods resume in the majority of cases, at a median of three months [18], the interval at which PTA was assessed in the present study. Menstrual blood loss and the resulting iron deficiency have accordingly been proposed as contributors to the higher frequency of PTA reported in female recipients [19].

The inverse association between hypertension and PTA was unexpected and is difficult to explain pathophysiologically. In our cohort, however, only six recipients did not have hypertension, so this finding is most likely a consequence of the small subgroup size and should be interpreted with caution.

The significantly lower Hb, Hct, and RBC observed in recipients with PTA at every post-transplant time point

were an expected finding, as these parameters are basic indicators of erythropoietic status and directly reflect the presence and severity of PTA. It should be noted that pre-transplant Hb already tended to be lower in recipients who subsequently developed PTA, although this difference was of borderline significance. Preexisting anemia is a recognized contributor to early PTA [4,7], and the lower pre-transplant Hb in this group most likely reflects its persistence into the early post-transplant period rather than a separate phenomenon. Notably, Hb in the PTA group improved gradually over the first post-transplant year, yet deterioration of graft function was more frequent in this group. This observation suggests that early exposure to anemia may have a lasting effect on the graft, which is in line with the finding that early PTA carries the highest risk of adverse outcomes [12]. Serum creatinine was significantly higher in the PTA group only immediately after transplantation; thereafter the difference attenuated and retained as only a strend towards higher values at one year. In contrast, eGFR was significantly lower in recipients with PTA both immediately after transplantation and at 12 months, indicating a more pronounced progressive decline in graft function in this group. Biologically, this may be explained by the mechanisms through which anemia contributes to graft injury: chronic hypoxia resulting from a reduced Hb concentration activates profibrotic mediators that promote tubulointerstitial fibrosis and progressive loss of graft function, while the hemodynamic adaptations accompanying anemia, including compensatory tachycardia and altered renal perfusion, may further contribute to ischemic injury and accelerate chronic graft dysfunction [9,10]. Similarly to our findings, another group of authors found no difference in serum creatinine between recipients with and without PTA at 12 or 36 months after transplantation [20].

Proteinuria was significantly higher in recipients with PTA immediately after transplantation, whereas this difference did not persist at later time points. A cross-sectional study likewise identified proteinuria as a significant risk factor for PTA, although in that cohort the association was observed at the 6- and 12-month post-transplant time points [21]. The proposed mechanism linking proteinuria to PTA may be urinary loss of erythropoietin, iron and other factors relevant for erythropoiesis, although its relevance for sub-nephrotic proteinuria and the transplant population remains uncertain [21].

The central finding of this study is that PTA independently predicted deterioration of graft function at one year after transplantation. The adjusted odds were approximately 8.5-fold higher for a serum creatinine increase ≥25% and 27.5-fold higher for an eGFR decline ≥30%. Larger cohorts have reported associations of PTA with acute rejection, graft loss, and mortality [6,7,11]. Our findings are consistent with the cohort of Kolonko *et al.*, in which recipients with PTA likewise had a significantly lower eGFR at one year after transplantation (43.9 vs. 55.3 mL/min/1.73 m²) and a higher long-term risk of graft loss [22]. A meta-analysis of 17 studies including 16,463 recipients confirmed the association of PTA with graft loss and overall mortality, with early PTA carrying the highest risk [12].

The evidence is nevertheless not uniform. In several cohorts, PTA was associated with graft loss but not with patient survival or cardiovascular events [13,22,23]. One study found no difference in graft function between recipients with and without PTA at 6 and 12 months [24].

Deceased-donor transplantation independently predicted a serum creatinine increase ≥25% in our cohort. This is in line with a systematic review and meta-analysis of 35 observational studies in which deceased-donor grafts were independently associated with one-year death-censored graft loss [25]. Another retrospective cohort study reported a shorter graft and patient survival after deceased-donor transplantation, although in that cohort the difference became apparent only after the first post-transplant year [26]. The functional deterioration of renal graft function observed at the 12-month time point in our cohort may therefore represent an earlier manifestation of the same process, preceding overt graft loss.

In the present study, the frequency of death and return to hemodialysis one year after transplantation did not differ between recipients with and without PTA. With only two deaths and one return to dialysis, the number of events was too small for a meaningful analysis of the composite outcome, and this finding should not be interpreted as evidence against an effect of PTA on recipient survival, that has been demonstrated in substantially larger cohorts and pooled analyses [11,12].

Our study has limitations. It was conducted in a single center with a relatively small sample size, and the low number of adverse events resulted in wide confidence intervals around the effect estimates, so the magnitude of the adjusted OR should be interpreted with caution. In addition, the follow-up was limited to one year, so the longer-term impact of PTA on graft function could not be assessed. In addition and unfortunately, the iron status, including ferritin levels, was not systematically assessed, so the contribution of iron deficiency to PTA and its evolution in the two groups could not be evaluated. The partly retrospective design carries a risk of information bias, four recipients who died within the first six months could not be included in the outcome analyses, and residual confounding cannot be excluded.

Conclusion

Post-transplant anemia, present in more than one quarter of recipients, independently predicted deterioration of

renal graft function one year after kidney transplan–tation. Unlike donor age, donor type, or the degree of human leukocyte antigen (HLA) matching, the PTA is modifiable, and it is detected by a laboratory test al–ready performed at every routine post-transplant visit. The Hb value obtained three months after transplan–tation identifies recipients who warrant closer sur–veillance of graft function, at negligible additional cost. Whether correction of PTA alters that trajectory, and at which Hb threshold, remains to be established in larger prospective studies with standardized defi–nitions of PTA.

Conflict of interest statement. None declared.

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Original article

Post-Transplant Infectious Complications Within a Five-Year Period: A Single-Center Experience

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Abstract

Introduction. Kidney transplant recipients (KTRs) are particularly vulnerable to post-transplant infectious complications. Immunosuppressive (IS) therapy prevents allograft rejection but also increases susceptibility to infections. Although infection rates have declined over recent decades, infections remain an important cause of mortality after kidney transplantation (KT), only after the cardiovascular disease. Infectious episodes may impair renal allograft function and contribute to chronic graft injury, potentially leading to graft failure and a return to renal replacement therapy (RRT). This study aimed to describe infections among KTRs followed at our center.

Methods. This retrospective observational study was conducted at the Department of Nephrology and Renal Replacement Therapy, Clinical Center, University of Sarajevo, between 2020 and 2025. Electronic health records were reviewed for 100 KTRs attending regular follow-up visits. All patients received induction therapy with anti-thymocyte globulin (ATG) or basiliximab, followed by triple maintenance IS therapy consisting of corticosteroids, mycophenolic acid, and a calcineurin inhibitor (CNI; tacrolimus or cyclosporine A).

Results. The mean patient age was 47.42±12.56 years, and 73% were male. Post-transplant complications were reported in 61.8% of patients, and 85% of these complications were described as infectious. Urinary tract infections (UTIs) were reported in 31% of patients with *Escherichia coli* as leading identified pathogen (11%). No statistically significant associations were observed between infectious complications and hypertension, diabetes mellitus, or anemia. The frequency of infectious complications did not differ significantly between living- and deceased-donor transplant recipients. Patients receiving tacrolimus had a higher reported risk of infectious complications compared to those receiving cyclosporine (relative risk [RR] 14.286, 95% confidence interval [CI] 1.41-178.8; p=0.01). Delayed graft function (DGF) was associated with overall complications (p=0.026), but not with infectious complications when analyzed separately. The duration of pre-transplant RRT (p=0.005) and lower estimated glomerular filtration rate (eGFR; p=0.018) were associated with overall complications that was not observed for infectious complications alone. Infectious complications were documented in all five patients who died during follow-up.

Conclusion. Our study concluded that infectious complications are frequently reported among KTRs, with UTIs representing the most commonly described infection. Individualized IS management and regular monitoring may support early detection and treatment and help improve patient and allograft outcomes.

Keywords: kidney transplantation, Infectious complications, Urinary tract infection

Introduction

Kidney transplant recipients (KTRs) are particularly vulnerable to infectious complications because the immunosuppressive (IS) therapy, while essential for preventing allograft rejection, increases susceptibility to a broad range of infections. Despite improvements in prevention and management, infections remain an important cause of mortality after kidney transplantation (KT), only after the cardiovascular disease. Previous infectious episodes may impair allograft function and contribute to chronic graft injury, potentially leading to graft failure and the need to resume renal replacement therapy (RRT) [1]. Treating infections in transplant recipients can be challenging because some antimicrobial agents are nephrotoxic, and interactions with IS drugs may increase treatment-related toxicity. When planning living-donor KT, particular attention should be also paid to latent infections that may reactivate during IS. Hence, an appropriate donor and recipient screening, together with preventive measures, may reduce the risk of post-transplant infectious complications [2-4].

Material and methods

This retrospective observational study was conducted at the Department of Nephrology and Renal Replace–ment Therapy, University Clinical Center of Sarajevo. The study included 100 KTRs who attended regular follow-up visits between December 2020 and December 2025, including recipients transplanted before the start of the study period. Data, including pre-transplant hyper–tension (HTA), diabetes mellitus (DM), and hemo–globin (Hb) levels, were obtained from electronic health records. Anemia was defined as an Hb level below 110 g/L. All patients received induction therapy with anti-thymocyte globulin (ATG) or basiliximab, followed by triple maintenance IS therapy consisting of corticosteroids, mycophenolic acid, and a calci–neurin inhibitor (CNI; tacrolimus or cyclosporine A). The primary aim was to describe post-transplant infectious complications at our center and assess their associations with selected risk factors and allograft function. Collected variables included the underlying kidney disease, type and duration of pre-transplant RRT, HTA, DM, and anemia, CNI use, donor type (living or deceased), delayed graft function (DGF), post-transplant complications, including infections, mortality, and renal allograft function. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 26. Continuous variables were expressed as mean ± standard deviation (SD) and compared using Student's t-test or the Mann–Whitney U test, as appropriate. Categorical variables were compared using the chi-square or Fisher's exact test. A p-value below 0.05 was considered statistically significant.

Results

The mean patient age was 47.42±12.56 years with 73% being males. The cause of end-stage renal disease (ESRD) was unknown in the largest group of patients (Figure 1). Post-transplant complications were identified in 61.8% of patients, and 85% of these complications were reported as infectious. Urinary tract infections (UTIs) were documented in 31% of patients. *Escherichia coli* was the most frequently isolated pathogen (11%), follo–wed by *Klebsiella pneumoniae* (9%) and *Enterobacter cloacae* (4%). Other infectious complications, including cytomegalovirus (CMV) viremia, BK polyomavirus (BK) viremia, and coronavirus disease 2019 (COVID-19), were also documented (Figure 2). No statistically significant association was found between infectious complications and the assessed pre-transplant risk fac–tors, including HTA, DM, and anemia. The occurrence of infectious complications did not differ significantly between living- and deceased-donor transplant recipients. Among patients with infectious complications, 84.3% had received hemodialysis (HD) before KT, 5.9% un–derwent preemptive transplantation, and the remaining patients had received peritoneal dialysis. Patients re–ceiving tacrolimus had a higher reported risk of in–fectious complications compared to those receiving cyclosporine (relative risk [RR] 14.286, 95% confidence interval [CI] 1.41-178.87; p=0.01). DGF was associated with a higher frequency of overall post-transplant com–plications (p=0.026); however, this association was not observed when infectious complications were analyzed separately. Overall post-transplant complications were associated with the duration of pre-transplant RRT (p

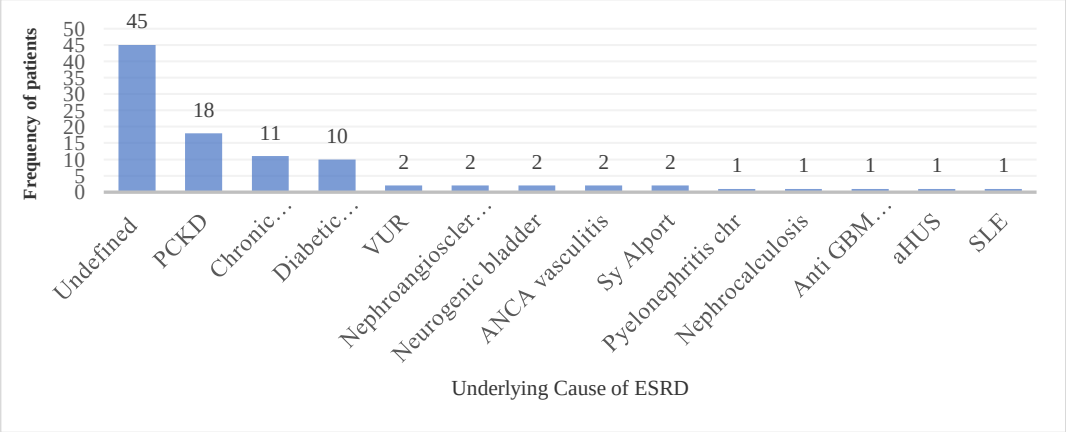

Fig. 1. Underlying causes of end-stage kidney disease in the study population.
Note: Values indicate the number of patients in each category. Abbreviations: ESRD, end-stage renal disease; PCKD, polycystic kidney disease; VUR, vesicoureteral reflux; ANCA, antineutrophil cytoplasmic antibodies; anti-GBM, anti-glomerular basement membrane antibodies; aHUS, atypical hemolytic uremic syndrome; SLE, systemic lupus erythematosus; Sy, syndrome; chr, chronic.

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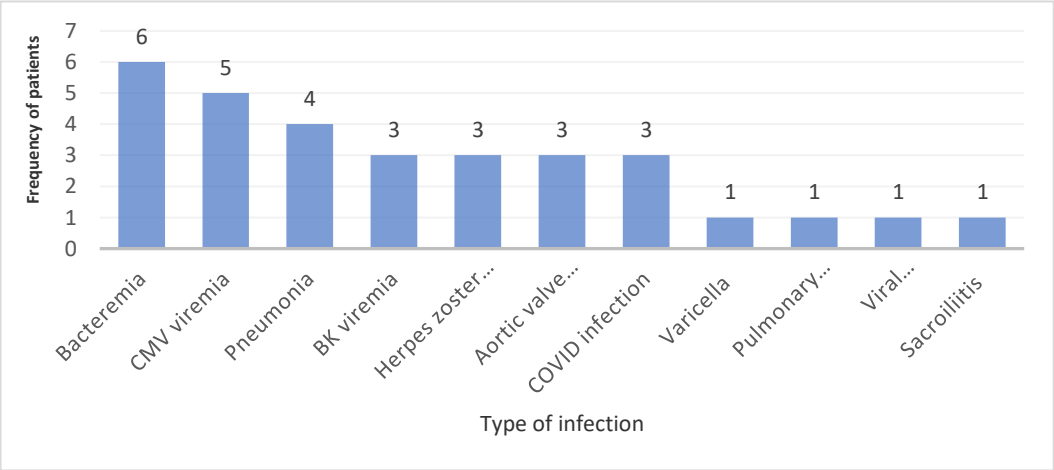

Fig. 2. Distribution of infectious complications other than urinary tract infections.
Note: Values indicate the number of patients with each reported infection. Abbreviations: CMV, cytomegalovirus, BK, BK polyomavirus, COVID, coronavirus disease 2019 (COVID-19).

=0.005) and a decrease in estimated glomerular filtration rate (eGFR) after complications (p=0.018). Neither association was statistically significant when infectious complications were analyzed separately. No significant association was found between time since KT and overall post-transplant complications. Five patients who died during the follow-up period, had experienced infectious complications. No statistically significant association was observed between mortality and overall post-transplant complications. In all five patients, infectious complications occurred within the first six months after KT. Two of these patients experienced both surgical and infectious complications: one presented with renal artery stenosis and a pulmonary infection, while the other had an urinoma and a UTI.

Discussion

In this retrospective single-center study, infectious constituted a high proportion of reported post-transplant complications (85%), with UTIs being the most frequently described type. This is consistent with previous retrospective studies in which UTIs were among the most common infections after KT [2]. Although all five patients who died in our study had experienced infectious complications, no statistically significant association with mortality was found. Alotaibi *et al.*, similarly reported no significant difference in mortality between patients with infections and controls [2]. Infections may impair allograft function through a direct tissue injury, inflammatory responses, acute or chronic rejection, antimicrobial nephrotoxicity, interactions affecting IS drug levels, and reactivation of latent viral infections. Severe systemic infections and sepsis may further compromise graft function through hemodynamic instability and acute kidney injury. In our study, previous infectious complications were not significantly associated with serum creatinine or eGFR when analyzed separately. An association with graft function was observed only when infectious, vascular, and surgical complications were combined. In contrast, Kaouiri *et al.*, (2025) reported persistent renal dysfunction after infection in 46% of patients and graft failure requiring a return to dialysis in 14.6% [5]. Differences in patient characteristics, infection type and severity, follow-up duration, IS regimens, and sample size may partly explain the discrepancy. This study was limited by its retrospective design, with potential selection bias, incomplete data, and residual confounding. The small sample size limited statistical power for analyses of allograft function, while the small number of deaths restricted the assessment of mortality. Further prospective multicenter studies are needed to confirm these findings and inform standardized infection-prevention strategies for KTRs.

Conclusion

Infectious complications represented a substantial proportion of post-transplant complications in this single-center cohort, with UTIs being the most frequently reported type. Individualized IS management, regular monitoring, early recognition of infection, and timely, appropriate antimicrobial treatment remain important components of post-transplant care. A multidisciplinary approach may help to improve patient and allograft outcomes.

Conflict of interest statement. None declared.

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Original article

Assessment of Retinal Microangiopathy in CKD and Dialysis Patients by Optical Coherence Tomography Angiography

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Abstract

Introduction. Ocular microvascular changes may reflect the progression of kidney damage in chronic kidney disease (CKD). The aim of this study was to investigate the association between retinochoroidal parameters, assessed by optical coherence tomography angiography (OCTA), and the degree of kidney deterioration in CKD and dialysis patients.

Methods. In this cross-sectional study, the study group comprised patients with arterial hypertension at different stages of CKD and patients receiving dialysis treatment. A complete eye examination, including OCTA imaging of the macular region, was performed in all participants. According to the estimated glomerular filtration rate (eGFR), non-dialysed patients were divided into low-eGFR (<60 mL/min) and high-eGFR (>60 mL/min) groups, and CKD patients on renal replacement therapy were further classified according to the dialysis modality (hemodialysis or peritoneal dialysis).

Results. The analysis included 136 eyes of 100 CKD patients. Mean retinal thickness (Rt) was 275.73±9.65 µm in the low-eGFR group and 274.36±10.77 µm in the high-eGFR group; in dialysis patients, Rt increased from 273.4 µm before to 277.2 µm after the dialysis session. OCTA showed significantly lower deep vascular density (DVD) in CKD patients with albuminuria than in those without albuminuria ($p<0.001$). Albuminuria was inversely related to retinal and choroidal thickness and to superficial (SVD) and deep (DVD) vascular density.

Conclusion. In patients with CKD, decreasing kidney function is associated by a reduction of retinal and choroidal vascular density, as assessed by OCTA.

Keywords: microvasculature, chronic kidney disease, OCTA, chorioretinal thickness, vascular density

Introduction

Chronic kidney disease (CKD) ranks among the most consequential public health problems of the modern era, with a steadily rising worldwide prevalence and a heavy contribution to overall morbidity and mortality. By current consensus, CKD is diagnosed when evidence of kidney damage persists for at least three months or when the estimated glomerular filtration rate (eGFR) remains below 60 mL/min/1.73 m². The Kidney Disease Outcomes Quality Initiative (KDOQI) classification stratifies the condition into five stages according to eGFR, the fifth of which, an eGFR below 15 mL/min/1.73 m², defines end-stage renal disease (ESRD) [1].

The disorder is remarkably prevalent. Community-based estimates suggest that 8-16% of adults are affected, with the figure rising steeply with age to approximately 30.8% among those aged 70 years or older [2]. CKD is also encountered in about 15% of non-diabetic hypertensive individuals and in 43-53% of patients with diabetes mellitus [3,4], and the overall burden is expected to double by 2035 as ageing populations and the diabetes epidemic continue to expand [5].

CKD is not confined to the kidneys. Its systemic reach extends to the cardiovascular, endocrine, gastrointestinal, and nervous systems, and the eye is a frequent target of the disease. Affected individuals carry an increased risk of cataract, glaucoma, age-related macular degeneration, retinopathy, and visual impairment [6-9], while coexisting diabetes mellitus and hypertension predispose specifically to diabetic and hypertensive retinopathy [10]. Beyond the eye, CKD is also linked to accelerated atherosclerosis, cerebrovascular disease, cognitive decline, and excess mortality [11-14]. Why ocular disease is so common in these patients remains debatable. Some authors emphasise the substantial overlap of risk factors-ageing, diabetes, hypertension, smoking, and obesity-between renal and ocular pathology. Others invoke mechanisms intrinsic to CKD itself, such as an oxidative stress triggered by the accumulation of nitrogenous waste products that generate free radicals, and inflammation sustained by activation of the renin-angiotensin system [15].

Once ESRD develops, renal replacement therapy (RRT) becomes necessary to preserve metabolic homeostasis,

the principal options being hemodialysis (HD), peri–toneal dialysis (PD), and kidney transplantation [16]. PD may be administered either as continuous ambula–tory peritoneal dialysis (CAPD) or as automated peri–toneal dialysis (APD), according to the center's protocol. Dialysis inherently disturbs systemic hemodynamics and osmolality, engendering rapid fluctuations in blood pressure, plasma osmolarity, and fluid balance [17]. These swings are of particular ocular relevance be–cause the retina and choroid are richly vascularized structures. Earlier work has suggested that dialysis may produce measurable changes in the thickness of the retina and choroid as well as in the retinal capillary perfusion, although the responsible mechanisms and their clinical significance remain poorly understood [18]. During hemodialysis in particular, ultrafiltration, osmotic shifts, and blood pressure variation can acutely influence ocular perfusion and tissue thickness, most notably in the choroid. In line with this, recent meta-analyses have documented a modest yet consistent re–duction in subfoveal choroidal thickness after HD sessions, whereas retinal thickness parameters are largely stable in the acute setting [19], supporting the view that choroidal circulation responds particularly sensitively to the fluid and hemodynamic burden imposed by dialysis.

Superimposed on these acute phenomena, CKD drives longer-term structural remodelling of the eye. Chronic alterations include narrowing of the retinal arterioles, progressive choroidal thinning, and atrophy of the retinal nerve fiber layer (RNFL) and the ganglion cell–inner plexiform layer (GCIPL) [20,21]. Retinal vessel analysis has further revealed decreased retinal vessel diameter, reduced fractal dimension, focal narrowing of arterioles, arteriovenous nicking, and arteriolar wall opacification in CKD [19]. Such retinal microvascular features are increasingly regarded as surrogate markers of cardiovascular risk, cognitive impairment, and worse–ning renal function [22]. The concept that the eye mirrors systemic microvascular health is reinforced by the structural and autoregulatory resemblance between the retinal and renal microvasculatures and by demon–strated correlations between ocular structural parameters and renal injury markers, including reduced eGFR and increased albuminuria [22]. Data at the capillary level, however, remain sparse. Although scanning laser Doppler flowmetry has disclosed an increased intercapillary distance in CKD, the behavior of individual retinal vas–cular plexuses is largely unknown, and the contribution of systemic comorbidities to these microvascular chan–ges has not been clarified [18].

Optical coherence tomography (OCT) and OCT angio–graphy (OCTA) have transformed the assessment of retinal and choroidal morphology. OCT provides high-resolution measurements of retinal thickness, including central macular thickness, while OCTA delivers non-invasive, depth-resolved imaging of the retinal micro–vasculature with quantitative metrics of perfusion. To–gether, these modalities constitute a convenient and reproducible window onto microvascular alterations in the systemic disease.

Against this background, the present study evaluated retinal and choroidal structural parameters by OCTA in CKD patients with different stages of kidney dys–function, and in patients treated with hemodialysis and peritoneal dialysis. In particular, it determined whether dialysis-related hemodynamic changes affect ocular measurements and characterized early microvascular changes in the superficial and deep retinal vascular ple–xuses, along with their systemic correlates. Comparative data on ocular structural parameters between CKD, HD and PD patients obtained with these techniques remain scarce, and clarifying these alterations may improve non-invasive monitoring of systemic microvas–cular dysfunction in CKD while yielding candidate biomarkers for disease-related vascular change.

Material and methods

This cross-sectional study was carried out at the Clinic for Nephrology and Renal Replacement Therapy of the Clinical Center, University of Sarajevo, Bosnia and Herzegovina. The study population comprised patients receiving maintenance hemodialysis (HD) or peritoneal dialysis (PD) who were under regular follow-up at the dialysis unit, together with non-dialysed patients whose eGFR was either below or above 60 mL/min/1.73 m². In total, 136 eyes of 100 patients with different stages of CKD were evaluated in the cross-sectional component of the study; within this cohort, ocular measurements obtained before and after a dialysis session were available for 100 patients.

Ophthalmic evaluation was scheduled at two time points, the exact timing being dictated by the dialysis modality. In HD patients, all measurements were taken at rest, 30 minutes before the start and 30 minutes after the end of the session. In PD patients, assessments were likewise performed at rest, 15 minutes after drainage of the dialysate and again 2 hours after its refill.

Individuals whose ocular status could interfere with retinal or choroidal measurements-including significant media opacity, previous retinal surgery, advanced glaucoma, and retinal vascular disease-were excluded. The investigation was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was granted by the Ethics Committee of the Clinical Center Training and Research Hospital (Appro–val No. 1142), and written informed consent was ob–tained from every participant. A comprehensive ophthal–mological examination was performed at each visit.

Clinical variables, urinalysis, and quantitative measu–rement of urinary albumin were collected for all par–ticipants. Albuminuria was defined as a urinary albumin excretion above 30 mg/day on a reliable 24-hour urine collection. The entire cohort was subsequently divided

into four subgroups according to two criteria: the level of kidney function (eGFR above or below 60 mL/min/ 1.73 m²) and the mode of renal replacement therapy (HD or PD).

Macular microvascular morphology was assessed with the Optovue OCTA instrument (AngioVue system, Optovue Inc., Fremont, CA, USA). Superficial and deep vascular density (SVD and DVD) were derived from 3×3 mm OCTA scans centred on the fovea. Using the built-in AngioVue software, the vascular compartment was automatically partitioned into four layers: superficial, deep, outer retinal, and choroidal. By default, SVD encompasses the vessels located between the internal limiting membrane and a plane 10 µm above the inner plexiform layer, whereas DVD covers the vasculature lying between 10 µm above the inner plexiform layer and 10 µm below the outer plexiform layer. Vessel density was expressed as the percentage of the region occupied by vessels and was computed automatically by the software for each plexus. Additional foveal metrics provided by the in–strument-foveal avascular zone (FAZ) area, FAZ peri–meter, and the presence of microaneurysms-were de–rived from the OCTA image of the inner retinal mic–rovasculature, which contains both the superficial and the deep plexus.

All computations were performed with IBM SPSS Statistics software; statistical analyses were run with SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). The normality of variable distributions was examined with the Kolmogorov–Smirnov and Shapiro-Wilk tests. Normally distributed data are presented as mean ± standard deviation, whereas non-normally distributed data are summarized as median and interquartile range. Group comparisons relied on Student's t-test or the Mann–Whitney U test, depending on the distribution, and categorical variables were compared using the chi-square test. Correlations were assessed with Pearson's or Spearman's coefficients, as appropriate. A two-sided p-value below 0.05 was considered statistically significant.

Results

Baseline characteristics

The baseline characteristics of the study population are summarized in Table 1. The analysis included 136 eyes from 100 patients with CKD and/or dialysis dependence. Demographic and clinical data comprised sex, age, the presence of diabetes mellitus, and systolic and diastolic blood pressure, while hemoglobin, eGFR, urinary pro–tein excretion, and per-session ultrafiltration volume served as indicators of health status. The mean duration of a dialysis session was 4.81±0.99 hours (4.00±0.00 hours in the HD group and 5.94±0.34 hours in the PD group). Average ultrafiltration volume amounted to 2730.95±1020.83 mL, with higher values in HD patients (3085.70±1248.24 i mL) than in PD patients (2222.98 ±184.8 mL). Age did not differ significantly between the high- and low-GFR groups, nor between the HD and PD groups. Notably, the PD subgroup with albu–minuria or gross proteinuria displayed significantly higher mean plasma glucose and urinary albumin concentra–tions than the other study groups ($p < 0.001$ for both).

Table 1. Main clinical characteristics of patients with different stages of kidney dysfunction

	eGFR ≤60 mL/min (n=30)	**eGFR >60 mL/min (n=30)**	**Hemodialysis (n=20)**	**Peritoneal dialysis (n=20)**
Age (years)	66(60-74.5)	64(56.5-71.5)	63(58.3-72.8)	66.5(60-73.3)
Gender (M/F)	68.1%/31.9%	70.3%/29.7%	69.8%/30.2%	68.3%/31.7%
BMI (kg/m²)	25.27±4.16	24.09±2.15	23.85±5.63	24.86±4.58
Smoking (yes)	45.6%	30.6%	34.9%	44.3%
SBP (mm Hg)	130 (120-140)	130(120-140)	130(120-140)	135(120-140)
DBP (mm Hg)	80 (70-90)	80(70-90)	80(77.5-82.5)	80(70-80)
Diabetes (yes)	34.8%	48.6%	16.3%	55.6%
Hb (g/L)	109.14±20.5	137.54±18.8	114.6±17.3	121.2±21.9
Proteinuria (g/day)	0.51 (0.2-1.5)	0.45(0.16-1.82)	0.19(0.13-0.28)	1.06(0.44-2.7)
Albuminuria (mg/L)	39.5(23-247.8)	61.5(21.5-297)	21(16.5-27)	204(75-282.3)
Cr. clear. (mL/min)	39.7(31.7-48.9)	74.8(65.7-94)		
Dialysis session duration (h)			4.00±0.00	5.94±0.34
Ultrafiltration volume (mL)			3085.70±1248.24	2222.98±184.8

Abbreviations: GFR-glomerular filtration rate, BMI-body mass index, SBP-systolic blood pressure, DBP-diastolic blood pressure, Hb-hemoglobin, Cr. clear.-creatinine clearance

Pharmacological treatment

Table 2 presents the distribution of pharmacological treatment according to the level of kidney function. Pa–tients in the low-GFR CKD group were more frequently prescribed antihypertensive agents-in particular angio–tensin-converting enzyme inhibitors and angiotensin II type 1 receptor blockers-than their counterparts. In the dialysis groups, diuretic use was markedly more common among PD than HD patients (52.4% vs. 6.5%, p= 0.001). Systemic comorbidities and the classes of antihypertensive drugs used are detailed in Table 2.

Table 2. Distribution of the patients pharmacologically treated for hypertension and of other cardiovascular drugs among the groups with different stages of kidney dysfunction

Drug class	GFR ≤60 mL/min	GFR >60 mL/min	P value	Hemodialysis	Peritoneal dialysis	P value
Anti-hypertensive drugs (%)						
ACE inhibitors	62.3	48.6	0.175	41.2	61.9	0.072
AT1 blockers	17.4	21.6	0.596	16.3	20.6	0.574
Calcium antagonists	49.3	51.4	0.839	55.8	46.0	0.323
Diuretics	55.1	40.5	0.154	6.5	52.4	0.001
β-blockers	31.9	29.7	0.819	17.9	23.3	0.554
Other cardiovascular drugs (%)						
Antiplatelet drugs	30.4	43.2	0.187	17.2	23.3	0.681
Statins	47.8	54.1	0.541	41.9	55.6	0.166

OCTA-derived parameters

OCTA-derived parameters are presented in Table 3. With respect to choroidal morphology, the low-GFR group exhibited substantially greater choroidal thinning than patients with an eGFR above 60 mL/min (p< 0.001), a difference that persisted after adjustment for antihypertensive treatment. In the parafoveal region, vascular density differed between subgroups for both the superficial and the deep plexus, with SVD being significantly lower in patients whose eGFR was ≤ 60 mL/min (p=0.03). FAZ perimeter, by contrast, did not differ between the two GFR categories (Table 3).

Table 3. OCTA parameters among the groups with different stages of kidney dysfunction

Parameter	eGFR ≤ 60 mL/min	eGFR > 60 mL/min	P value
Rt total area (μm)	274.4±10.7	275.7±9.7	0.52
Rt central ring (μm)	245.3(240.7-247.8)	246(241.6-247.7)	0.462
Cht central ring (μm)	286.2(246.4-290.1)	276.6(250.2-292.6)	0.36
Cht total area (μm)	271.2(249.7-276.7)	270.3(264.5-275.9)	0.59
Area of FAZ (mm²)	0.29(0.27-0.33)	0.28(0.25-0.31)	0.06
SVD (%)	46.6(44.9-47.9)	47.3(45.9-49.6)	0.03
DVD (%)	48.7(47.3-49.3)	48.7(47.7-49.2)	0.44
MA (up to 10)	29%	64.9%	<0.001
FAZ perimeter (μm)	2197(2168.5-2267)	2177(2157-2259)	0.263

Abbreviations: GFR-glomerular filtration rate, CKD-chronic kidney disease, Rt-retinal thickness, Cht-choroidal thickness, FAZ-foveal avascular zone, SVD-superficial vascular density, DVD-deep vascular density, MA-microaneurysms

Table 4 lists the ocular parameters measured before and after the dialysis session. Prior to dialysis, the mean FAZ area was 0.3 mm² and the mean FAZ perimeter 2199 μm; mean vessel density amounted to 46.3% (SVD) and 48.1% (DVD) over the whole image, while mean total-area choroidal thickness was 266.9 μm.

Table 4. OCTA parameters among the groups on renal replacement therapy

Parameter	Before dialysis Mean ± SD	Post-dialysis Mean ± SD	P value
Rt total area (μm)	273.4(266.8-280.6)	277.2(271.2-280.5)	0.116
Rt central ring (μm)	244.8(240.6-247.5)	246.3(242.2-247.9)	0.312
Cht central ring (μm)	264.5(245.1-288.7)	290.2(286.1-294.1)	<0.001
Cht total area (μm)	266.9(249.4-273.9)	273.5(269.8-278.1)	0.001
Area of FAZ (mm²)	0.3(0.3-0.34)	0.28(0.26-0.3)	0.03
SVD (%)	46.3(44.8-48.6)	47.3(46.3-48.3)	0.06
DVD (%)	48.1(47.1-48.9)	49.1(48.6-49.4)	<0.001
MA (up to 10)	23(36.5%)	21(48.8%)	0.206
FAZ perimeter (μm)	2199(2166–2285)	2177(2156-2201)	0.009

Abbreviations: GFR-glomerular filtration rate, CKD-chronic kidney disease, Rt-retinal thickness, Cht-choroidal thickness, FAZ-foveal avascular zone, SVD-superficial vascular density, DVD-deep vascular density, MA-microaneurysms

Following dialysis, the corresponding values were 0.28 mm² for FAZ area, 2177 μm for FAZ perimeter, 47.3% for SVD, 49.1% for DVD, and 273.5 μm for total-area choroidal thickness (Table 4).

Comparison between dialysis modalities

Changes in ocular and systemic parameters from before to after the session were compared between HD and PD patients using the Mann–Whitney U test. The two modalities differed significantly with respect to the change in FAZ area (p=0.04) as well as to the changes in SBP (p<0.001), DBP (p=0.017), and intraocular pressure (p=0.006). In contrast, none of the OCTA-derived retinal microvascular measures-SVD, DVD, FAZ metrics, or choroidal thickness-changed significantly between HD and PD patients (all p >0.05, Table 5).

Table 5. Comparison of parameter changes between HD and PD

Parameter	HD Δ (Mean ± SD)	PD Δ (Mean ± SD)	P value
ΔFAZ area (mm²)	0.0039±0.0909	-0.0191±0.074	0.047
ΔFAZ perimeter (mm)	-0.0067±0.315	-0.0228±0.325	0.986
ΔSVD whole (%)	0.24±3.92	0.23±2.31	0.986
ΔDVD whole (%)	0.54±5.03	-0.30±3.24	0.206
ΔChoroidal thickness(μm)	6.59±20.36	3.31±24.59	0.516
ΔSystolic BP (mm Hg)	17.22±18.68	-4.20±11.77	<0.001
ΔDiastolic BP (mm Hg)	8.82±10.64	2.83±10.98	0.017

Correlation analyses. Spearman correlation analysis disclosed a moderate negative association between the change in choroidal thickness and the change in SBP (r=-0.372, p<0.001), and a moderate positive association between dialysis session duration and the change in choroidal thickness (r=0.320, p=0.003). Ultrafiltration volume correlated weakly and negatively with the change in whole-image DVD (r=-0.239, p=0.028) and with no other OCTA parameter (all p>0.05; Table 6). In bivariate analyses, kidney function and albuminuria emerged as the strongest correlates of choroidal measures (Table 6). Choroidal thickness-but not retinal thickness-was significantly associated with eGFR, as were SVD and DVD. Among the OCTA metrics, parafoveal vascular density in both plexuses was inversely related to albuminuria, and foveal SVD and DVD, FAZ area, and FAZ perimeter were all associated with eGFR and albuminuria. In subjects with positive albuminuria, urinary albumin excretion was inversely correlated with choroidal thickness in the central ring and in the total area. Associations with the remaining clinical variables were inconsistent.

Table 6. Correlations of the chorioretinal parameters assessed by OCTA in the overall study population

OCTA parameter	GFR (rho)	Albuminuria (rho)	Hb (rho)	SBP (rho)	DBP (rho)
Rt total area (μm)	0.180	-0.223*	0.254**	-0.197*	0.072
Cht total area (μm)	0.187	-0.398**	0.232*	-0.083	0.168
Area of FAZ (mm²)	-0.26**	0.291**	-0.27**	0.168	-0.047
SVD (%)	0.32**	-0.275**	0.352**	-0.095	0.143
DVD (%)	0.203*	-0.490**	0.185	-0.088	0.114
FAZ perimeter (mm)	-0.233*	0.389**	-0.081	-0.103	-0.058

Abbreviations: GFR-glomerular filtration rate, Hb-hemoglobin, SBP-systolic blood pressure, DBP-diastolic blood pressure, Rt-retinal thickness, Cht-choroidal thickness, FAZ-foveal avascular zone, SVD-superficial vascular density, DVD-deep vascular density, *p<0.05. **p<0.01

Discussion

The retinal and choroidal microvasculature is increasingly regarded as a readily accessible surrogate of systemic microvascular health. Because the retinal circulation shares numerous anatomical and physiological features with other end-organ capillary beds, non-invasive imaging with OCT and OCTA offers a means of examining systemic vascular alterations in vivo. In CKD and ESRD, systemic microvascular dysfunction, chronic inflammation, endothelial injury, and metabolic derangement act in concert to produce widespread vascular damage that may well extend to the ocular circulation.
Two principal findings emerged from this study. First, CKD was associated with retinal thinning and with a progressive decline in retinal-choroidal vascular density as kidney function deteriorated. Second, the microvasculature of different retinal layers appeared to respond differentially to systemic comorbidity.

It is well established that long-term microvascular structural and functional changes accompany diabetes mellitus, and comparable alterations are encountered in the retina, in neural tissue, and in the kidney. Whereas the progression of CKD is traditionally monitored by invasive means-most often kidney biopsy-retinal microvascular abnormalities may serve as a window onto systemic microangiopathy in renal vascular disease and arterial hypertension, and their objective quantification has become a topic of active investigation [10]. The choroid, despite being a highly vascular structure with a key role in ocular volume regulation and metabolism, has received considerably less attention in this respect [11]. Earlier epidemiological work has linked CKD to a higher prevalence of visual impairment and ocular disease [9,12,13]. OCTA enables repeatable, high-resolution evaluation of retinal and choroidal volume and thickness [3], and recent studies have applied it to the non-invasive interrogation of ocular microcirculatory

flow without the need for contrast agents [14]. From a nephrological perspective, OCTA therefore represents a readily available instrument for the rapid detection of retinal microvascular alterations that may mirror sys–temic circulatory and renal status.

Only a limited number of studies have so far compared OCTA metrics across stages of CKD. In our cohort, patients with an eGFR above 60 mL/min differed sig–nificantly from those with lower eGFR values in se–veral microvascular parameters, including FAZ area, FAZ perimeter, and radial peripapillary capillary density.

Hemodialysis, although indispensable for the elimination of metabolic waste and excess fluid, exposes patients to rapid hemodynamic and osmotic fluctuations that may affect both the systemic and the ocular circulation [12]. Ultrafiltration and osmotic shifts during a session provoke swift changes in intravascular volume and blood pressure, with the potential to disturb ocular perfusion. Earlier studies have demonstrated that such physiological stress can induce transient structural and vascular changes in the retina and choroid. For instance, Chen *et al.*, described increased macular retinal nerve fiber layer thickness together with reduced choroidal thickness shortly after hemodialysis, attributing these changes to rapid fluid redistribution and osmotic shifts [13]. Consistent with this, several OCT and OCTA investigations have reported a decrease in subfoveal choroidal thickness after HD sessions, particularly in the temporal and nasal regions; a pooled self-controlled case series by Su *et al*., confirmed a moderate but con–sistent reduction across studies [14]. Beyond structural effects, dialysis-related circulatory stress may also compromise ocular perfusion itself, as reflected in re–ports of enlarged choriocapillaris non-perfusion areas after HD despite largely unaltered retinal vascular density [13,16]. Taken together, these observations su–ggest that the choroidal circulation is more vulnerable to the hemodynamic stress of dialysis than the retinal vasculature, which benefits from stronger autoregu–latory capacity.

Our data are in partial agreement with those of Balmforth *et al.*, [23], who demonstrated a direct relationship between GFR and choroidal thickness, an inverse relationship between choroidal thickness and proteinuria, and thinning of both retinal and choroidal layers in CKD patients compared with healthy and hypertensive controls. In contrast with that study, we did not detect a correlation between retinal thickness and estimated kidney function. It is conceivable that the relationship between GFR and retinal thickness evolves progressively as renal function declines.

A substantial body of evidence links retinal microvascu–lar abnormalities and vessel caliber changes to renal impairment in CKD [17,18]. In one study of 184 diabetic patients, retinal capillary rarefaction was shown to correspond to coexisting microcirculatory damage in the kidney [22]. Furthermore, the OCTA findings mirrored earlier histopathological observations of endothelial alterations and capillary dropout in diabetic retinas. In that cohort, the mean and the largest ten intercapillary areas correlated significantly with glomerular filtration, and previous reports had already demonstrated associations between OCTA metrics such as FAZ area, FAZ perimeter, and vessel density and diabetic retinopathy. In the present study, FAZ area, FAZ perimeter, and choroidal capillary flow area were markedly modified with advancing disease.

Our findings both corroborate and extend the existing literature data. Comparing OCTA parameters between HD and PD patients, the most striking observation was a significant difference in choroidal thickness between the two modalities, suggesting that HD may elicit more pronounced acute structural changes in the macula. Most OCTA-derived vascular indices-FAZ area and perimeter, and vessel density in both capillary plexu–ses-neither differ between the groups, nor had changed choroidal thickness. These results are consistent with the physiological contrast between the two treatments: HD is characterized by intermittent sessions with re–latively rapid fluid removal and pronounced hemody–namic swings, whereas PD achieves slower, more continuous ultrafiltration. The sharper intravascular volume and osmotic shifts experienced by HD patients could therefore be expected to translate into larger short-term structural changes in retinal tissue. Accor–dingly, the absence of any association between ultra–filtration volume and ocular parameters in our analysis suggests that the observed retinal changes relate chiefly to the speed of hemodynamic shifts rather than to the absolute amount of fluid removed.

Notably, in the CKD groups albuminuria, unlike eGFR, showed significant inverse associations with retinal and choroidal thickness. Our study design did not per–mit an explanation of this divergent behavior of eGFR and albuminuria. Nevertheless, available evidence in–dicates that microalbuminuria is more closely tied to the progression of diabetic retinopathy than a moderate reduction in eGFR [19]. It is also worth emphasizing the independent association we observed between eGFR and retinal vascular density, evaluated as parafoveal SVD and DVD by OCTA. Although the cross-sectional design precludes causal inference, one plausible inter–pretation is that the oxidative stress, inflammation, and endothelial damage inherent to CKD from its earliest stages intensify as kidney function worsens, thereby explaining the relationship between choroidal attenuation and lower eGFR, particularly in albuminuric patients [16].

Several limitations deserve mentioning. The sample size was relatively small, which may have limited the statistical power to detect subtle differences between dialysis modalities. The cross-sectional design precludes evaluation of the long-term ocular consequences of dialysis therapy and of the direction of the observed associations, where no longitudinal follow-up data were

available. Finally, although systemic dialysis-related parameters such as ultrafiltration volume and session duration were examined, they were not significantly associated with most ocular imaging variables; nevertheless, transient hemodynamic fluctuations during dialysis cannot be excluded as a source of residual confounding. Consequently, our results may reflect early microvascular alterations rather than late-stage retinopathy.

Conclusion

OCTA offers an attractive, non-invasive means of exploring the interrelation between the retinal-choroidal circulation and other vascular beds. The present study demonstrates that patients with CKD exhibit a significant reduction in retinal microvascular density, affecting both the superficial and deep plexuses. Furthermore, although most OCTA-derived retinal microvascular parameters remained stable when HD and PD patients were compared, macular thickness changes appeared to differ between the modalities, in parallel with the greater hemodynamic and osmotic stress of intermittent HD relative to the gradual fluid removal achieved by PD. These observations reaffirm the close coupling between ocular microcirculatory alterations and kidney function, and provide insight into the subclinical retinal changes associated with the systemic disease. Further studies are required to clarify the mechanisms underlying our findings and to establish whether imaging information derived from OCTA carries prognostic value for the progression of CKD.

Conflict of interest statement. None declared.

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The 21th Congress of the Balkan Association of Nephrology, Dialysis, Transplantation and Artificial Organs (BANTAO)

Abstract Book

29 – 31 October, 2026, Sarajevo, Bosnia and Herzegovina

Invited Speakers (IS)

IS-01

Highly Sensitized Kidney Transplantation: From Challenge to Opportunity

Nikolina Basic-Jukic

Abstract: Highly sensitized patients continue to represent one of the greatest challenges in kidney transplantation. Extensive HLA sensitization reduces the likelihood of finding a compatible donor, prolongs time on the waiting list, and is associated with an increased risk of antibody-mediated rejection. For many years, these patients had limited chances of receiving a transplant. Today, however, advances in immunology, organ allocation, and targeted therapies are changing this outlook. This lecture will review the current management of highly sensitized kidney transplant candidates, with an emphasis on practical approaches that improve access to transplantation. It will discuss the role of allocation strategies such as acceptable mismatch programs and kidney paired donation, as well as recent developments in immunological assessment, including molecular HLA matching and donor-specific antibody evaluation. The lecture will also summarize the emerging evidence for novel desensitization therapies, including imlifidase and other agents targeting B cells, plasma cells, IL-6 signalling, and FcRn, highlighting where these treatments may fit into clinical practice. Finally, the lecture will consider how a more individualized approach to immunological risk assessment is helping to expand transplant opportunities for patients who were previously considered extremely difficult to transplant. Together, these advances are redefining what is possible for highly sensitized kidney transplant candidates and offer new hope for improving both access to transplantation and long-term outcomes.

IS-02

The obesity paradox in ESKD, revisited

Adalbert Schiller, Alexandru Motofelea, Nicu Olariu, Adelina Mihaescu, Oana Schiller

Abstract: Obesity has a positive epidemiology worldwide and it is estimated that until 2035 obesity would be identifiable in 24% of the population. This positive epidemiology will have devastating consequences on world health since obesity is risk factor for many lethal chronic diseases. Related to kidney, obesity is risk factor for CKD initiation, progression and pre dialysis mortality (mainly by cardiovascular complications). In the 1980-ties the obesity paradox was identified in hemodialysis treated CKD patients. According to those findings ESKD patients on HD therapy presented an improved survival rate if obese (according to BMI). The survival benefit was attributed to better nutrition status of the obese patients as compared to patients with lean mass or protein caloric nutrition deficit. However, significant advancements in obesity management, pre-dialysis care, and HD technologies have emerged since these initial observations. This lecture re-evaluates the modern relevance of the obesity paradox in HD-treated ESKD patients using recent clinical data. We will critically analyze whether the survival advantages of a high BMI persist under current treatment paradigms. Furthermore, the presentation explores the safety, feasibility, and potential therapeutic benefits of both voluntary and medically assisted weight loss interventions for this specific patient population.

IS-03

Recurrence of the underlying disease in the renal allograft: Clinical Experience and Current Perspectives

Ulkem Cakir

Abstract: Kidney transplantation restores renal function but does not necessarily eliminate the systemic, immunologic, genetic, or metabolic mechanisms responsible for the recipient's original kidney disease. Consequently, recurrence in the renal allograft remains an important cause of graft dysfunction and late graft loss. The frequency, timing, and clinical consequences of recurrence vary substantially according to the underlying disease. Primary focal segmental glomerulosclerosis may recur shortly after transplantation and frequently presents with abrupt nephrotic-range proteinuria. IgA nephropathy often recurs gradually over several years, while membranous nephropathy may be anticipated through monitoring of disease-specific antibodies such as anti-PLA2R. C3 glomerulopathy, immune-complex mem–branoproliferative glomerulonephritis, and complement-mediated atypical hemolytic uremic syndrome are associated with particularly significant recurrence risks and require detailed complement, genetic, infectious, autoimmune, and monoclonal-protein evaluation. In contrast, clinically significant recurrence of lupus nephritis, ANCA-associated vasculitis, and anti-glomerular basement membrane disease is relatively uncommon when transplantation is performed during sustained remission. Effective management begins with accurate classification of the native kidney disease and individualized pretransplant risk assessment. Post-transplant surveillance should include renal function, quantitative proteinuria, urine sediment, disease-specific antibodies, complement markers,

and early allograft biopsy when recurrence is suspected. Light microscopy, immunofluorescence, and electron microscopy are often required to distinguish recurrent disease from rejection, transplant glomerulopathy, infection, drug toxicity, and de novo glomerular disease. Treatment is increasingly mechanism directed, incorporating plasma exchange, B-cell-targeted therapy, clone-directed treatment, or complement inhibition in selected patients. However, transplant-specific randomized evidence remains limited. Advances in genetic testing, molecular classification, biomarker surveillance, and targeted therapies support a transition toward precision management, offering opportunities for earlier diagnosis and improved long-term allograft survival.

IS-04

2026 KDIGO Diabetes & ESC/ERA CV management in context

Christoph Wanner

Abstract: In 2026 KDIGO (Kidney Disease Improving Global Outcomes) has released an update of their 2022 guidelines on the Diabetes Management in CKD as well as the European Society of Cardiology (ESC) in collaboration with the European Renal Association (ERA) have published guidelines on cardiovascular management in CKD. KDIGO has revised core elements such as chapter 1-Definitions, prevention, case-finding, staging, and cardiovascular risk assessment, chapter 2 -Glycemic monitoring and targets in people with diabetes and CKD, and chapter 4-Pharmacotherapy in people with diabetes and CKD. A new focus is on Continuous glucose monitoring (CGM) to be offered to all people with T1D and to people with T2D especially those receiving insulin therapy and at risk of hypoglycemia. Potential glycemic targets for those who use CGM are given (time in, below or above range). In chapter 4 a comprehensive strategy and goals for comprehensive care are given for pharmacotherapy to reduce risks of kidney disease progression and cardiovascular disease. A personalized approach to implement combinations of lifestyle and pharmacologic interventions for individual people is suggested. Initiating multiple interventions simultaneously may accelerate achievement of optimal individualized combination regimens when adverse effect profiles are nonoverlapping. Among the foundational therapies statins, SGLT2-inhibitors and RAS blockers are listed. Additional risk based pharmacotherapy consists of non-steroidal mineralocorticoid receptor antagonism, a GLP-1-based therapy and antiplatelet agents for secondary prevention. Treatment targets for blood pressure control, lipid management and glycemic control are given. Lifestyle management is the forth pillar of the comprehensive personalized strategy. It is important to understand and apply treatments according to their evidence based grading. Whereas SGLT2i, nsMRA and GLP1-RA have received a 1A grading, RASi remained at 1B. Low dose aspirin for prevention of recurrent ischemic cardiovascular disease events in people with established ischemic cardiovascular disease has received a 1C. Metformin has remained in the recommendations for people with an eGFR ≥30 ml/min per 1.73 m2 who have not achieved individualized glycemic targets despite use of SGLT2i and GLP-1-based therapies, or who are unable to use those medications (Grading 1B). New recommendations for people with T1D have been included. New is also the recommendations to maintaining kidney health in diabetes and a consensus has been reached (all aligned) with guidelines of the American Diabetes Association (ADA). The future will show how many patients with T2D and CKD achieve a clinical meaningful remission in order to avoid kidney replacement therapy. The tools are available. Since ESC/ERA CV management guidelines in people with CKD are under embargo until late August 2026 the presentation of this cooperation will be hot off the press.

IS-05

The gerosuppressive function of the kidneys: therapeutic impact

Alberto Ortiz

Abstract: Chronic kidney disease (CKD) causes one death every 20 seconds globally and is among the fastest growing causes of death, set to become the third cause of death in Western Europe by 2050 and growing equally fast in Central and Eastern Europe. This may come a surprise, given the availability of dialysis and kidney transplantation. However, current kidney replacement therapy fails to fully correct the altered homeostasis of CKD and does not contribute to the gerosuppressor factors secreted by healthy kidneys. Consequently, CKD is associated with accelerated biological aging, which is most extreme in people on dialysis: a 25-year-old-woman on dialysis in Europe has a biological age of 70 years. While CKD is part of the cardiovascular-kidney-metabolic (CKM) syndrome, its systemic pro-aging impact extends beyond the cardiovascular system and metabolism: in addition to an increased risk of peripheral vascular disease, heart failure, atrial fibrillation, stroke, myocardial infarction and premature cardiovascular death, CKD is associated with an increased risk of other age-associated conditions such as infection and cancer. The most interesting part is that accelerated biological aging is already observed when glomerular filtration rate (GFR) is still normal but albuminuria is increased. Indeed, there is a biological plausibility for this observation, since albuminuria suppresses the kidney production of the kidney-produced gerosuppressor Klotho and is associated with lower serum levels of the kidney-produced gerosupresor betaine. Klotho represents a kidney function that is not assessed in the clinic, but that is known to be lost when albuminuria is high. Loss of Klotho, by itself, already reproduces the

cardiovascular phenotype of CKD, even when GFR remains normal. This information may be translated into action that decreases the adverse personal and societal impact of CKD: albuminuria should be tested and treated, since albuminuria-stage CKD may still be reversible, contrary to CKD diagnosed based on a decreased GFR. Additionally, albuminuria lowering drugs such as renin-angiotensin system (RAS) blockers, SGLT2 inhibitors and mineralocorticoid receptor antagonists may restore Klotho production and/or decrease the negative impact of losing Klotho production.

IS-06

Peritoneal Dialysis in Special Populations

Rümeyza Kazancıoğlu

Abstract: Peritoneal dialysis (PD) is an effective kidney replacement therapy for many patients with end-stage kidney disease (ESKD), yet there might be some questions related to its preference in several special populations, particularly older adults, frail individuals, people with diabetes, and those with obesity. The growing proportion of elderly patients with ESKD, together with increasing frailty, cognitive impairment, and multiple comorbidities, requires a patient-centered approach that prioritizes quality of life, preservation of functional independence, and treatment goals aligned with patient preferences rather than solely conventional adequacy targets. Evidence demonstrates that PD offers several advantages for older adults, including preservation of residual kidney function, reduced hemodynamic instability, home-based treatment, and improved satisfaction, while assisted PD can overcome physical and cognitive barriers and reduce peritonitis risk. Diabetes, the leading cause of ESKD worldwide, presents unique challenges related to glycemic management, glucose exposure from dialysis solutions, cardiovascular disease, and functional impairment. However, there are recommendations regarding glucose monitoring, insulin administration, glucose-sparing PD prescriptions, and emerging therapeutic interventions in diabetic PD patients. For patients with obesity, there might be concerns regarding catheter insertion, dialysis adequacy, infectious complications, and survival. On the contrary, current evidence indicates that obesity alone should not preclude PD, as appropriate catheter placement techniques and individualized prescriptions can achieve outcomes comparable to those in non-obese patients. Across all three populations, successful PD requires comprehensive assessment of medical, functional, nutritional, psychosocial, and cultural factors. Shared decision-making, multidisciplinary care, caregiver involvement, and individualized dialysis prescriptions are the center of optimizing outcomes. Rather than viewing advanced age, diabetes, or obesity as contraindications, clinicians should recognize that appropriate patient selection, education, and tailored support enable PD to remain a safe, effective, and patient-centered treatment option for these increasingly prevalent populations.

IS-07

Peritoneal Dialysis and Heart Failure

Anila Duni

Abstract: Kidney failure and heart failure frequently coexist with the reciprocal interference of each condition complicating the other's management, culminating in detrimental patient outcomes. The aim of this lecture is to address the utilization of peritoneal dialysis (PD) in patients with heart failure, including its potential advantages as well as its challenges. Peritoneal dialysis may mitigate cardiovascular risk factors in patients with kidney failure undergoing replacement therapy, largely by optimizing volume and blood pressure management, thus limiting the progression of left ventricular hypertrophy and minimizing episodes of myocardial stunning. Among patients with kidney failure and prevalent heart failure, PD may offer particular advantages including efficient relief of intravascular congestion and less hemodynamic fluctuation in comparison to conventional hemodialysis. Furthermore, accumulating evidence supports the role of PD as a viable and beneficial adjunct to medical therapy alone in patients with chronic refractory heart failure without kidney failure. Ultimately, optimizing PD for sodium clearance remains the foremost objective in the context of heart failure. Consequently, a range of therapeutic approaches should be implemented to tailor the treatment according to the specific characteristics of the patient.

IS-08

Challenging surgical cases in kidney transplantation (20')

Ibrahim Berber

Abstract: The number of patients with end-stage renal failure (ESRD) is steadily increasing worldwide. The best treatment for patients with end-stage renal disease is kidney transplantation for many years. Therefore, the number of patients requiring kidney transplants is increasing every day. Complex kidney transplants constitute a significant portion of these kidney transplants. The increasing age of donors and recipients is leading to an increased complexity of kidney transplant implantation surgery. Complex kidney transplantation cases consist of medical and surgical reasons in the donor and recipient. Nowadays, a significant portion of kidney transplant candidates are elderly, have had a previous transplant, have severe peripheral and coronary vascular atherosclerosis, are immunologically high risk, require simultaneous surgeries, and require multiorgan transplantation. Urinary tract anomalies are the importent problem especially in pediatric and young patients. For increasing the acceptance and treatment of these complex patients, transplant teams should have innovative solutions to prevent and

manage complications that may occur pretransplant, intraoperative, and posttransplant period in complex patients with ESRD. The peripheral vascular disease increases difficulty of surgery and may effects transplant morbidity, mortality, and long-term outcomes. But, vascular complex kidney transplants offer comparable outcomes in the long term to conventional population when technically well menaged. Dialysis alternative has worse outcomes in terms of mortality, with a proportional risk of death 2.66 higher compared with transplanted patients. Second kidney transplant is considered a good therapeutic option for patients who have a previous graft failure, because second transplants show similar graft survival and complications rate as first transplants. Although there is controversy regarding the benefit of continuing dialysis or third and fourth kidney transplant, third and fourth kidney transplant is a valid treatment option with reasonable short- and long-term patient and graft survival outcomes. Other challenging surgical situations encountered in kidney transplant surgery include paired kidney exchange transplantation, pediatric kidney transplantation, simultaneous surgery during kidney transplantation (e.g., native nephrectomy for polycystic kidney disease), multiorgan transplantation, and kidney transplantation for patients with urinary tract anomalies. I would like to share our approach and experience in surgical techniques for minimally invasive living donor nephrectomy, management of donor-related recipient surgical challenges, complex vascular recipients, urologically challenging recipients, concurrent surgeries, paired kidney exchange transplantation, and second and third kidney transplantation.

IS-09

Managing inflammation in CKD: are we doing enough?

Flaviu Bob

Abstract: Inflammation is an important pathway involved in the cardio-reno-metabolic syndrome, and it acts as a self-amplifying feedback loop. It has been proven that despite treatment there is a constant residual risk. The question arises if applying the guideline directed medical therapy, this risk is reduced, and if there is prove that this treatment is reducing inflammation as well. Regarding, the anti-inflammatory effect of statins, it is due to the fact that statins reduce NF-κB signalling, and lower production/ release of pro-inflammatory cytokines (IL-6, TNF-α). By targeting AngII, ACEIs and ARBs are believed to exert potent antiatherosclerotic effects, not only through their antihypertensive pathway but also through anti-inflammatory, antiproliferative, and antioxidant properties. Overactivation of the aldosterone production and mineralocorticoid receptor expression in obesity, diabetes has further been implicated in the promotion of inflammation and fibrosis. Antagonism of the MR with steroidal (e.g. spironolactone), and non-steroidal (finerenone) MRAs suppresses expression of pro-inflammatory and pro-fibrotic genes in macrophages, myofibroblasts, podocytes and mesangial cells. Regarding SGLT2i the question is if inflammation is directly lowered by SGLT2i or it is lowered indirectly because of improved glucose control, reduced kidney injury, or less oxidative stress. Activation of the GLP1R reduces production of proinflammatory chemokines, cytokines, adhesion molecules and pro-fibrotic factors via inhibition of NF-κB binding. The anti-inflammatory effect of guideline directed medication is not proven in clinical trials, however is an additional reason to use it (in combination). The fact that it is not proven represents reason to look for new pillars of treatment targeting directly inflammatory pathways (IL1beta, IL6, etc).

IS-10

Update on therapies in podocytopathies

Ivica Horvatic

Abstract: The lecture reviews evidence of new therapies for managing patients with podocytopathies, minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS), building on the 2021 KDIGO glomerular disease guidelines. Although MCD and FSGS are traditionally regarded as distinct histopathological entities, they may represent different manifestations along the same disease spectrum characterized by podocyte injury. The accurate classification of FSGS into primary, secondary, or genetic forms is of utmost importance because treatment strategies differ substantially. Immunosuppressive therapy should generally be reserved for patients with primary FSGS, whereas secondary and genetic forms are managed primarily with supportive care. Comprehensive supportive care includes strict dietary sodium restriction, renin-angiotensin system blockers (RASB), titrated to the maximally tolerated dose and also sodium-glucose cotransporter 2 (SGLT2) inhibitors. Large trials, including DAPA-CKD and EMPA-KIDNEY, have demonstrated notable renal benefits in patients with glomerular disease, but such effects were not so clearly evident in the FSGS subgroup, possibly related to the limited sample size. Additional data suggest that SGLT2 inhibitors may stabilize kidney function and reduce proteinuria in patients with podocytopathies. Furthermore, dual endothelin-angiotensin receptor antagonist sparsentan, explored in the phase III DUPLEX trial significantly reduced proteinuria compared with irbesartan. However, the primary endpoint of eGFR slope was not met, and longer follow-up may be necessary to assess its full impact. Recently, finerenone showed significant renal benefit in patients with non-diabetic glomerular disease in subanalysis of FIND-CKD trial. For adults with MCD, and primary FSGS high-dose glucocorticoids are the recommended first-

line treatment, although prolonged steroid exposure is associated with significant adverse effects. Steroid resistance occurs in approximately 8–25% of patients with MCD and is more common in FSGS (up to 50%). Lack of response to glucocorticoids remains a key determinant of prognosis. The review discusses steroid-dependent and frequently relapsing disease, highlighting the role of steroid-sparing therapies such as calcineurin inhibitors, cyclophosphamide, and mycophenolate mofetil. Cyclophosphamide and mycophenolate remain an effective option but require careful consideration of its risks, including infertility, infections, and malignancy. Calcineurin inhibitors are effective but require monitoring for nephrotoxicity and are associated with relapse after discontinuation. In FSGS, multidrug resistance should prompt reassessment of the diagnosis and evaluation for genetic or secondary causes. In steroid-resistant cases, genetic causes are identified in up to 20% of patients and are associated with a high risk of progression to kidney failure. Genetic testing is increasingly important, particularly in younger patients, those with a family history, syndromic features, or resistance to immunosuppressive therapy, as identifying a genetic cause can prevent unnecessary exposure to ineffective immunosuppression. Among novel immu–nesuppressive strategies, B-cell–targeted therapies have garnered increasing attention. Rituximab reduces relapse rates in steroid-dependent and frequently relapsing nephrotic syndrome, although most evidence derives from cohorts dominated by MCD patients. In FSGS, efficacy is more limited, with more favourable responses observed in steroid-dependent than in steroid-resistant cases. These patterns are reflected in larger cohort studies. The RITERM study, which included 183 patients with podocytopathies, reported an overall response rate of 82% over a follow-up period of at least three years. Outcomes differed by subgroup, with lower response rates in steroid-resistant patients (51%) and complete remission in only 18%, particularly in those with FSGS. The TURING trial, so far the only randomized control trial in adults with rituximab, showed that rituximab is safe and effective in nephrotic MCD/FSGS in delaying relapse, it increases proportion of FSGS patients reaching remission and also this study showed that faster prednisone wean is equally effective as slower. Second-generation anti-CD20 monoclonal antibodies, such as obinutuzumab, may achieve more sustained B-cell depletion. However, their efficacy in steroid-resistant disease remains modest (approximately 50%). Other promising agents are TRPC5/TRPC6 ion channels inhibitors acting on podocyte cytoskeleton stabilisation and subsequently on reduction in proteinuria. Overall, the review advocates a personalized approach that combines precise disease classification, supportive care, judicious use of immunosuppressive agents, and incorporation of emerging evidence to optimize long-term renal outcomes while minimizing treatment-related toxicity.

IS-11

CKD-MBD: New Insight and Opportunities for Pharmacological Treatment

Marija Milinkovic

Abstract: Chronic kidney disease–mineral and bone disorder (CKD-MBD) is defined as a systemic disorder of mineral and bone metabolism due to CKD, manifested by abnormalities in calcium, phosphate, parathyroid hormone (PTH), or vitamin D metabolism; abnormalities in bone turnover, mineralization, volume, linear growth, or strength (renal osteodystrophy, ROD); and vascular or other soft-tissue calcifications. In 1994, the World Health Organization defined osteoporosis as a disease characterized by reduced bone mass and deterioration of bone microarchitecture, resulting in increased bone fragility and fracture risk. More broadly, osteoporosis may be considered as any condition that compromises bone strength and increases fracture risk. Bone strength depends on both bone quantity (density) and bone quality (microarchitecture). Bone abnormalities associated with ROD impair bone quality and strength, thereby increasing fracture risk independently of bone density. Moreover, fracture risk is further increased by hormonal disturbances, which are common in both men and women with CKD, as well as by frequent falls and the high prevalence of sarcopenia. These observations have brought skeletal complications to the forefront of nephrology and supported a broader understanding of bone disease within the spectrum of CKD-MBD. Accumulating evidence from both experimental and clinical studies suggests that fibroblast growth factor 23 (FGF-23) exerts a direct pathogenic effect on the development of left ventricular hypertrophy (LVH). Independently of Klotho, FGF-23 activates fibroblast growth factor receptor 4 (FGFR4), promoting LVH and myocardial fibrosis. In addition, through Klotho-dependent activation of the serine/threonine protein kinase WNK4, FGF-23 enhances sodium and calcium reabsorption in the distal nephron by upregulating the apical Na-Cl cotransporter and epithelial calcium channels. Thus, FGF-23 appears to play a pivotal role in myocardial remodeling and the progression of cardiovascular disease, whereas convincing evidence linking FGF-23 directly to vascular calcification remains lacking. Therapeutic strategies are evolving in parallel with advances in our understanding of the pathophysiology of CKD-MBD. Current approaches include non-calcium-based phosphate binders, expanded hemodialysis, medical nutritional therapy, calcimimetics (both oral and intravenous), vitamin K supplementation, and magnesium-based interventions. In addition, several novel therapeutic strategies are under investigation, including denosumab, the recombinant Klotho protein, extended-release calcifediol, tenapanor, and other emerging

agents. Taken together, these advances highlight the importance of a deeper understanding of the mechanisms underlying CKD-MBD, with the ultimate goal of improving patient outcomes and reducing the burden of skeletal and cardiovascular complications in individuals with CKD, including those receiving maintenance dialysis.

IS-12

The Child Behind the Kidney: Born Equal, but Treated Equally? The Global Challenge of Pediatric Kidney Disease

Ayse Balat

Abstract: According to the UN Convention on the Rights of the Child, one of the fundamental rights highlighted is "every child's right to access education and health services." Despite the existence of legally guaranteed children's rights and the understanding that healthy children form the foundation of a healthy society, many children face disparities beginning in the intrauterine period, largely due to sociodemographic and economic inequalities. These factors create significant barriers to early diagnosis, specialized care, and life-saving treatments, disproportionately affecting vulnerable populations. Children's biological characteristics differ from those of adults, making them the most vulnerable group to disease. Childhood kidney disease, particularly in its chronic forms, exemplifies health inequality at almost every stage of life. Research indicates that inequalities in the care of childhood kidney disease are not due to biological differences but rather arise from a combination of social, structural, and health system factors. Issues such as poverty, limited health knowledge among caregivers, geographic barriers, and health systems that do not prioritize children's needs limit access to kidney disease prevention, early diagnosis, and kidney replacement therapies. These inequalities are particularly pronounced in resource-constrained settings and challenging geographic areas, resulting in delayed diagnoses, poorer clinical outcomes, impaired growth and development, and long-term negative impacts on individuals. Although every child is born equal, the quality of care they receive for kidney-related problems can vary significantly for several reasons. In summary, inequality in child health services is a significant issue that requires coordinated, multi-sector strategies that extend beyond medical care. The primary strategies should focus on improving health literacy, implementing early interventions, building equitable health systems, strengthening the pediatric nephrology workforce and infrastructure, and enacting policies that address the social determinants of health.

IS-13

Is there still a role for plasma exchange in complement-mediated TMA/aHUS?

Mirna Aleckovic-Halilovic

Abstract: Complement mediated TMA/aHUS is organ and life-threatening condition for which prompt initiation of curative, but also empiric and supportive therapy is of great importance. It results from overactivation of alternative pathway of complement. Current main stray of treatment is C5 inhibition. Prior to its approval, plasma exchange (PLEX) was first line treatment although overall efficacy was poor with exception of aHUS with factor H Ab, where it is used in combination with immunosuppression. Circumstances in which PLEX still might be used and rationale for it will be elaborated together with literature review on the topic. Although terminal complement inhibition is effective and current first line therapy for aHUS, main limitations is its cost and unavailability in some countries and risks of severe infections and allergic reactions. Short-and long-term management of patients with aHUS should be tailored individually considering patient's clinical course, underlying genetic abnormality and current conditions of healthcare systems of countries. PLEX is important initial therapy if high clinical suspicion of aHUS in countries where eculizumab is difficult to attain or resources are limited. Therefore, alternative approaches, including PLEX, are certainly needed and research on these approaches, varied responsiveness to PLEX, dialysis, and C5 inhibition may guide future directed therapy. Research should also focus on quicker and more readily available diagnostic modalities that will ensure timely management and rehabilitation.

IS-14

The impact of Epigenomics on chronic kidney disease

Ingrid Prkačin

Abstract: This abstract emphasizes genome-wide profiling of DNA and RNA methylation and histone modifications in chronic kidney disease (CKD) and the impact of disregulation of epigenome, future challenges, new tools, treatment options and earlier intervention. The epigenome, includes covalent modifications of chromatin components such as DNA, RNA, and proteins, ensures that cells maintain their differentiated states through epigenetic mechanisms. Proper kidney development relies on specific methylation abnormalities, like adding a methyl group to cytosine, via the enzyme DNA methyltransferase (DNMT). Renal disorders often involve epigenetic modifications such as DNA/RNA methylation and acetylation, which affect gene expression. Dysregulation of DNA methylation represents a hallmark of the fibrotic process, characterized by genomic hypomethylation, genomic instability and the aberrant hypermethylation of specific tumor suppressor

and anti-fibrotic gene promoters with functional impairments and structural damage of kidney tissue. Patients with hypertension and diabetes related CKD, have differentially methylated positions, influenced by genetic variants. Decreased methylation may influence gene expression and progression of disease, making these regions potential biomarkers. Monitoring the epigenome could lead to new therapies and biomarkers, with drugs like 5-azacitidine and decitabine by reducing DNMT1 expression and enhancing podocyte function. Histone modifications are vital in various biological processes, impacting gene expression and chromatin structure influencing transcription and DNA repair. Clinical studies highlight the reno-protective effects of histone modification inhibitors, and incretin-related medications. MicroRNAs (miRNAs) are short, noncoding RNAs (18-25 nucleotides) vital in regulating gene expression in eukaryotes and play a crucial role in diabetic nephropathy and polycystic kidney disease. The evidence on the impact of renal function on circulating miRNA levels is inconsistent. Dysregulation of epigenome in CKD, has role in pro-fibrotic pathways, suggesting potential new biomarkers and therapeutic targets. Methylation plays a crucial role in kidney diseases, and demethylating agents may improve outcomes by reversing abnormal patterns. Precision medicine may help us understanding and improve patient outcomes in kidney diseases. Identifying methylation and histone changes in patients vs. healthy individuals is vital for developing targeted new therapies. Future nephrology research will identify novel tools and biomarkers. Bioelectrical impedance spectroscopy could be some of new tools in early recognition, provides early disturbances in cellular health and fluid distribution that may precede clinically detectable kidney dysfunction. Incorporating bioelectrical impedance spectroscopy with phase angle and other parameters into routine management in patients with risk factors for CKD could improve early risk stratification.

IS-15

The role of immunological parameters in treatment and outcomes of ANCA-associated vasculitis

Nebojsa Miric

Abstract:

Introduction. ANCA-associated vasculitis (AAV) represents a heterogeneous group of autoimmune disorders characterized by inflammation of small blood vessels. Immunological parameters provide valuable insights into disease activity, contribute to predicting therapeutic response, and support more effective treatment and monitoring strategies, highlighting the need to evaluate their role in clinical practice. Therefore, this study aimed to assess the role of immunological parameters in treatment and clinical outcomes of patients with ANCA-associated vasculitis.

Methods. A retrospective study included 38 patients with ANCA-associated vasculitis, hospitalized or followed up at the Clinic of Nephrology and Clinical Immunology, University Clinical Center of Vojvodina, between 2020 and 2023. Clinical data, biochemical and immunological parameters, as well as disease activity assessed by BVAS and FFS scores, were analyzed. Results: A correlation was observed between ANCA titers, complement components, and ESR with pulmonary involvement (r=0.202), as well as a negative association between ANCA titers and renal function markers (creatinine and eGFR). Patients in serological remission had significantly lower ANCA titers (p=0.03). The need for acute hemodialysis and plasmapheresis correlated strongly with higher ANCA titers (r=0.503; r=0.502). The presence of PR3-ANCA was associated with higher FFS values (p=0.032). Higher BVAS scores correlated with corticosteroid use and plasmapheresis.

Conclusion. Predicting relapses using immunological markers offers the possibility of early identification and timely treatment, which can significantly reduce disease progression and minimize complications. These findings support the routine assessment of immunological parameters in the management of patients with ANCA-associated vasculitis.

IS-16

CKD screening: urinary albumin or urinary DKK3 or both?

Danilo Fliser

Abstract: Approximately 750 million people worldwide suffer from chronic kidney diseases (CKD)-a leading cause of cardiovascular morbidity and premature mortality-but early identification of progressive kidney function decline in patients at risk is still a challenge. CKD diagnosis relies on estimated glomerular filtration rate (eGFR) and albuminuria screening, primarily reflecting glomerular injury. Nevertheless, in a substantial proportion of affected subjects progressive CKD initially remains undetected, since kidney function deteriorates through ongoing tubulointerstitial injury without significant albuminuria, a condition known as “non-albuminuric“ CKD. Urinary Dickkopf-3 (uDKK3) has emerged as an innovative biomarker of progressive CKD, which is expressed by proximal tubular epithelial cells as a response to continuing injury. It is secreted into the urine, where it signals ongoing fibrogenic activity within the kidney. Clinical studies across a broad range of CKD etiologies-in adults and children alike-have shown that elevated uDKK3 significantly improved detection and prediction of progressive CKD after adjustment for established CKD risk markers including albuminuria. Moreover, in primarily non-albuminuric populations, e.g. those with type 2 diabetes and patients with heart or lung diseases, uDKK3 identifies high-risk individuals for future decline of kidney function. These findings support

the hypothesis that CKD progression follows different pathways of mainly glomerular or tubulointerstitial injury. It is therefore plausible to use complementary biomarkers for CKD screening-albuminuria and uDKK3-each reflecting a distinct biological dimension of kidney injury. We discuss the limitations of albuminuria screening and propose a framework for integrating tubular markers like uDKK3 into future CKD screening strategies.

IS-17

Measured vs estimated GFR in deceased-donor KTx recipients

Zhaklina Shterjova-Markovska, Irena Rambabova-Bushljetik, Tanja Makazlieva, Aleksandra Peshevska, Venjamin Majstorov, Nikola Gjorgjievski, Galina Severova, Igor Nikolov, Vlatko Karanfilovski, Julijana Usprcov, Goce Spasovski

Abstract:

Introduction. Serum creatinine (sCr)-derived estimated glomerular filtration rate (eGFR) equations are routinely employed to monitor graft function, though their accuracy in kidney transplant recipients (KTRs) can be affected by transplant-specific clinical variables.

The aim was to assess the agreement between 99mTc-DTPA measured glomerular filtration rate (mGFR) and sCr-based eGFR equations in deceased-donor KTRs, while evaluating the impact of cold ischemia time (CIT), delayed graft function (DGF), and human leukocyte antigen (HLA) matching on this agreement. Methods: This single-center, cross-sectional method-comparison study analyzed 30 adult deceased-donor KTRs at 1-3 years post-transplantation. 99mTc-DTPA plasma clearance via the three-plasma sample method (TPSM) served as the comparator method (CM) for mGFR. eGFR was estimated using the CKD-EPI 2021, MDRD, and EKFC equations. Statistical agreement was measured using Bland-Altman analysis, mean bias with 95% confidence intervals, 95% limits of agreement, mean absolute error, and P30 accuracy. Pearson correlation was applied to assess inter-method relationships. Subgroup analyses were stratified by CIT duration, presence of DGF, and degree of HLA matching. **Results:** Mean mGFR was 51.50±16.12 mL/min/1.73 m². Equation accuracy varied across transplant-related subgroups. Prolonged CIT and DGF were associated with reduced agreement between methods. HLA matching demonstrated a nuanced pattern, showing higher P30 accuracy in recipients with ≥4 matches without a consistent reduction in bias. The MDRD equation exhibited the most stable overall performance across all analyzed subgroups.

Conclusion. In deceased-donor KTRs, sCr-based eGFR equations exhibit variable performance depending on key transplant-related characteristics. Direct mGFR determination remains valuable when precise evaluation of graft function is required.

IS-18

New Classification of Monoclonal Gammopathies-Associated with Kidney Lesions

Danica Galesic Ljubanovic

Abstract:

Introduction. Monoclonal gammopathy of renal significance (MGRS) refers to clonal plasma-cell or B-cell proliferative disorders that secrete a nephrotoxic monoclonal immunoglobulin without meeting the haematological criteria for a malignancy requiring specific treatment. Over the past two decades the spectrum of monoclonal gammopathy-associated kidney lesions has expanded considerably, with new entities and morphological variants continually being described. Because pathologic diagnosis depends heavily on electron microscopy and ancillary techniques and has long been hampered by inconsistent terminology, the Renal Pathology Society (RPS) and the International Kidney and Monoclonal Gammopathy Research Group (IKMG) convened a 27-member international working group of nephropathologists, nephrologists and a haematologist to establish consensus terminology and diagnostic criteria. The Six *Diagnostic Categories:* The 2025 consensus organizes monoclonal gammopathy-associated lesions into six major categories: light chain cast nephropathy, immunoglobulin amyloidosis, monoclonal immunoglobulin deposition disease (MIDD), monoclonal gammopathy-associated glomerulonephritides (including PGNMID, monoclonal membranous nephropathy, monoclonal immunotactoid glomerulopathy, cryoglobulinaemic glomerulonephritis types I and II, intracapillary monoclonal IgM glomerulopathy, and C3 glomerulopathy with monoclonal gammopathy), monoclonal gammopathy-associated crystalline nephropathies, and non-crystalline light chain proximal tubulopathy. For every entity the group adopted a two-tiered structure: mandatory prerequisite diagnostic criteria that must all be met, alongside supportive, non-mandatory features that strengthen but are not required for the diagnosis. Key Novelties in the 2025 *Classification:* As emphasized in the accompanying presentation, the consensus now recognizes 16 distinct monoclonal gammopathy-associated kidney lesions comprising 22 morphological variants and explicitly acknowledges that two or more of these lesions may coexist within the same biopsy, demanding systematic examination by light microscopy, immunofluorescence and electron microscopy. Newly defined entities include PGNMID, C3 glomerulopathy associated with monoclonal gammopathy, crystalglobulin-induced nephropathy and light chain crystalline podocytopathy, while newly recognized variants include light chain (or light-and-heavy-chain) deposition disease by immunofluorescence only, non-crystalline light chain proximal tubulopathy, heavy chain fibrillary glomerulonephritis, light chain-only PGNMID and immunotactoid glomerulopathy,

IgD/IgE variants of MIDD, and amyloidogenic light chain cast nephropathy. Terminology was also revised for clarity: “light chain cast nephropathy” now replaces “myeloma cast nephropathy,” since the lesion is not exclusive to multiple myeloma, and “intracapillary monoclonal IgM glomerulopathy” replaces the older “Waldenström macroglobulinaemia glomerulopathy” to avoid confusion with MIDD. As highlighted in the presentation, reaching these diagnoses remains technically demanding and depends on electron microscopy at high magnification and ancillary techniques-IgG subclass staining, protease-digested paraffin immunofluorescence (IF-P), mass spectrometry, and immunoelectron microscopy-that are not widely available, particularly in developing countries. Clinical *Relevance:* Precise lesion-specific diagnosis is far more than an academic exercise: individual entities differ markedly in their haematological associations, extrarenal manifestations, kidney survival, and post-transplant recurrence rates, and this distinction is essential for designing the systemic work-up, selecting clone-directed therapy, and planning transplant and follow-up monitoring. By eliminating ambiguous and inconsistent terminology, this consensus aims to harmonize kidney biopsy reporting reporting worldwide, improve communication between pathologists, nephrologists and haematologists, and support patient stratification for future clinical trials.

Oral Communications (OC)

OC-01

Why do we still miss Fabry disease? Lessons from a three-year selective screening program in Bosnia and Herzegovina

Nejra Prohic, E. Begic

Abstract: Fabry disease is an X-linked lysosomal storage disorder caused by pathogenic variants in the GLA gene, resulting in deficient α-galactosidase A activity and progressive glycosphingolipid accumulation. Its heterogeneous multisystem phenotype contributes to diagnostic delay, as renal, cardiac and cerebrovascular manifestations are often evaluated separately. Chronic kidney disease, unexplained proteinuria, left ventricular hypertrophy and stroke of uncertain etiology represent important clinical red flags. We aimed to evaluate the diagnostic yield of selective Fabry disease screening in a high-risk population and the additional value of cascade family screening. Between 2023 and 2026, a selective Fabry disease screening program was conducted in Bosnia and Herzegovina. A total of 575 patients with clinical features suggestive of Fabry disease were evaluated. The main indications were chronic kidney disease and/or unexplained proteinuria, unexplained left ventricular hypertrophy, and cerebrovascular events of uncertain etiology, particularly in younger patients. Diagnostic evaluation included α-galactosidase A activity and lyso-Gb3, followed, when indicated, by molecular genetic analysis of the GLA gene. After identification of index cases, pedigree assessment and cascade testing of available relatives were performed. Among 575 selectively screened patients, Fabry disease was identified in two unrelated families. Overall, seven affected family members were identified through evaluation of index cases and subsequent cascade screening. Three affected members of the first family carried the GLA variant c.540G>C p.(Leu180Phe), while four members of the second family carried c.334C>G p.(Arg112Gly). Identification of index cases enabled recognition of additional affected relatives. Renal, cardiac and cerebrovascular abnormalities represented the principal clinical triggers for diagnostic evaluation. Fabry disease may remain unrecognized because its manifestations are interpreted as isolated organ-specific disorders rather than components of a multisystem disease. Our real-world experience supports a kidney-heart-brain approach to selective screening, particularly in patients with unexplained chronic kidney disease/proteinuria, left ventricular hypertrophy or cerebrovascular events. Combining targeted screening with cascade family testing may improve recognition and facilitate earlier diagnosis.

OC-02

Secondary Glomerular Diseases in University Clinical Center of Republika Srpska Banja Luka – Results of Kidney Biopsies in Period 2007–2025

Milorad Grujicic

Abstract: Kidney biopsy plays a key role in the diagnosis of glomerular kidney diseases and serves as a guide for therapy. To present all patients with secondary glomerular diseases at the University Clinical Center of Republika Srpska during the period from 2007 to 2025. We performed 368 native kidney biopsies, representative sample was in 328 patients. Complete preparation, processing of preparations and pathohistological diagnosis was made at Clinic for Pathology University clinical centre of Republik of Srpska. In 11 patients we also took a third sample for electron microscopy-preparation, processing and pathohistological diagnosis was made at the Institute for Pathology of Faculty of Medicine in Zagreb. We divided patohistological diagnoses in 5 groups according to Italian registry kidney biopsies: primary glomerular diseases (49.4% of all patients), secondary glomerular diseases (35.6%), vascular diseases (7%), tubulointerstitial diseases (2.4%) and miscellaneous (4.8%). Patients with secondary glomerular diseases were divided in three groups: 1. immune-mediated glomerulonephritis 67 patients (lupus nephritis 38 patients, ANCA vasculitis 26 patients, Goodpasture syndrome 4 patients); 2. glomerulonephritis caused by dysgammaglobulinaemia and paraproteinaemia 28 patients (amiloidosis 15 patients, light chain disease 7 patients, myeloma cast nephropathy 3 patients and crioglobulinemia one patient). Metabolic and hereditary disorders 22 patients (diabetic nephropathy 19 patients, thin basement membrane disease 2 patients, Alport syndrome one patient). Most frequent diagnoses of all patients with secondary glomerular disease were lupus nephritis, ANCA vasculitis, diabetic nephropathy (isolated or combined with non-diabetic kidney disease) and amiloidosis. Out of 48 patients over the age of 65, secondary glomerular diseases had 18 patients, most commonly pANCA vasculitis, amyloidosis, and diabetic nephropathy. Patients with secondary glomerular diseases were the second most common group of patients in whom we performed kidney biopsy, and the most common diagnoses were lupus nephritis, ANCA vasculitis, amyloidosis, and diabetic nephropathy,

which is consistent with data from most kidney biopsy registries from Europe.

OC-03

Early Worsening of Renal Function Identifies High-Risk Patients After Non-ST-Elevation Myocardial Infarction

Emir Becirovic, Minela Becirovic, Amir Becirovic

Abstract: Early deterioration of kidney function is a frequent manifestation of cardiorenal interaction in patients with acute cardiovascular disease and may identify individuals at increased risk of adverse outcomes. This study aimed to determine the incidence and admission predictors of early worsening of renal function and to assess its association with short-term outcomes in patients hospitalized with non-ST-elevation myocardial infarction. This prospective observational study included 170 consecutive patients with non-ST-elevation myocardial infarction. Serum creatinine and other laboratory parameters were measured at admission and after 24 hours. Early worsening of renal function was defined as an increase in serum creatinine of ≥26.5 μmol/L within the first 24 hours. Clinical, biochemical, inflammatory and echocardiographic parameters were evaluated as potential predictors. Receiver operating characteristic analysis was used to assess discrimination, and multivariable logistic regression was performed to identify factors independently associated with early renal deterioration. Patients were followed for three months for major adverse cardiovascular events and all-cause mortality. Early worsening of renal function occurred in 25 of 170 patients (14.7%). At admission, affected patients had higher median serum creatinine (150 vs. 92 μmol/L, p<0.001), urea (10.4 vs. 6.6 mmol/L, p<0.001), C-reactive protein (27.7 vs. 9.0 mg/L, p<0.001), and glucose (9.1 vs. 7.2 mmol/L, p=0.006). Admission creatinine demonstrated the highest individual discrimination for early renal deterioration (AUC 0.778), followed by urea (AUC 0.759) and C-reactive protein (AUC 0.752). A creatinine threshold of 122 μmol/L provided 72% sensitivity and 80% specificity. In multivariable analysis, admission creatinine (OR 1.048 per 10 μmol/L increase, 95% CI 1.009-1.089; p=0.016) and C-reactive protein (OR 1.076 per 10 mg/L increase, 95% CI 1.004-1.153; p=0.038) remained independently associated with early worsening of renal function. Three-month mortality was markedly higher in patients with early renal deterioration (40.0% vs. 10.3%; OR 5.78, 95% CI 2.21-15.12; p<0.001). Early worsening of renal function occurred in approximately one in seven patients with non-ST-elevation myocardial infarction and identified a subgroup with nearly six-fold higher odds of short-term mortality. Admission creatinine and systemic inflammatory activity may facilitate early recognition of patients at increased risk of renal deterioration and adverse outcomes.

OC-04

Metabolic-kidney-cardio (MKC) axis and early kidney dysfunction begins with central obesity

Ingrid Prkacin, Mateja Muric Begic, Damir Rebic

Abstract: Obesity is a chronic metabolic dysfunction driven by visceral adiposity. Central obesity, defined by a waist-to-height ratio (WHtR) ≥0.5, precedes and predicts the development of heart failure, but data regarding its association with chronic kidney disease (CKD) are limited. Obesity is an important risk factor for CKD; however, conventional laboratory markers often remain within the normal range until substantial renal damage has occurred. Central obesity, liver fat, blood pressure, lipid profile and HbA1c are markers of broader metabolic health. This study evaluated whether selected metabolic parameters could identify early CKD vulnerability in untreated normal-weight, overweight and stage 1 obesity individuals without established kidney disease. Prospective observational study included 271 healthy adults assessed between 1 March and 1 April 2026 in two outpatient settings (167 females, age 42.3±9.1 years; 104 males, age 43.5±10.1 years). Renal function, blood pressure (normal value <130/80 mmHg on two measurements), anthropometric parameters (waist-to-height ratio [WHtR], body mass index [BMI]) and laboratory parameters were recorded. Participants were categorized according to metabolic-kidney-cardio (MKC) stage: stage 0 (171 participants, 125 F/46 M, with no MKC risk factors) or stage 1 (100 participants, 42 F/58 M, with overweight [BMI 25–29.9 kg/m²] or stage 1 obesity [BMI 30-34.9 kg/m²]). All participants were non-smokers and had no known arterial hypertension, diabetes mellitus, CKD, liver disease, heart failure, dyslipidemia or established cardiovascular or cerebrovascular disease. Participants with diagnosed MKC stage ≥2 were excluded (additional 70 participants, 20%). Kidney function was assessed using estimated glomerular filtration rate (eGFR; normal >60 mL/min/1.73 m²), and albuminuria using the urine albumin-to-creatinine ratio (UACR; A1 category <3 mg/mmol). Associations between WHtR and markers of early renal vulnerability, including UACR, were analysed, with statistical significance set at p<0.05. In MKC stage 0, median BMI was 24.3 kg/m², and WHtR ≥0.5 was detected in 10% of males and 7% of females. In MKC stage 1, 70% of males and 80% of females were overweight, with a median BMI of 26.4 kg/m². Stage 1 obesity was present in 30% of males and 20% of females, with a median BMI of 32.1 kg/m². WHtR ≥0.5 was detected in 80% of males and 54% of females. In MKC stage 0 and stage 1 participants were similar age (median 40 vs. 39 years) and blood pressure values (125/75 vs. 126/74 mmHg), with preserved kidney function (median eGFR 90 vs. 91 mL/min/1.73 m²; and UACR 1.5 vs. 1.7 mg/mmol). However, WHtR differed between groups, with median values of 0.53 in MKC stage 0 and 0.58 in MKC stage 1. Among

participants with WHtR ≥0.5, after 6 months we observed a non-significant difference in median eGFR and UACR between groups: median eGFR decreased to 88 and 87 mL/min/1.73 m², while median UACR increased to 1.9 and 2.0 mg/mmol, respectively. These findings suggest that early alterations and accelerated changes in kidney function may precede clinically detectable kidney dysfunction. Recognising metabolic dysfunction as a unified, multisystem condition supports a broader metabolic health framework with early central obesity prevention and management. Timely intervention may be crucial for preventing disease progression and reducing morbidity and mortality across the MKC spectrum.

OC-05

Lupus nephritis flare versus preeclampsia in pregnancy: a scoping review of diagnostic strategies

Prohovic S, Popovic M, Djurovic V, Strazmester Majstorovic G, Petrovic L, Knezevic V.

Abstract: Systemic lupus erythematosus (SLE) with lupus nephritis (LN) imposes a diagnostic dilemma in pregnancy: LN flare and preeclampsia (PE) share an overlapping phenotype of hypertension, proteinuria, thrombocytopenia, and renal impairment, yet require opposite management. Reported PE rates are approxi–mately 25-30% in women with LN versus under 3% in non-renal SLE. We aimed to map the available evidence on strategies for distinguishing LN flare from PE in pregnancy, and to appraise the strength of the evidence supporting each proposed diagnostic parameter. We conducted a scoping review following Joanna Briggs Institute methodology and PRISMA-ScR reporting guidance. Eligibility was defined using a Population-Concept-Context framework (pregnant women with SLE/LN; clinical, laboratory, serological, angiogenic-biomarker, or histological differentiation strategies; antenatal care). MEDLINE/PubMed was searched using four search strings spanning angiogenic, serological, and histological domains, supplemented by hand-searching of reference lists. Screening was performed independently by two reviewers. Of 57 records identified, 32 were included by database search and 16 by hand-search (48 total). No single clinical parameter reliably distinguished the two conditions in isolation. Gestational age under 20 weeks favoured LN flare, as did active urinary sediment with a falling complement/ rising anti-dsDNA trend. The soluble fms-like tyrosine kinase-1/placental growth factor (sFlt-1/PlGF) ratio was the most extensively studied biomarker: in the largest available dataset (68 women, 107 samples, conference-abstract level), a ratio ≤38 carried a negative predictive value (NPV) >95% in women without pre-existing proteinuria, but only 80% at 4 weeks in women with pre-existing proteinuria-the subgroup in whom the differential is hardest. A larger, peer-reviewed longitudinal cohort (163 women, 527 samples) independently corroborated the direction of this biomarker change without itself providing diagnostic-accuracy figures. Renal biopsy in the second trimester was reported as safe in experienced centres but used selectively rather than routinely. Distinguishing LN flare from PE in pregnancy requires a structured, multi-parameter approach integrating gestational timing, urinary sediment, serial serology, and angiogenic biomarkers, with renal biopsy reserved for discordant or clinically pivotal presentations. The evidence base for angiogenic biomarkers in this population remains limited to a small number of studies, the largest of which is unreplicated abstract-level data; prospective, adequately powered validation is the most pressing research priority.

OC-06

Lower is not always better: the non-linear effect of individualized dialysate sodium on volume, thirst and cardiac remodeling

Eftimovska-Otovikj N, Nakovska M, Poposka E, Ristovski O, Krstaveska T, Zlatevska K, Nikolova E, Ilioska S.

Abstract: Individualized dialysate sodium (iDNa), prescribed according to predialysis serum sodium, is considered a physiological approach to sodium and volume management in hemodialysis. However, whether progressively lower iDNa provides additional clinical benefit remains uncertain. We investigated the relationship between iDNa and volume status, thirst, blood pressure and cardiac remodeling. Seventy-seven stable, non-diabetic maintenance hemodialysis patients receiving iDNa based on predialysis serum sodium were stratified into three groups: 134-136 mmol/L (n=39), 137-138 mmol/L (n=33), and >139 mmol/L (n=5). Interdialytic weight gain (IDWG), blood pressure, thirst assessed by the Dialysis Thirst Inventory (DTI), and echocardiographic parameters were compared across sodium strata. Mean IDWG was 1.97±0.58, 1.88±0.73 and 1.98±0.21 kg in the 134-136, 137-138 and >139 mmol/L groups, respectively, with no significant between-group difference. Thirst also showed no dose-dependent relationship with iDNa (Kruskal-Wallis p=0.774), with DTI scores of 10.55±3.25, 10.72±3.41 and 12.20±4.81, respectively. Left ventricular diastolic and systolic diameters tended to be lower in the 134-136 mmol/L group compared with 137-138 mmol/L (44.61±7.41 vs. 48.34±7.34 mm, p=0.060; 30.34±6.48 vs. 34.07±7.24 mm, p=0.074). Left ventricular mass and mass index were comparable. Notably, relative wall thickness was significantly higher in the lowest sodium group (0.49±0.08 vs. 0.42±0.06, p=0.002). The effects of individualized dialysate sodium were not linearly dose-dependent. Lower iDNa was not associated with significantly lower IDWG or thirst, while cardiac geometry showed potentially relevant differences. These findings suggest that sodium matching to the individual patient may be

more important than simply prescribing lower dialysate sodium concentrations.

OC-07

Medical nutritional therapy and sarcopenia management in advanced stages of CKD: a case study

Ana-Maria Damian

Abstract: Adherence to personalized nutritional medical therapy in advanced stages of CKD can improve the status of metabolic disorders and also delay the initiation of hemodialysis, but where the risk of malnutrition and muscle mass loss becomes an important concern. The purpose of this case study is to emphasize the importance of nutritional medical therapy in the management of the pre-dialysis patient. A 75-year-old male, BMI=27.1kg/m2, with type 2 diabetes for 15 years treated with insulin glargine 16 units and dapagliflozin, with chronic pancreatitis and renal imbalance-CKD stage G5A2 (Hb 9.8mg/dl, serum creatinine 7 mg/dl, eGFR 6.9 ml/min/1,73m2, K=6.6 mmol/L, urea 200 mg/dl, uACR 200 mg/g) addresses for nutritional counseling. Nutritional assessment identified an increased intake of hyperlipidemic foods and animal protein, food choices with a high glycemic index, a low-fiber diet, and moderate fluid intake (1500ml). The medical nutritional therapy was based on the personalization of macronutrients and gastro-technical elements (culinary techniques such as boiling, blanching, and soaking foods in water before cooking/consuming). It was recommended an individualized dietary plan, with 3 meals and 2 snacks: normocaloric-2000kcal, hypoglycemic-240g CH, hypolipidemic 60g L, and low-protein with 43g P (0.8g P due to renal context), fluid intake-2000ml water/day (diuresis/24h>2000ml), low-sodium <2300mg/day, low in potassium 1900-2700 mg/day, physical activity within the tolerance limit and adjustment of insulin doses according to self-monitoring; the patient's body composition was assessed using BiA (bioelectrical impedance analysis) to evaluate SMM (Skeletal Muscle Mass) in order to control the risk of sarcopenia : periodic visits were carried out to acquire information and create a sustainable approach for the patient's health. The evolution of biological parameters-serum creatinine decreased to 4.6 mg/dL, serum potassium dropped to 4.8 mmol/L (in conjunction with sodium zirconium cyclosilicate), uACR fell to 76 mg/g, and serum urea decreased to 164mg/dl. In terms of body composition, SMM increased by 0.3 kg, while VFA (Visceral Fat Area) decreased by 0.6 cm2; ECW (Extracellular Water) showed a decrease of 0.002, and the SMI (Skeletal Muscle Index) remained stable at 8.6 kg/m2. Following a 16-week collaborative effort, the patient's biological parameters showed favorable improvement, allowing the arteriovenous fistula procedure to be postponed. Multidisciplinary collaboration plays a vital role in the management of patients with CKD, and medical nutrition therapy has a key part to play-both in implementing dietary recommendations tailored to the underlying condition and in preventing sarcopenia.

OC-08

Left Atrial Enlargement Despite Preserved Ejection Fraction in Chronic Kidney Disease: Association With Advanced Disease and Hemodialysis

Eneida Hoxha, Ledio Collaku, Somida Kuka, Pandush Pojani, Xhesika Habilaj, Margarita Resuli Gjata

Abstract: Cardiovascular involvement in chronic kidney disease (CKD) may be present despite preserved left ventricular systolic function. Left ventricular ejection fraction (LVEF) alone may therefore underestimate structural cardiac abnormalities in this population. We aimed to evaluate left atrial enlargement in patients with preserved LVEF across CKD severity and to explore its association with maintenance hemodialysis. We performed a cross-sectional analysis of 100 patients with CKD stages G2–G5 who underwent transthoracic echocardiography by a single experienced operator. CKD stage was classified according to eGFR, with patients receiving maintenance hemodialysis categorized as G5. Left atrial enlargement was graded echocardiographically as absent, mild, moderate, or severe. Preserved LVEF was defined as ≥50%. Patients with atrial fibrillation were excluded from the left atrial analysis to minimize rhythm-related confounding. Patients with preserved LVEF were stratified into three groups: CKD G2–G3, advanced CKD G4-G5 not receiving hemodialysis, and maintenance hemodialysis. Preserved LVEF was present in 74 of 100 patients. Among patients with preserved LVEF and without atrial fibrillation (n=49), left atrial enlargement showed a marked increase across clinical groups: 3 of 18 patients with CKD G2–G3 (16.7%), 5 of 15 patients with advanced non-dialysis CKD (33.3%), and 14 of 16 patients receiving maintenance hemodialysis (87.5%; overall $p<0.001$). Among patients with advanced CKD, left atrial enlargement was significantly more frequent in those receiving hemodialysis than in those not receiving dialysis (87.5% vs 33.3%; $p=0.003$). In contrast, the difference between G2–G3 and advanced non-dialysis CKD did not reach statistical significance. Left atrial enlargement was common in CKD despite preserved LVEF and was particularly frequent among patients receiving maintenance hemodialysis. The substantially higher prevalence in hemodialysis patients suggests that cardiac structural remodeling in advanced CKD may be associated with factors beyond loss of kidney function alone, including dialysis status. Assessment of left atrial remodeling may provide additional

cardiovascular information beyond conventional systolic function in patients with CKD.

OC-09

Renal Biomarkers Identify Patients at High Risk of Death and Renal Replacement Therapy in Cardiorenal Syndrome Type 2

Minela Becirovic, Emir Becirovic, Amir Becirovic

Abstract: Cardiorenal syndrome type 2 is characterized by chronic kidney dysfunction developing in the setting of chronic heart failure and is associated with substantial morbidity and mortality. Early identification of patients at increased risk of renal deterioration and death remains challenging. This study aimed to evaluate the prognostic value of routinely available renal biomarkers for early adverse outcomes in patients with cardiorenal syndrome type 2 hospitalized for decompensated heart failure. This prospective observational cohort study included 200 consecutive adult patients hospitalized for decompensated chronic heart failure between April and October 2025. Cardiorenal syndrome type 2 was identified in 130 patients based on documented chronic heart failure preceding chronic kidney disease. Renal function and injury were assessed at admission using serum urea, creatinine, cystatin C, estimated glomerular filtration rate, uric acid, serum albumin, and urinary albumin-to-creatinine ratio. Patients were followed for 90 days. The primary composite outcome was all-cause mortality or initiation of renal replacement therapy. Receiver operating characteristic analysis, Kaplan-Meier analysis, and Cox proportional hazards regression were used to assess prognostic performance. Cardiorenal syndrome type 2 was present in 65.0% of the study population. Compared with patients without cardiorenal syndrome, affected patients had markedly higher rates of renal replacement therapy (22.3% vs. 2.9%, p<0.001), in-hospital mortality (32.3% vs. 11.4%, p=0.002), and 90-day mortality (44.6% vs. 21.4%, p=0.002). Among patients with cardiorenal syndrome type 2, those reaching the primary outcome had higher cystatin C [2.85 (2.12-3.55) vs. 1.69 (1.31-2.38) mg/L, p<0.001] and urinary albumin-to-creatinine ratio [28.34 (12.79-101.25) vs. 7.99 (2.92-20.37) mg/mmol, p<0.001], and lower estimated glomerular filtration rate [30.10 (19.38-36.30) vs. 46.10 (38.40-54.98) mL/min/1.73 m², p<0.001]. Urea demonstrated the highest discrimination for the primary outcome (AUC 0.806), followed by estimated glomerular filtration rate (AUC 0.788), cystatin C (AUC 0.739), and urinary albumin-to-creatinine ratio (AUC 0.733). Cystatin C was strongly associated with adverse outcomes in Cox analysis (HR 1.534, 95% CI 1.263-1.863; p<0.001). Renal dysfunction is strongly associated with early adverse outcomes in patients with decompensated heart failure and cardiorenal syndrome type 2. Admission cystatin C, albuminuria, estimated glomerular filtration rate, and urea provide clinically relevant short-term risk stratification and may help identify patients requiring intensified renal monitoring during the vulnerable early period after hospitalization.

OC-10

Historical Spectrum and Outcome of Biopsy-Proven Glomerular Diseases in Adults: A Single-Center Experience between 2002 and 2010

Leyla Koc, Kubra Kaynar, Sevdegul Mungan, Şukru Ulusoy, Gulsum Ozkan, Muammer Cansiz, Nuray Misir

Abstract: Prior to the 2009 establishment of kidney biopsy registries in Turkiye, the histopathological spec–trum of biopsy-proven kidney diseases in Northeastern Turkiye was not well defined. This study aimed to describe the demographic characteristics, biopsy indi–cations, histopathological findings, and clinical outcomes of adult patients undergoing native kidney biopsy during the pre-registry era. We conducted a retrospective, single-center study of 113 adult patients who underwent percutaneous native kidney biopsy from January 2002 to December 2010. Clinical, laboratory, and histopatho–logical data were extracted from hospital and pathology records. The study protocol was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of Helsinki. Patients (67.2% men) had a mean age of 43.9±15.4 years, with nephrotic syndrome acting as the leading biopsy indication. Primary glomerulonephritis was the predomi–nant histopathological category (n=73). Focal segmental glomerulosclerosis and membranous nephropathy were the most frequent primary glomerular diseases, while amyloidosis was the most common secondary cause. Hypertension was the most frequent comorbidity. Outcome data were missing for 37.1% of patients. Of the evaluated cohort, 28(24.8%) achieved complete remission, and 21(18.6%) progressed to ESKD. Primary glomerulonephritis was the primary histopathological finding in Northeastern Türkiye during the pre-registry era, with focal segmental glomerulosclerosis and membranous nephropathy being the leading causes at that time. Notably, IgA nephropathy was less frequent compared to later national registry reports. This cohort provides an important historical baseline for future regional and national comparison.

OC-11

Chronic pain and its association with depression in patients on maintenance hemodialysis

Trbojevic-Stankovic J, Damnjanovic N, Hadzibulic S, Hadzibulic E

Abstract: Chronic pain is a common symptom among patients with end-stage renal disease. Its multifaceted origin may be related to underlying renal disease, comorbidities, or treatment itself. The discomfort may strongly affect everyday functioning and even predispose patients to consider withdrawal from dialysis. This investigation aimed to examine the incidence of chronic

pain among patients on chronic hemodialysis and explore its association with depression. This cross-sectional study included 120 maintenance hemodialysis patients. General demographic, clinical and laboratory data were collected from the patients' medical records. Pain was assessed using the Brief Pain Inventory (BPI), yielding data on the prevalence of chronic pain, pain severity and pain interference with daily activities. Presence of depressive symptoms was evaluated with the Beck Depression Inventory (BDI-II) and the Cognitive Depression Index (CDI). BDI scores of 14 and above were considered the threshold for clinically significant symptoms. The study population included 71 (59%) males. Mean age was 62.9±11.01 years, dialysis vintage 4-283 months (Med 54), body mass index 24.6±4.5. Diabetes, secondary hyperparathyroidism and hypertension were present in 37%, 12% and 87.5% of patients, respectively. Two-thirds of patients (80; 66.7%) reported chronic pain. Pain severity was reported as mild, moderate or severe by 57.5%, 27.5% and 15.0% of subjects, respectively. Accordingly, the majority of patients (65.5%) consumed pain medications occasionally, while 16.4% took them daily. Further–more, 74.4% practised alternative methods for alleviating pain. Patients rated pain interference with daily activity as none, mild, moderate and strong in 17.5%, 15.0%, 36.3% and 31.3% of cases, respectively. The majority reported one (40.0%) or two (25.0%) areas affected with pain. Mean BDI was 9.75±8.82 (range 0-40), and mean CDI was 5.33±5.9 (range 0-27). Depressive symptoms were present in 32 (26.7%) patients. Patients with chronic pain had significantly higher BDI (6.35±5.41 vs 11.45±9.70; $p<0.01$) and CDI (3.50±3.78 vs 6.25±6.55; $p=0.004$), with similar Charson Comorbidity Index (6.03±2.34 vs 6.18±2.19; $p=0.743$). Depressed patients reported significantly more painful spots (3.78±3.1 vs 2.17±2.09; $p=0.02$). Depression was not significantly associated with pain severity (4.50±2.27 vs 3.72±2.02; $p=0.138$), but depressive patients reported significantly higher pain interference with everyday activities (5.26±2.15 vs 3.43±2.8; $p=0.002$). Chronic pain and depression are important, concomitant issues among maintenance HD patients. Preventive and coping strategies should be consistently explored among affected patients.

OC-12

Calcineurin Inhibitor-Induced Pain Syndrome in a Kidney Transplant Recipient With Ellis-van Creveld Syndrome

Mirha Pjanic, Alma Klapic, Maida Taletovic-Dugonjic, Eldina Pjanic, Nadina Kurtanovic, Mirna Aleckovic-Halilovic

Abstract: A 28-year-old male, 1 month after receiving a kidney transplant (KT) from his sister, presented with sudden-onset, bilateral, symmetrical leg pain, primarily involving the heels and knees. The pain was so severe that he soon required a wheelchair. The patient was diagnosed with Ellis-van Creveld (EVC) syndrome in childhood and had bilateral kidney cysts, as well as a 3-year history of hemodialysis before KT. The post-KT course was complicated by high trough tacrolimus levels, requiring multiple dose reductions, with a tacrolimus concentration to dose ratio of 5.01. These findings raised clinical suspicion of slow tacrolimus metabolism; however, genetic testing was not available. X-rays of the painful areas were unre–markable. A review of the literature revealed case reports of KT recipients (KTRs) with calcineurin inhibitor-induced pain syndrome (CIPS), a condition characterized by sudden-onset, bilateral, symmetrical pain in the lower extremities. A dihydropyridine calcium channel blocker was initiated to counteract vasoconstriction associated with calcineurin inhibitors, which facilitated further tacrolimus dose reduction and achieved a trough level of 6.1 ng/ml. Dexamethasone was introduced as antiedematous therapy, alongside vitamin D supple–mentation and physical therapy. Magnetic resonance imaging revealed bone marrow edema of the knees, a radiologic hallmark of CIPS. At follow-up 15 days after discharge, bone pain had significantly decreased. In the meantime, densitometry was performed, showing severe osteoporosis. At the recent follow-up, symptoms had nearly resolved, and the patient was able to walk without assistance. However, given the bone density scores and high fracture risk, we decided to proceed with our plan to supplement therapy with bisphosphonates.

OC-13

Can complete blood count-derived inflammatory indices predict diabetic microvascular complications? Insights into nephropathy and retinopathy in type 2 Diabetes Mellitus

Mutevelic-Turkovic A, Kujundzic-Begovic E, Pleh H, Mahmuljin A, Coric A, Ajanovic S, Grosa E

Abstract: Diabetes mellitus (DM) is a common metabolic disorder associated with significant morbidity and mortality. Hyperglycemia affects complete blood count (CBC) parameters and CBC-derived inflammatory indices, which may reflect the development of diabetic microvascular complications. This study aimed to evaluate the association between CBC-derived inflammatory indices and the severity of diabetic nephropathy and retinopathy in patients with type 2 diabetes mellitus (T2DM). This cross-sectional study included 100 outpatients with T2DM followed at the Ophthalmology Clinic between September 2025 and February 2026. Renal function was assessed using estimated glomerular filtration rate (eGFR) calculated by the CKD-EPI equation, and patients were categorized into two groups with eGFR ≥60 and <60 mL/min/1.73 m². Based on fundus examination, patients were classified as having non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR). CBC-derived

inflammatory indices were calculated, including neut–rophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic inflammation response index (SIRI), systemic immune-inflammation index (SII), aggregate index of systemic inflammation (AISI), and derived NLR (dNLR). Associations were evaluated using logistic regression and ROC curve analyses. The study population comprised 58% men with a mean age of 65.0±10.9 years. Reduced renal function (eGFR <60 mL/min/1.73 m²) was present in 24% of patients, while 50% had PDR. No significant association was observed between eGFR and retinopathy severity. Among patients with diabetic nephropathy, PLR was the only inflammatory index significantly associated with renal impairment. Patients with eGFR <60 mL/min/ 1.73 m² had higher PLR values compared with those with preserved renal function (139.20 vs. 110.71, p=0.013). Logistic regression identified PLR as an independent predictor of reduced renal function (OR=0.989, 95% CI 0.981-0.998, p=0.020). ROC analysis showed a modest discriminatory ability of PLR for eGFR <60 mL/min/1.73 m² (AUC=0.643, p=0.035). Patients with PDR demonstrated higher NLR (2.10 vs. 1.88, p=0.035) and SIRI (1.29 vs. 0.91, p=0.035), and lower LMR values (3.86 vs. 4.78, p=0.011) compared with NPDR patients. In logistic regression analysis, only LMR was independently associated with a lower likelihood of PDR (OR=0.78, 95% CI 0.623-0.977, p=0.031). ROC analysis confirmed the discriminatory ability of LMR for PDR (AUC= 0.648, p=0.011). CBC-derived inflammatory indices are associated with the severity of diabetic microvascular complications. LMR emerged as a potential marker of proliferative diabetic retinopathy, whereas PLR was associated with reduced renal function. These inexpensive and widely available biomarkers may assist in identifying patients at increased risk of advanced diabetic nephropathy and retinopathy.

OC-14

Divergent one-year cognitive trajectories in chronic kidney disease and kidney transplant recipients

Cadri V, Pasko N, Cenaj S, Rista E, Pilika A, Strakosha A

Abstract: Cognitive impairment is increasingly recognized as an important complication of chronic kidney disease. However, cross-sectional cognitive assessment may fail to capture clinically relevant changes occurring over time. We aimed to compare one-year cognitive trajectories in patients with non-dialysis chronic kidney disease and kidney transplant recipients and to determine whether these trajectories differed between the two renal populations. This prospective longitudinal cohort study included 200 adults: 100 patients with non-dialysis chronic kidney disease and 100 kidney transplant recipients. Cognitive performance was assessed using the Montreal Cognitive Assessment in the same individuals at baseline and after one year. Individual change in Montreal Cognitive Assessment score was calculated, and participants were categorized as improved, stable, or deteriorated. Within-group changes and between-group differences in cognitive trajectories were evaluated. Multivariable analysis assessed the association between transplant status and follow-up cognitive performance after adjustment for baseline Montreal Cognitive Assessment score, age, and education. The two groups demonstrated markedly divergent one-year cognitive trajectories. In patients with chronic kidney disease, mean Montreal Cognitive Assessment score decreased from 25.73 at baseline to 24.77 at follow-up (mean change -0.96 points), whereas kidney transplant recipients improved from 23.69 to 24.88 (mean change +1.19 points). The between-group difference in one-year cognitive change was 2.15 points (p<0.001). Cognitive deterioration occurred in 66% of patients with chronic kidney disease compared with 13% of kidney transplant recipients, whereas improvement occurred in 6% and 58%, respectively. After adjustment for baseline cognitive performance, age, and education, transplant status remained independently associated with a more favorable follow-up cognitive score (adjusted difference +1.96 points; 95% confidence interval 1.52-2.40; p<0.001). Patients with non-dialysis chronic kidney disease and kidney transplant recipients demonstrated divergent cognitive trajectories over one year. Cognitive decline predominated in chronic kidney disease, whereas improvement was substantially more frequent among kidney transplant recipients. These findings highlight the added value of longitudinal cognitive assessment over single-time-point screening and suggest that transplant status is independently associated with more favorable follow-up cognitive performance after accounting for baseline cognition, age, and education. Serial cognitive assessment may identify clinically relevant changes in the kidney–brain axis that remain undetected by cross-sectional evaluation.

OC-15

Use of Sildenafil in Renal Transplant Patients with Pulmonary Hypertension: A Case Report

Alan Horvat, Nikolina Basic-Jukic

Abstract: Pulmonary hypertension (PH) is associated with increased morbidity and mortality in chronic kidney disease and renal transplant recipients. Although sildenafil is established in pulmonary arterial hypertension, evidence in renal transplant patients remains limited. We report two female renal transplant recipients with heart failure and severe PH treated with sildenafil. A 55-year-old woman with previous myocardial infarctions and reduced left ventricular ejection fraction (40%) developed severe PH and worsening heart failure despite conventional therapy and ultrafiltration. Sil–

denafil 20 mg twice daily was initiated but subsequently reduced to 20 mg once daily due to renal and hepatic dysfunction, followed by clinical and laboratory improvement. A 41-year-old woman developed right-sided heart failure and PH following sepsis. PH was confirmed by echocardiography and right heart catheterization. Sildenafil 10 mg three times daily resulted in rapid clinical improvement. Sildenafil may be beneficial in selected renal transplant patients with PH, but careful monitoring and individualized dosing are essential.

Poster Sessions (PS)

P-01

Dynamic Prediction of Acute Kidney Injury 24–72 Hours Before Onset Using Routine Intensive Care Unit Measurements

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Abstract:

Introduction and Aims. Acute kidney injury (AKI) frequently complicates critical illness; however, admission-based prediction models may not capture evolving haemodynamic and metabolic changes preceding renal dysfunction. We evaluated whether routine intensive care unit (ICU) measurements could predict first AKI within 24-72 hours.

Methods. This prospective cohort included 342 adults admitted to three ICUs at two hospitals in Tirana, Albania, from May 2024 to March 2026. Participants were ≥18 years old with eGFR>90 mL/min/1.73 m². Those with pre-existing renal disease or early serum creatinine decline > 0.3 mg/dL were excluded. AKI was defined by KDIGO creatinine criteria. First, we compared first-24-hour mean arterial pressure (MAP), lactate, bicarbonate, and day-1 non-renal Sequential Organ Failure Assessment (SOFA) among no AKI, early AKI (days 1-4), and late AKI (day ≥5). For dynamic prediction, each AKI-free ICU days served as a rolling landmark, with same-day measurements predicting first AKI 24-72 hours later. Pooled logistic regression included age, diabetes, lactate, bicarbonate, MAP, and $\log_2$-transformed creatine kinase (CK), accounting for within-patient clustering. Internal validation used 2,000 patient-level bootstrap resamples.

Results. Within the first 14 ICU days, 168/342 patients (49.1%) developed AKI. Compared with no AKI (n=174), those with early AKI (n=113) had lower MAP (72 [60-90] vs 89 [80-100] mmHg), higher lactate (3.9 [3.0-5.3] vs 2.4 [1.9-3.1] mmol/L), lower bicarbonate (20 [18-23] vs 22 [20-25] mmol/L; all p<0.001), and higher non-renal SOFA scores (5 [3-6] vs 4 [3-6]; p=0.020). In contrast, late AKI (n=55) had similar MAP, lactate and bicarbonate to no AKI (all p≥0.518), but higher non-renal SOFA scores (6 [4.5–7]; p<0.001), support a dynamic prediction approach. The dynamic analysis included 516 AKI-free measurements from 340 patients, with 130 (25.2%) followed by AKI within 24-72 h. Older age, diabetes, higher lactate, lower bicarbonate, lower MAP, and higher CK were independently associated with subsequent AKI. Adjusted odds ratios were 1.34 per 10-year age increase, 2.06 for diabetes, 1.30 per 1 mmol/L lactate increase, 1.50 per 5 mmol/L bicarbonate decrease, 1.20 per 10 mmHg MAP decrease, and 1.22 per CK doubling. Apparent and optimism-corrected AUCs were 0.814 and 0.802.

Conclusion. Routine clinical and biochemical measurements can support dynamic, repeatedly updated prediction of AKI 24–72 hours before onset. A dynamic prediction model combining age and diabetes with contemporaneous lactate, bicarbonate, MAP, and CK showed good internally validated discrimination and may enable earlier identification of ICU patients at risk of AKI. External validation is required before clinical implementation.

P-02

A comparative analysis of clinical characteristics, laboratory findings, and radiological manifestations of hospitalized COVID-19 patients with and without atopy: a single-center cross-sectional study with matched controls

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Abstract:

Introduction and Aims. Patients with chronic kidney disease on hemodialysis face disproportionately high morbidity and mortality from SARS-CoV-2 infection. Atopy-encompassing asthma, allergic rhinitis, and atopic dermatitis-is characterized by Th2-skewed immunity and elevated immunoglobulin E responses. Emerging evidence suggests that Th2 polarization may attenuate the cytokine-mediated inflammatory cascade of severe COVID-19, yet its clinical impact in hemodialysis patients remains poorly characterized. This study aimed to investigate clinical characteristics, laboratory findings, and radiological manifestations of COVID-19 in hemodialysis patients, comparing those with and without atopic comorbidity to identify patterns of disease severity, progression, and outcomes.

Methods. A single-center cross-sectional study with matched controls was conducted at the Department of Nephrology, General Hospital Struga, North Macedonia. Consecutive patients with confirmed COVID-19 (rapid antigen or PCR) were enrolled during 2022. A total of 84 patients were included: 48 male (57.1%) and 35

female (41.7%), mean age approximately 63 years; 53 (63.1%) were on chronic hemodialysis. Patients were classified as atopic or non-atopic based on documented medical history and matched for age, sex, and primary diagnosis. Comorbidities recorded included arterial hypertension (n=49, 58.3%), diabetes mellitus type II (n=24, 28.6%), and chronic pulmonary disease (n=12, 14.3%). Laboratory parameters-eukocyte count, C-reac–tive protein (CRP), lactate dehydrogenase (LDH), and D-dimer-were assessed serially. All patients un–derwent serial chest radiography. Treatment modalities (oxygen therapy, corticosteroids, antibiotics, antico–agulants) and outcomes were systematically docu–mented. Statistical analysis employed chi-square and Mann-Whitney U tests; $p<0.05$ was considered signi–ficant.

Results. Arterial hypertension (58.3%), diabetes mellitus type II (28.6%), and chronic pulmonary disease (14.3%) were the most prevalent comorbidities. Approxima–tely 59.5% of patients had received prior COVID-19 vaccination (Sinopharm, Pfizer/BNT162b2, AstraZeneca, or Sinovac). Oxygen supplementation was required in 21 patients (25.0%), corticosteroids in 36(42.9%), anti–biotics in >85%, and anticoagulation in 55(65.5%). Inflammatory markers showed marked elevation during the acute phase: CRP 1.6->175 mg/L, LDH 63-3508 U/L, D-dimer 272->10,000 ng/mL, and leukocyte count 1.8-50.8×10⁹/L. Serial laboratory values demonstrated progressive normalization in recovering patients. Chest radiographs universally revealed bilateral bronchovascular and bronchitic changes with perihilar predominance; fibrostripe shadows and focal zones of reduced pulmonary transparency were common, with sequential imaging showing gradual improvement in most cases. Sixteen patients (19.0%) died; 65(77.4%) achieved recovery. Patients with atopy showed distinct inflammatory and radiological profiles compared to non-atopic controls, with differences in CRP and D-dimer levels, oxygen therapy requirement, and radiological severity, while mortality did not significantly differ between groups ($p >0.05$). Vaccinated patients demonstrated a more favorable clinical course.

Conclusion. This study provides clinically relevant insights into COVID-19 in a predominantly hemodialysis nephrology cohort. Despite representing a high-risk population, systematic management-including serial laboratory monitoring, chest radiological assessment, anticoagulation, and targeted anti-inflammatory therapy-was associated with favorable outcomes in the majority. Atopy appears to modulate the inflammatory and ra-diological manifestations of COVID-19, consistent with an immunomodulatory role of Th2 immunity, without significantly altering in-hospital survival. Vaccination was associated with a positive impact on disease severity. These findings support the importance of individualized monitoring protocols for nephrology patients with COVID-19 and contribute to the growing evidence base regarding outcomes in immunocompro–mised, specialized populations.

P-03

Discordance Between Negative Urine Sediment and Elevated Urinary Albumin-to-Creatinine Ratio: Clinical Implications for Kidney Disease Screening

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Abstract:

Introduction and Aims. Proteinuria assessment through urine sediment analysis is a widely used screening tool in clinical practice for detecting kidney damage. However, the sensitivity of this method compared to quantitative measurements like urinary albumin-to-creatinine ratio (UACR) remains debatable. This study aimed to investigate the prevalence and characteristics of patients presenting with negative urine sediment despite having elevated UACR (>30 mg/g), focusing on the potential limitations of relying solely on qualitative urine sediment analysis for kidney disease screening.

Methods. A cross-sectional analysis was conducted on patients who underwent both urine sediment analysis and UACR measurement. Elevated albuminuria was defined as UACR>30 mg/g. The study population was stratified based on urine sediment results, and those with negative sediment were further analyzed. UACR values were categorized into three groups: moderately increased (30-300 mg/g), severely increased (300-1000 mg/g), and nephrotic range (>1000 mg/g). Statistical analysis included descriptive statistics and correlation analysis between UACR and HbA1c levels in patients with negative sediment and elevated UACR.

Results. Descriptive Statistics for UACR in Patients with Negative Urine Sediment and UACR>30: The study identified 36 patients with negative urine sediment despite having elevated UACR (>30 mg/g). In this discordant group, the mean UACR was 222.6±288.7 mg/g, with values ranging from 31.0 to 1417.0 mg/g. The median UACR was 118.0 mg/g, indicating sig–nificant albuminuria despite negative sediment fin–dings. Correlation coefficient (UACR vs HbA1c): -0.207 P-value: 0.2254. The severity distribution analysis re–vealed: 1. Moderatly increased (30-300): 30, 2. Severely increased (300-1000): 5, and 3. Nephritic range (>1000): 1. This distribution shows that among patients with negative sediment, 30(83.3%) had moderately increased albuminuria, 5(13.9%) had severely increased albumi–nuria, and 1(2.8%) presented with nephrotic-range proteinuria, all despite showing negative results on urine sediment analysis.

Conclusion. This study demonstrates a significant clinical discordance between urine sediment analysis and UACR measurements, with 36 patients showing elevated UACR despite negative sediment findings.

The majority of these cases (83.3%) presented with moderate albuminuria, but notably, 16.7% had severe or nephrotic-range proteinuria that would have been missed by sediment analysis alone. The weak correlation between UACR and HbA1c in this group suggests that the discordance is not significantly influenced by glycemic control. These findings highlight the potential limitations of using urine sediment analysis as the sole screening method for kidney disease and emphasize the importance of incorporating quantitative UACR measurements into routine clinical practice. The results suggest that reliance on urine sediment alone might lead to missed diagnoses of significant kidney damage, particularly in cases of moderate albuminuria. Implementation of regular UACR screening, even in patients with negative urine sediment, may be crucial for early detection and management of kidney disease.

P-04

From Anuria to Dialysis Independence: Late Kidney Recovery after Twelve Months of Haemodialysis in Hepatorenal Syndrome Associated with Alcohol-Related Cirrhosis

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Abstract:

Introduction and Aims. Hepatorenal syndrome (HRS) is potentially reversible in advanced cirrhosis, but prolonged dialysis dependence carries poor renal prognosis. We report late partial kidney recovery with sustained dialysis independence after twelve months of haemodialysis in alcohol-related cirrhosis initially presenting as HRS-acute kidney injury (HRS-AKI).

Methods. We retrospectively reviewed the clinical course, serial biochemical parameters, urine output, dialysis requirement, paracenteses and liver-related management of a 39-year-old man from April 2025 to August 2026. Presentation supported HRS-AKI with cirrhosis, ascites, acute kidney injury and anuria, previously normal renal function, normal ultrasonography, and no proteinuria, shock or nephrotoxic exposure. Persistent kidney dysfunction beyond 90 days was classified as HRS-chronic kidney disease (HRS-CKD).

Results. The patient, whose alcohol-related cirrhosis had been diagnosed three months earlier, presented in April 2025 with oedema, fatigue, dyspnoea, anuria, hyperkalaemia (6.9 mmol/L), creatinine 622 µmol/L, metabolic acidosis (pH 7.19), portal hypertension and tense, refractory ascites. As terlipressin was unavailable, haemodialysis was initiated on 24 April 2025 three times weekly. MELD score was 22; transjugular intrahepatic portosystemic shunt (TIPS) was considered high-risk, and liver transplantation was not performed because no suitable donor was available. Between May and August 2025, nine large-volume paracenteses removed approximately 79 L with volume substitution, and dry weight fell from 82 to 67 kg. He remained abstinent from alcohol. Urine output increased from anuria to 100-800 mL/day by October 2025, 1400 mL/day in November and 2600 mL/day by April 2026. Haemodialysis was reduced to twice weekly in December 2025 and once weekly in February 2026. The final session was on 23 April 2026. Dialysis independence remained sustained: creatinine was 287 µmol/L in May, 258 µmol/L in June and 244 µmol/L in August 2026. At latest assessment, eGFR was 29 mL/min/1.73 m², urine output >2 L/day, potassium 4.4 mmol/L, albumin 48 g/L, total bilirubin 11.6 µmol/L and INR 1.14. He was normotensive, euvolaemic and asymptomatic.

Conclusion. Late partial kidney recovery sufficient for sustained dialysis independence may occur despite prolonged dialysis dependence in selected patients with HRS. This course illustrates progression from HRS-AKI to HRS-CKD followed by recovery to CKD G4 without TIPS or transplantation. Alcohol abstinence, hepatic stabilisation, careful volume management and serial reassessment of residual kidney function accompanied recovery. Prolonged dialysis dependence in HRS should not automatically be considered irreversible.

P-05

Post-Transplant Infectious Complications Within a Five-Year Period: A Single-Center Experience

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Abstract:

Introduction. The kidney transplant recipient population is particularly vulnerable to post-transplant infectious complications. Immunosuppressive therapy, while suppressing the host immune response to prevent rejection of the renal allograft, simultaneously increases susceptibility to a wide range of infections. Although the incidence of infections has decreased over the past several decades, infections remain the second leading cause of mortality in this population, after cardiovascular diseases. Previous infectious episodes may affect renal allograft function and contribute to the development of chronic allograft nephropathy, ultimately resulting in graft failure and the need for renal

replacement therapy. Aim of this study was to observe infections in transplant patients at our Center. **Methods.** A retrospective observational study was conducted at the Clinical Center of the University of Sarajevo, Department of Nephrology and Renal Replacement Therapy, over a five-year period from 2020 to 2025. Data were obtained from the electronic medical records of 100 kidney transplant recipients who regularly attended follow-up visits. All patients received induction therapy (Anti-thymocyte globulin or Basiliximab) followed by triple immunosuppressive therapy, steroids, mycophenolic acid and calcineurin inhibitors (tacrolimus or cyclosporin A).
Results. Mean age of patients was 47.42+12.56 years, 73% were male and 27% female. In 61.8% of patiens post-transplant complications were detected, in which 85% of them were infectious. In 31% of patients urinary tract infection was described with Escherichia coli as leading cause with 11%. No statistically significant association was found between the assessed risk factors-hypertension, diabetes mellitus and anaemia-and the occurrence of post-transplant infectious complications. There were no association within living donor and cadaveric transplantation according the occurence of infectious complications. Patients receiving tacrolimus had a 14.3-fold higher risk of developing infectious complications compared with patients receiving cyclo–sporine (RR 14.286, 95% CL:1.41-178.8, p=0.01). Patients with delayed graft function had more complications (p=0.26), this association was not observed when in–fections were analyzed separately. There was a sta–tistical significant association between length of renal replacement therapy and onset of complications (p=0.005); lower eGFR and onset of complications (p= 0.018), yet this association was not described at infectious complications separately. In five patients, who died during the following period, were infectious complications described.
Conclusion. Our study concluded that infectius com–plications are the most often complications in renal transplant recipients with high prevalence of urinary tract infections. Individualized adjustment of immune–suppressive therapy and regular monitoring are crucial for early detection and treatment, aiming to improve renal alograft and patient survival.

P-06

Preserve more, dialyze less: clinical outcomes of incremental hemodialysis

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Abstract:
Introduction and Aim. Incremental hemodialysis (iHD) is an individualized approach that reduces dialysis frequency in patients with preserved residual kidney function (RKF), potentially minimizing dialysis-related burden while maintaining adequate metabolic control. We compared clinical characteristics and long-term survival between patients receiving iHD and conventional thrice-weekly hemodialysis (cHD).
Methods. This retrospective observational study in–cluded 32 maintenance hemodialysis patients: 16 treated with iHD (≤2 sessions/week) and 16 with cHD (3 sessions/week). All patients in the iHD group had preserved urine output at dialysis initiation and were followed for a mean of 2.7 years. Nutritional, infla–mmatory, hematological and biochemical parameters, erythropoiesis-stimulating agent (ESA) requirements, and 5-year survival were evaluated. Results: Patients receiving iHD had significantly higher serum albumin compared with cHD patients (4.1±0.3 vs. 3.7±0.4 g/dL, $p<0.05$). Hemoglobin levels were comparable, whereas ESA requirements were lower in the iHD group. CRP levels were significantly lower with iHD (4.2 vs. 8.9 mg/L, $p<0.01$). Serum phosphate and potassium remained within acceptable ranges in both groups, with no apparent increase in hyperphosphatemia or hyperkalemia among iHD patients. Five-year survival was higher in the iHD group (81% vs. 62%). Conclusion: In carefully selected patients with preserved RKF, iHD was asso–ciated with better nutritional status, lower inflamma–tory burden, reduced ESA requirements, and favorable long-term survival without compromising biochemical control. These findings support incremental hemo–dialysis as a patient-centered strategy that may reduce dialysis burden while preserving the benefits of residual kidney function.

P-07

Severe Reversible Acute Kidney Injury in a 93-Year-Old Man With Advanced Ulcerated Tophaceous Gout

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Abstract:
Introduction and Aims. Advanced tophaceous gout may be complicated by ulceration, intense tissue inflammation, infection, and renal dysfunction. We report a 93-year-old man with extensive tophaceous gout, marked systemic inflammation, severe metabolic

derangement, and acute kidney injury (AKI) followed by complete return to baseline renal function.
Methods. Clinical, laboratory, microbiological, and imaging data were reviewed throughout hospitalization. Serial renal function, acid-base status, inflammatory markers, serum uric acid, plain radiographs, and computed tomography (CT) findings were assessed.
Results. The patient presented with extensive chronic tophi involving the hands, elbows, and feet, including inflamed foot lesions with chalky-white material and surrounding erythema. Plain radiographs showed advanced erosive and deforming arthropathy with periarticular soft-tissue deposits, compatible with chronic tophaceous gout. Initial laboratory evaluation showed leukocytosis 27.7×10^9/L, C-reactive protein 11.9 mg/dL, urea 255 mg/dL, serum creatinine 3.7 mg/dL, and uric acid 10.7 mg/dL. Severe metabolic acidosis was present (pH 7.19, bicarbonate 10.5 mmol/L; calculated anion gap approximately 23.5 mmol/L), together with hypokalemia (3.0 mmol/L). Urine culture yielded Pseudomonas aeruginosa at 100,000 CFU/mL. CT demonstrated bilateral age-related renal parenchymal reduction without calculi or hydronephrosis, excluding postrenal obstruction. Following correction of volume, electrolyte, and acid-base disturbances, antimicrobial therapy, and local wound care, renal function improved progressively. At discharge, urea decreased to 40 mg/dL and serum creatinine to 1.0 mg/dL, returning to the patient's previously documented normal baseline.
Conclusion. Severe AKI in advanced tophaceous gout may be multifactorial and fully reversible despite profound metabolic abnormalities and very advanced age. Intense gout-associated local inflammation may coexist with documented infection and complicate interpretation of systemic inflammatory markers. Careful identification and correction of reversible precipitating factors are essential, while acute urate nephropathy should not be assumed solely from marked tophaceous burden and hyperuricemia.

P-08

Two decades of peritoneal dialysis: patient and technique survival in a single-center cohort from Bosnia and Herzegovina

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Abstract:
Introduction and aims. Peritoneal dialysis (PD) remains underutilized in Bosnia and Herzegovina (B&H), and long-term outcome data are lacking. We report survival analysis of a 23-year PD cohort from our center.
Methods. Retrospective observational analysis of all consecutive adults treated with PD at the Clinic for Nephrology, Clinical Center University of Sarajevo (January 2003-August 2026). Patient and technique survival were estimated by Kaplan-Meier. Multivariable Cox regression was used as independent predictors of mortality. Competing risks calculated by Aalen–Johansen and Fine-Gray models (R 4.3.3).
Results. A total of 198 patients were included. Mean age at PD initiation was 56.6±15.8 years; 52.5% were male; diabetic nephropathy was the leading cause of ESRD (38.4%); prior hemodialysis exposure 8.6%; CAPD 96.8%. During follow-up, 80 patients (40.4%) died, 38 (19.2%) permanently transferred to hemodialysis, and 24 (12.1%) underwent kidney transplantation. Estimated patient survival at 1, 5, and 10 years was 81.6%, 42.8%, and 16.4% (median 4.0 years); technique survival 91.6%, 67.1%, and 39.5% (median 7.0 years). Cumulative incidence of death at 10 years: 55.5%. In multivariable Cox regression, older age (HR 1.04 per year, 95% CI 1.02-1.06; $p<0.001$) and prior HD exposure (HR 5.05, 95% CI 2.49-10.24; $p<0.001$) were the only independent predictors of all-cause mortality. Pooled peritonitis rate was 0.40 episodes per patient-year.
Conclusion. Long-term PD outcomes in Sarajevo are comparable to European and regional cohorts. Older age and prior HD exposure are the dominant independent predictors of mortality. Expansion of PD utilization in B&H remains a priority.

P-09

Effect of Dapagliflozin on the Activity of Sodium-Glucose Cotransporter Type 2

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Abstract:
Introduction and Aims. Type 2 diabetes is a chronic metabolic disease that requires reliable and accessible methods for evaluating the action of therapeutic agents. Dapagliflozin inhibits sodium-glucose cotransporter type 2 (SGLT2) at the renal level, thereby preventing glucose reabsorption. Although the mechanism of action of dapagliflozin is well established, the kinetic parameters of its binding have rarely been determined using simpler, laboratory-accessible biochemical methods such as ELISA, as opposed to more costly functional cell-based transport assays. The aim of this study was

to determine the type of inhibition, IC50, and kinetic binding constants of dapagliflozin for SGLT2 using the ELISA method, and to compare these findings with published values obtained from functional assays.
Methods. The mechanism of action of dapagliflozin on the SGLT2 transporter was monitored using a spectrophotometric ELISA method at 37°C, at a wa–velength of 450 nm. Measurements were performed both without and in the presence of various concen–trations of dapagliflozin (1-20 µg/mL) in phosphate buffer, pH 7.4.
Results. Dapagliflozin binds to the SGLT2 transporter as a competitive inhibitor, preventing glucose reabsorp–tion in the renal proximal tubules. The inhibition constant (Ki) determined by the ELISA method was 0.07 µM (70 nM), confirming the competitive mechanism of inhibition. Compared with published IC50 values for dapagliflozin obtained from functional cell-based transport assays (0.49-1.1 nM), the measured Ki value was approximately 60-140 times higher. This difference is consistent with the expected discrepancy between biochemical binding assays on isolated protein and functional transport assays in living cells, where membrane context and substrate availability can significantly affect binding affinity.
Conclusion. Dapagliflozin acts as a competitive in–hibitor of the SGLT2 transporter, as confirmed by the ELISA method used in this study. The obtained Ki value (70 nM), although higher than values obtained from functional cell-based assays, indicates that the spectrophotometric ELISA method is a reliable and accessible tool for preliminary assessment of SGLT2 inhibitor binding kinetics, particularly in laboratories without access to cell-based transport assays. These findings contribute to the understanding of method–logical differences in determining SGLT2 inhibitor affinity and may serve as a basis for further com–parisons of different analytical approaches.

P-10

Use of sodium-glucose cotransporter 2 inhibitors in patients with hereditary porphyria: two case reports

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Abstract:

Introduction. Hereditary porphyrias are disorders of heme biosynthesis in which acute attacks may be pre–cipitated by medications, infections, dietary changes, and other stressors. Evidence regarding the use of sodium-glucose cotransporter 2 (SGLT2) inhibitors in patients with hereditary porphyria is limited. We describe two patients with hereditary porphyria and chronic kidney disease treated with dapagliflozin.
Case. A 51-year-old woman with hereditary copro–porphyria and chronic kidney disease stage G3aA2 was started on dapagliflozin at the standard dose. Close clinical monitoring was performed after treatment ini–tiation. No acute porphyria attacks occurred. During follow-up, proteinuria decreased and renal function remained stable. She developed one urinary tract in–fection. Ciprofloxacin was discontinued after an erythematous skin reaction, and trimethoprim-sulfa–methoxazole was administered without further reac–tion. Dapagliflozin was subsequently continued. A 60-year-old woman with hereditary porphyria, obesity, type 2 diabetes mellitus, and chronic kidney disease stage G3bA3 was receiving metformin adjusted to renal function. Dapagliflozin was added to therapy. During follow-up, no acute porphyria attacks, urinary tract infections, or other treatment-related complications were observed, while renal function remained stable.
Discussion. In both patients, dapagliflozin use was not temporally associated with an acute porphyria attack. The first patient experienced a urinary tract infection, but dapagliflozin treatment could be continued after infection resolution. These observations suggest that SGLT2 inhibitor therapy may be feasible in selected patients with hereditary porphyria and chronic kidney disease when accompanied by individualized risk assessment and clinical monitoring. However, conclu–sions regarding safety cannot be drawn from two cases.
Conclusion. Dapagliflozin was used without acute porphyria attacks in two patients with hereditary porphyria and chronic kidney disease, with stable renal function during follow-up.

P-11

Growth hormone therapy before kidney transplantation in a child with congenital nephrotic syndrome: a case report

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Abstract:

Introduction. Growth impairment is a common com–plication of chronic kidney disease in children and may persist before and after kidney transplantation. Recombinant human growth hormone can improve linear growth in selected pediatric patients with chronic kidney disease, although concerns regarding its use around transplantation have limited its application. We report the long-term growth and graft outcome of a patient in whom growth hormone therapy was initiated shortly before kidney transplantation.
Case. A 19-year-old male was diagnosed at birth with congenital nephrotic syndrome, Finnish type, described as corticosteroid-sensitive. Progressive chronic kidney disease led to kidney failure, and peritoneal dialysis was initiated at 2 years of age. At 3 years and 9 months, he underwent deceased-donor kidney transplantation. Growth hormone therapy had been introduced three months before transplantation. The early post-trans–

plant course was uncomplicated. Maintenance immu–nosuppression consisted of cyclosporine, mycophe–nolate mofetil, and corticosteroids, with gradual ste–roid dose reduction. During long-term follow-up, the patient achieved a height of 202 cm with appropriate development of secondary sexual characteristics. Graft function remained stable, with no documented episodes of rejection or graft dysfunction. Cyclosporine was later replaced by tacrolimus. Arterial hypertension and hypothyroidism developed during follow-up and were successfully treated. Bone mineral density was within the reference range.

Discussion. In this patient, growth hormone therapy initiated before transplantation was followed by satisfactory long-term linear growth and preserved graft function without documented rejection. Although a causal relationship cannot be established from a single case, this observation supports consideration of growth hormone therapy in carefully selected pediatric patients with chronic kidney disease and significant growth impairment.

Conclusion. Growth hormone therapy initiated before kidney transplantation was associated with favorable long-term growth and stable graft function in this patient, without documented rejection episodes.

P-12

Lung abscess in patient after kidney transplantation

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Abstract:

Introduction and aims. Solid organ transplant re–cipients are at increased risk of opportunistic infec–tions due to long-term immunosuppressive therapy, including invasive fungal infections. Candida species most commonly cause candidemia, while localized pulmonary infections such as lung abscesses are rare and diagnostically challenging. Objective of this case report is to emphasize the importance of early recognition of invasive candidiasis in immunocompromised patients through a rare case of pulmonary abscess following kidney transplantation.

Methods. Clinical data were retrospectively collected from medical records, including clinical presentation, laboratory results, microbiological findings, and radio–logical imaging. Results: We report a 49-year-old male patient, six months after cadaveric kidney transplan–tation, who developed a pulmonary abscess caused by Candida non-albicans (Candida glabrata). Initial treat–ment with voriconazole resulted in a decrease in inflammatory markers and partial clinical improvement. However, follow-up radiological imaging demonstrated progression of the pulmonary abscess. A multidis–ciplinary team consisting of a nephrologist, infectious disease specialist, pulmonologist, anesthesiologist, and thoracic surgeon decided on surgical management. The patient underwent successful surgical resection with continuation of antifungal therapy. Despite initial postoperative stability, the patient developed respi–ratory failure and hemodynamic instability, resulting in a fatal outcome.

Conclusion. This case highlights the diagnostic and therapeutic challenges of invasive candidiasis in trans–plant recipients. Discordance between clinical and radiological response may indicate the need for aggre–ssive and multidisciplinary management, although outcomes may still be unfavorable.

P-13

Bioelectrical Impedance Spectroscopy Identifies Early Alterations Associated with Chronic Kidney Disease

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Abstract:

Introduction and Aims. Hypertension is one of the leading risk factors for chronic kidney disease (CKD), yet conventional laboratory markers often remain within the normal range until substantial renal damage has occurred. Bioelectrical impedance spectroscopy (BIS) enables non-invasive assessment of hydration status and cellular integrity and may detect early phy–siological disturbances preceding overt kidney dys–function. This study evaluated whether BIS-derived pa–rameters identify early CKD vulnerability in treated hypertensive patients without established kidney disease.

Methods. A cross-sectional study included 60 adults (61% female, 60.5±6.1 years old) with controlled pri–mary arterial hypertension, on one or two antihy–pertensive drugs, non-smokers. Patients with diabetes mellitus, chronic kidney disease, heart failure, dysli–pidemia or established cardio-neuro-vascular disease were excluded. BIS (5-1000 kHz), Multiscan 5000 system (BodyStat Ltd.) was performed to assess total body water, intracellular water (ICW), extracellular water (ECW), ECW/ICW ratio, overhydration index, body cell mass (BCM), reactance, and phase angle (PhA). Renal function, blood pressure (normal value < 130/80mmHg in two measurements), anthropometric (body mass index, BMI kg/m2) and laboratory parameters were recorded. Albuminurija measured via a urine Albumin-to-Creatinine Ratio (ACR, A1 is normal <30 mg/g (or <3 mg/mmol)), estimated glomerular filtration rate (normal eGFR>60 mL/min/1.73 m²). Associations between BIS parameters and markers of early renal vulnerability were analysed (Mann-Whitney U test), with a significance level of $p<0.05$.

Results. Despite similar body mass index (median 28.30) and blood pressure values (median 128/78 mmHg), preserved kidney function (eGFR>60 ml/min/ 1.73 m2 and albuminuria A1), hypertensive patients demonstrated variability in hydration status and cellular health. Patients were categorized into two groups: In hypertensive patients with eGFR 71±6 ml/min/1.73 m2 median level of phase angle was 4.84, while in patients with eGFR 85±7 ml/min/1.73 m2 median phase angle level was 5.90 (p<0.001). Lower phase angle and body cell mass were associated with less favorable intracellular hydration, higher ECW/ICW ratio, and increased extracellular fluid expansion. These findings indicate early disturbances in cellular health and fluid distribution that may precede clinically de–tectable kidney dysfunction.

Conclusion. BIS provides clinically relevant information beyond conventional assessment in patients with hypertension. Phase angle and hydration-related parameters may identify individuals at increased risk for future CKD before measurable deterioration of renal function occurs. Lower phase angle indicates impaired cellular membrane integrity. Incorporating BIS into routine hypertension manage–ment may improve early risk stratification and support preventive nephrology strategies.

P-14

Determinants of peripheral neuropathy differ in pre-dialysis and dialysis chronic kidney disease: kidney function versus serum potassium

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Abstract:

Introduction. Peripheral neuropathy becomes more frequent as chronic kidney disease (CKD) advances, but it is not known whether the same factors drive it before and during dialysis. Chronic hyperkalemia depolarises the axonal membrane and may directly injure nerves; unlike declining kidney function, it is modifiable.

Methods. We studied 126 CKD patients across all stages, including 62 on hemodialysis (mean age 62 years, 24% diabetic). We confirmed or excluded neuro–pathy by electroneuromyography (ENMG) and graded it with the Michigan Neuropathy Screening Instrument (MNSI). We recorded eGFR, pre-dialysis serum potassium, biochemistry, dialysis vintage, and dietary compliance. We analysed pre-dialysis and dialysis patients separately.

Results. Neuropathy was confirmed in 86 of 126 patients (68%), rising with disease severity: 0% in stage 3a, 42% in 3b, 81% in stage 4, 100% in stage 5, and 76% on dialysis (79% in end-stage disease com–bined); 80% of advanced versus 29% of early CKD patients were affected (p<0.001). Before dialysis (n=64) eGFR was the dominant determinant (AUC 0.91; odds ratio 0.07 per standard deviation, p<0.001); potassium was associated with neuropathy on its own (AUC 0.77, p<0.001) but showed no association independent of eGFR (adjusted odds ratio 0.98 per standard deviation, 95% CI 0.40-2.43), with no gain in discrimination (AUC 0.913 to 0.916). On dialysis (n=62), where kidney function no longer varies, potassium became the dominant determinant, 5.9 versus 4.5 mmol/L in affected and unaffected patients (p<0.001, AUC 0.90), with a clear dose–response: neuropathy affected 25% of patients below 4.5 mmol/L, 74% between 4.5 and 5.5, and 97% above 5.5 mmol/L (ρ=0.58, p<0.001). This association persisted after adjustment for age, diabetes, Kt/V, and dialysis vintage (adjusted OR 9.1 per standard-deviation increase; p=0.013), while longer dialysis vintage was independently associated with neuropathy (OR 5.0; p=0.026). Higher serum potassium also correlated with greater neuropathy severity on the MNSI (ρ=0.54; p<0.001). In contrast, diabetes was not significantly associated with neuropathy (73% vs 67%; p=0.65). Dietary non-adherence, reported in 57% of patients, was associated with both higher serum potassium (p=0.017) and greater neuropathy prevalence (76% vs 57%; p=0.03).

Conclusions. Neuropathy affects two-thirds of CKD patients and, before dialysis, it tracks the loss of kidney function, and potassium shows no association independent of eGFR. On dialysis, where kidney function is no longer a variable, serum potassium becomes the dominant and dose-dependent determinant, alongside time on dialysis. Potassium is modifiable: these findings support tighter potassium control in dialysis patients and routine neuropathy screening.

P-15

Significance and applicability of some inflammatory markers in patients undergoing hemodialysis

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Abstract:

Introduction. Patients with end-stage renal disease treated with hemodialysis are increasing worldwide and the main reasons for their shortened survival are cardiovascular and infectious events. The aim of our study was to monitor the levels of the most commonly used inflammatory markers in practice and to clarify their applicability in this subgroup of patients.

Methods. We studied the values of C-reactive protein, interleukin-6, procalcitonin, ferritin and uric acid in 69 patients treated with hemodialysis for more than 90

days. Those who had clinical evidence of infection or active neoplasm were excluded from the study. We compared the data with sex, age, main diagnosis and vascular access. By age, patients were divided into those under and over 65 years of age. The data were processed with Statistical Package for Social Sciences (SPSS), version 20.0 (IBM Corp., Armonk, NY). Statgraphics plus, version 2.1 and EXCEL for Windows.

Results. We found that the data for procalcitonin, interleukin-6, ferritin and uric acid were significantly higher than the reference values for healthy individuals. The only indicator that showed comparable values with healthy individuals was CRP. At the same time, the results for CRP and IL-6 were significantly higher in the groups over 65 years of age (0.025 and 0.006, respectively).

Conclusion. According to our results, the only well-correlated and significant indicator in patients on he–modialysis treatment is CRP. Other markers should be used primarily to monitor the effect of the treatment.

P-16

Peripheral neuropathy across CKD stages and hemodialysis vintage: structural and functional assessment by nerve ultrasound and electrophysiology

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Abstract:

Introduction. Peripheral neuropathy (PN) is the commonest and most underdiagnosed complication of chronic kidney disease (CKD). High-resolution ultra–sound (HRUS) enables rapid, non-invasive nerve assessment, but whether structural change tracks func–tional severity across CKD stages and on haemo–dialysis (HD) is unclear.

Methods. We prospectively studied 126 CKD patients (3a n=9, 3b n=19, 4 n=26, 5 n=10, HD n=62; mean age 62±12 years; diabetes 24%) and 28 healthy controls. Tibial, peroneal and sural nerves were examined by HRUS (cross-sectional area [CSA], echogenicity, fas–cicular architecture, intraneural Doppler) and correla–ted with electroneuromyography (ENMG), Michigan Neuropathy Screening Instrument (MNSI), Total Neuro–pathy Score (TNS), biochemistry, dialysis vintage and dietary compliance.

Results. ENMG confirmed PN in 86/126 (68%), rising from 0% in stage 3a to 42% (3b), 81% (4), 100% (5), and 76% on HD. Tibial CSA was larger in patients than controls (13 [12-14] vs 10 [10-11] mm², p<0.001); peroneal CSA was also increased (p<0.001), sural CSA was not (p=0.83). Tibial CSA detected ENMG-confirmed PN with an AUC of 0.86 (95% CI 0.79-0.92); a cut-off of ≥13 mm² gave 85% sensitivity and 75% specificity (diabetic AUC 0.88, non-diabetic 0.86). Fascicular architecture was lost in 73% of patients and 0% of controls (sensitivity 91%, OR 18.1, p<0.001), and intraneural Doppler signal was lost in 41% versus 0% (p<0.001). CSA increased from 10.7 mm² (stage 3a) to 15.7 mm² (stage 5) (ρ=0.60, p<0.001) but was lower on HD (13.1 mm², p=0.011 vs stage 5), where it rose again with vintage (p=0.002), while symptom burden remained higher than in stages 4-5 (p=0.006). CSA correlated with MNSI (ρ=0.60), eGFR (ρ=-0.58), creatinine (ρ=0.51), potassium (ρ=0.40) and PTH (ρ=0.31) (all p<0.001). Severity tracked dialysis vintage, not dialysis itself: beyond 5 years, 97% were ENMG-positive versus 56% below (p<0.001; 100% beyond 7 years), with higher MNSI (9 vs 7.5, p<0.001), TNS (23 vs 14, p=0.023) and CSA (p=0.010). Dietary non-compliance (57%) was asso–ciated with higher potassium, larger CSA, higher MNSI and more ENMG-confirmed PN (all p<0.05).

Conclusions. Tibial HRUS detects CKD-associated PN accurately and non-invasively, and qualitative features, particularly fascicular architecture loss, add sensitivity to CSA. Structural enlargement peaks in advanced pre-dialysis CKD and does not progress on HD, whereas symptomatic and functional burden accumulates with dialysis vintage, reaching universal ENMG positivity beyond 7 years. These findings, and a large untreated symptom burden, support systematic neuropathy screening in CKD.

P-17

Factors Affecting Patient And Graft Survival in Kidney Transplant Recipients: A Single-Center Study Between 2009 and 2015

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Abstract:

Introduction and Aims. Chronic Kidney Disease (CKD) is a prevalent and significant health problem both in our country and worldwide. Patients progre–ssing from CKD to End-Stage Renal Disease (ESRD) can sustain their lives through renal replacement the–rapies (RRT). Kidney transplantation, the most out–standing among RRT options, had been successfully performed at Karadeniz Technical University (KTU) between March 2009 and 2015. This study aims to determine the factors affecting graft and patient sur–vival in patients who underwent kidney transplantation at the KTU Faculty of Medicine.

Methods. The study included 42 patients over the age of 18 who underwent kidney transplantation at the

KTU Faculty of Medicine between March 2009 and November 2015. Recipient and donor demographic findings, post-transplantation follow-ups, and the treat–ment regimens and dosages used were retrospectively analyzed. Statistical analyses of the data were per–formed using the SPSS 13.0 for Windows statistical software package. Retrospective pre- and post-transplant data of the patients were obtained by scanning their medical records.

Results. Of the patients who underwent kidney transplantation, 13(31%) received grafts from living donors, and 29(69%) from deceased (cadaveric) donors. According to the Kaplan-Meier method, excluding death, graft survival for living donor transplantations was 100% at year 1 and 100% at year 5. For deceased donor transplantations, these rates were 90% at year 1 and 78% at year 5. When patient survival was evaluated, the rates for living donor transplantations were 92% at year 1 and 92% at year 5; for deceased donor transplantations, the rates were calculated as 86% at year 1 and 86% at year 5. In our study, post-transplantation blood transfusion and the presence of delayed graft function were found to be statistically significant in patients with graft loss compared to those without graft loss. When evaluating patient survival, advanced recipient and donor age, the pre–sence of coronary artery disease, a history of post-transplantation blood transfusion, and a high Kidney Donor Profile Index (KDPI) were found to be sta–tistically significant when comparing deceased and surviving patients.

Conclusion. In our study, graft and patient survival rates at the KTU Faculty of Medicine were found to be compatible with national and international literature. Minimizing post-transplantation blood transfusions and carefully evaluating high KDPI donors as well as advanced-age recipients are critical to improving long-term survival outcomes.

P-18

Treatment outcomes in primary nephrotic syndrome: a single-centre experience

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Abstract:

Introduction and Aims. Treatment response and long-term outcomes in primary nephrotic syndrome vary according to the underlying glomerular disease and treatment strategy. This study aimed to describe clinical characteristics, treatment response, relapse patterns, and renal outcomes in patients with nephrotic syndrome due to primary membranous nephropathy (MN), focal segmental glomerulosclerosis (FSGS), and minimal change disease (MCD) treated at a single tertiary center.

Methods. We conducted a retrospective, single-center descriptive study including 30 adult patients with primary nephrotic syndrome due to MN, FSGS, or MCD. Patients with secondary causes of nephrotic syndrome and other glomerular diseases were excluded. Demographic characteristics, laboratory parameters, treatment response and clinical outcomes were analyzed. Complete remission (CR) was defined as proteinuria <0.3 g/24 h, and partial remission (PR) as a ≥50% reduction from baseline to <3.5 g/24 h, with stable kidney function. Continuous variables were expressed as median and interquartile range (IQR), and cate–gorical variables as number and percentage.

Results. Among 30 patients, 19(63.3%) were male, with a median age of 55 years (IQR 44.3–62.8). MN was the predominant diagnosis (22/30; 73.3%), followed by FSGS (5/30; 16.7%) and MCD (3/30; 10.0%). Hyper–tension was present in 23 patients (76.7%) and diabetes mellitus in 3 (10.0%) at baseline. New-onset diabetes during treatment occurred in 5 patients (16.7%) and was reversible in one. Median baseline proteinuria was 8.88 g/24 h (IQR 5.93–17.75), serum creatinine 87.5 µmol/L (IQR 75.5–119.8), and serum albumin 24.5 g/L (IQR 21.0–28.8). The best achieved response was CR in 11 patients (36.7%), PR in 15 (50.0%), and no remission (NR) in 4(13.3%); overall, 86.7% achieved at least PR. Relapse occurred in 8 patients (26.7%), with two or more relapses in 4(13.3%). At the last available follow-up, median proteinuria was 0.62 g/24 h (IQR 0.31-2.23), serum creatinine 95 µmol/L (IQR 81-121.5), and serum albumin 40 g/L (IQR 36.3–43.0). One patient progressed to end-stage kidney disease (ESKD).

Conclusion. In this single-center cohort, most patients with primary nephrotic syndrome achieved complete or partial remission despite marked proteinuria at presentation. Relapses occurred in approximately one-quarter of patients, while kidney function was generally preserved during follow-up. New-onset diabetes was observed in every sixth patient, emphasizing the im–portance of monitoring both treatment effectiveness and metabolic complications during long-term management.

Free Communications (FC)

FC-01

Renal outcomes following SGLT2 inhibitor initiation in non-diabetic patients with chronic kidney disease: a pilot observational study

Hamza-Mahmutovic I, Prohic N, Kajevic E, Salkic-Smailbegovic E, Mujakovic A

Abstract: Chronic kidney disease (CKD) is one of the leading causes of mortality worldwide. Over the past six years, the introduction of SGLT2 inhibitors has transformed the approach to slowing the progression of CKD. Given their established renoprotective effects in diabetes, real-world evidence in non-diabetic CKD remains needed, providing the rationale for this pilot study and the ongoing prospective cohort. Of 79 initially identified patients, 37 non-diabetic patients with CKD (stages G2-G4, predominantly attributed to hypertensive nephroangiosclerosis) and sufficient longitudinal data following SGLT2 inhibitor initiation were included in the final analysis. These patients were managed as outpatients at General Hospital "Prim. Dr. Abdulah Nakas" and evaluated retrospectively using medical records from August 2025 to September 2026. Longitudinal paired and complete-case subgroup analyses were performed across baseline (T0), 3-months (T1), and 6 months (T2) follow-ups. Primary renal parameters (eGFR, urea and creatinine, proteinuria for subgroup) and secondary markers (hemoglobin, hematocrit, electrolytes) were evaluated using paired Student's t-tests or Wilcoxon signed-rank tests based on normality (Shapiro-Wilk test). UACR values were harmonized with 24-hour proteinuria by conversion to estimated 24-hour protein excretion, yielding 11 paired measurements for longitudinal analysis. For exploratory purposes, the total eGFR slope was estimated from the change between baseline and T2, while chronic eGFR slope was calculated from T1 to T2 standardized to an annual rate. Baseline eGFR and serum creatinine levels remained stable without significant deterioration across all timepoints (T0 vs T2 eGFR: p=0.922; serum creatinine: p=0.242). Neither the total nor chronic eGFR slope differed significantly from zero (-1.20 mL/min/1.73 m2, p=0.792 and -2.29 mL/min/1.73 m2/year, p=0.747, respectively). Harmonized 24-hour proteinuria (N=11) showed a 75.5% median reduction from baseline to 6 months (0.310 to 0.076 g/24h), with 81.8% (9/11) achieving a ≥30% response. SGLT2 inhibitor initiation was associated with an acute, statistically significant increase in hemoglobin levels (T0 to T1, p=0.005) and a significant increase in hematocrit at 6-month follow-up. Serum potassium (T0: 4.69±0.57 mmol/L vs T2: 4.79±0.77 mmol/L; p=0.129) and serum sodium (140±1.97 mmol/L vs 140±3.63 mmol/L; p=0.947) remained within normal physiological ranges without significant electrolyte derangements. In this pilot study SGLT2 inhibitor initiation was associated with stable eGFR and marked reduction in proteinuria, alongside significant hematocrit elevation and stable electrolyte levels. Study limitations include the retrospective observational design, single-center setting, and limited longitudinal follow-up data. Prospective data collection is ongoing for newly enrolled cohort patients awaiting scheduled follow-ups.

FC-02

Falsely elevated iPTH in a patient after total parathyroidectomy with forearm auto-transplantation

Selma Ajanovic, Aida Coric, Alma Mutevelic-Turkovic, Fahrudin Masnic, Emir Grosa

Abstract: Secondary hyperparathyroidism (SHPT) is characterized by excessive synthesis and secretion of parathyroid hormone (PTH), accompanied by progressive enlargement and hyperplasia of the parathyroid glands. Total parathyroidectomy with forearm autotransplantation (TPTX-AT) is an established treatment option for severe SHPT in patients receiving dialysis. Following surgery, patients require close monitoring because postoperative hypocalcemia and recurrent or persistent hyperparathyroidism may occur. We present a hemodialysis patient who developed unexpectedly high intact parathyroid hormone (iPTH) concentrations one month after TPTX-AT, raising suspicion of recurrent hyperparathyroidism. During routine postoperative iPTH monitoring, a blood sample was obtained from the right forearm, where the parathyroid autograft had been implanted. The patient's arteriovenous fistula (AVF) was located in the left arm, necessitating blood sampling from the right arm. The iPTH concentration was markedly elevated at 4495 pg/mL. Two days later, during hemodialysis, a blood sample obtained from the nongrafted left arm revealed an iPTH concentration of 288.4 pg/mL. This case demonstrates that blood sampling from the forearm containing a parathyroid autograft may result in a spuriously elevated systemic iPTH measurement due to localized hormone secretion from the graft into the adjacent venous circulation. Such a localized elevation may mimic recurrent hyperparathyroidism and potentially lead to misdiagnosis and unnecessary treatment. Awareness of the sampling site is therefore essential

when interpreting iPTH concentrations in patients who have undergone TPTX-AT, particularly in those re–ceiving hemodialysis.

FC-03

Metabolic dysfunction-associated steatotic liver disease and renal function: preliminary findings from an ongoing study

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Abstract: Metabolic dysfunction-associated steatotic liver disease is a systemic metabolic disorder asso–ciated with multiple extrahepatic complications, inclu–ding chronic kidney disease. Insulin resistance, chronic inflammation, oxidative stress and endothelial dys–function may contribute to the complex interplay between hepatic steatosis, liver fibrosis and renal impairment. In this context, this study aimed to further explore the relationships between the severity of hepatic steatosis, non-invasive markers of liver fibrosis and renal function in patients with metabolic dys–function-associated steatotic liver disease. This preliminary cross-sectional analysis included the first 18 patients enrolled in an ongoing study. Clinical, biochemical and anthropometric characteristics were systematically assessed, while renal function was evaluated using estimated glomerular filtration rate (eGFR), chronic kidney disease stage, albuminuria and proteinuria. Hepatic steatosis and fibrosis were assessed by transient elastography using controlled attenuation parameter (CAP) and liver stiffness measurement (LSM), respectively. The fibrosis-4 index (FIB-4) was calculated as an additional non-invasive marker of liver fibrosis. All 18 patients had hepatic steatosis on ultrasonography. Renal function varied considerably across the cohort, with eGFR ranging from 16.76 to 95.04 mL/min/1.73 m²; most patients had chronic kidney disease stage G3a or G3b. LSM ranged from 1.5 to 20.2 kPa, FIB-4 from 0.58 to 3.40, and CAP from 178 to 352 dB/m. No statistically significant correlation was observed between LSM and eGFR (ρ=0.159, p=0.528) or between FIB-4 and eGFR (ρ=0.212, p=0.399). CAP showed a moderate inverse correlation with eGFR (ρ=−0.370), although this finding did not reach statistical significance (p=0.130). No statistically significant associations were observed between LSM, FIB-4 or CAP and chronic kidney disease stage. These preliminary findings from the initial study cohort did not demonstrate statistically significant associations between non-invasive markers of liver fibrosis and renal function. However, the moderate inverse correlation between CAP and eGFR suggests a possible relationship between greater hepatic steatosis and reduced renal function. Continued patient recruitment and expansion of the study cohort are needed to further investigate the relationship between hepatic steatosis, liver fibrosis and chronic kidney disease severity.

FC-04

Antihypertensive Medication Use and Inflammatory Burden in Hemodialysis: A Comparative Analysis of Serum Interleukin-6

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Abstract: Interleukin-6 (IL-6) is an important marker of systemic inflammation in patients undergoing main–tenance hemodialysis. Antihypertensive medications may influence inflammatory activity beyond their blood pressure-lowering effects. This study compared serum IL-6 concentrations according to beta-blocker and calcium channel blocker (CCB) use. A retrospective analysis included 96 patients receiving maintenance hemodialysis at the American Hospital in Tirana, Albania, during 2024. Patients were categorized into four groups: beta-blocker use without CCBs, CCB use without beta-blockers, concurrent use of both classes, or use of neither class. Serum IL-6 concentrations were summarized as mean ± standard deviation. Overall between-group differences were evaluated using Welch's analysis of variance. Among the 96 patients, 24(25.0%) received beta-blockers without CCBs, 20 (20.8%) received CCBs without beta-blockers, 12(12.5%) received both classes, and 40 (41.7%) received neither class. Mean IL-6 concentrations were 22.4±16.8 pg/mL, 19.6±13.9 pg/mL, 14.8±7.6 pg/mL, and 31.7±26.4 pg/mL, respectively. The overall comparison indicated differences across groups (p=0.008). Concurrent users had the lowest mean IL-6 concentration, whereas patients receiving neither class had the highest concentration and greatest between-patient variability. Antihypertensive medication patterns were associated with differences in circulating IL-6 concentrations, with the lowest mean level observed among concurrent beta-blocker and CCB users. These unadjusted associations do not establish an anti-inflammatory benefit or synergistic treatment effect. Prospective studies accounting for clinical characteristics and treatment indications are needed to clarify the relationship.

FC-05

Impact of anemia on kidney transplant outcome

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Abstract: Post-transplant anemia (PTA) is a frequent complication of kidney transplantation that has been linked to graft loss, cardiovascular events, and increased mortality. Reduced hemoglobin (Hb) concentration leads to chronic hypoxia of the renal graft, which may promote interstitial fibrosis, tubular atrophy, and prog–ressive loss of graft function. The aim of this study was to investigate the association between anemia diagnosed three months after kidney transplantation and renal graft function one year after transplantation. This retrospective-prospective longitudinal observational

study included 95 kidney transplant recipients followed one year after transplantation at the Nephrology Clinic, Clinical Center University of Sarajevo. Relevant clini–cal and laboratory parameters were collected for each recipient. Anemia was defined as an Hb concentration <110 g/L three months after transplantation, and recipients were divided into two groups according to the presence of PTA. Deterioration of graft function was defined as a serum creatinine increase ≥25% or an estimated glomerular filtration rate (eGFR) decline ≥30% at the 12-month compared to the 3-month post-transplant time point. The prevalence of PTA in our cohort was 27.37%. PTA was significantly more frequent in women than in men (42.86% vs. 20.90%; p=0.029). Recipients with PTA had significantly lower Hb, he–matocrit, and red blood cell counts at all post-transplant time points and significantly lower eGFR at one year post-transplant compared to recipients without PTA. A serum creatinine increase ≥25% (23.08% vs. 4.35%; p=0.005) and an eGFR decline ≥30% (19.23% vs. 1.45%; p=0.001) were significantly more frequent in the PTA group. In multivariable logistic regression analyses, PTA was independently associated with a serum creatinine increase ≥25% (OR 8.485, 95% CI 1.111-64.83, p=0.039) and an eGFR decline ≥30% (OR 27.54, 95% CI 2.28-340.4, p=0.010). Furthermore, deceased-donor transplantation independently predicted a serum creatinine increase ≥25% (OR 17.54, 95% CI 1.335-230.38, p=0.029). PTA independently predicts deterioration of renal graft function one year after transplantation, and can be helpful in identifying reci–pients who warrant closer surveillance of graft function.

FC-06

Vascular Access Complications in Hemodialysis: The Influence of Diabetes and Body Mass Index

Mukinovic D, Jasarevic A, Pjanic M, Aleckovic Halilovic M

Abstract: Vascular access complications are an important cause of morbidity in patients on intermittent hemo–dialysis. Diabetes mellitus and obesity have been reported as potential risk factors, but their association may differ depending on the type of vascular access and complication. Aim of this study was to assess the impact of diabetes mellitus and body mass index (BMI) on infectious and mechanical complications of vascular access. We conducted a cross-sectional study in our institution, which included 140 patients on intermittent hemodialysis at the Department of Nephrology, Dialysis and Kidney Transplantation, University Clinical Center Tuzla. Data on primary renal disease, duration of dialysis treatment, presence and duration of diabetes mellitus, BMI, sepsis associated with vascular access, arteriovenous fistula (AVF) dysfunction or malfunction, and catheter malfunction were analyzed. Categorical variables were compared using the chi-square test, while multivariate logistic regression was used to assess factors associated with AVF dysfunction and sepsis. A significance level of α=0.10 was applied. Diabetes mellitus was present in 50 patients (35.7%). Vascular access-related sepsis occurred in 49 patients (35.0%) and was more common among patients with diabetes than among those without diabetes (44.0% vs. 30.0%; p=0.096). Neither diabetes nor body mass index (BMI) were individually associated with AVF dysfunction in univariate analysis (p=0.523 and p=0.617). However, the multivariate model for AVF dysfunction was statistically significant (χ^2=14.273; p=0.027), with diabetes showing a borderline association (OR 4.89; p=0.061). Of note, a significant interaction was observed between diabetes and BMI (p=0.008), suggesting that the association of patient characteristics with AVF dysfunction may depend on their co-presence. In contrast, neither diabetes nor BMI were associated with catheter failure (p=0.874 and p=0.837, respectively). The multivariate model for sepsis was not statistically significant (p=0.137). In this single-center hemodialysis cohort, diabetes was associated with a higher incidence of vascular access-related sepsis at a pre-specified α=0.10 level, whereas no individual association of diabetes or body mass index (BMI) with AVF dysfunction was observed. The significant interaction of diabetes and BMI in the multivariable AVF model suggests a potentially specific and combined effect of metabolic risk factors on access.

FC-07

Renoprotection beyond diabetes: a case of obesity-related proteinuria treated with GLP-1 receptor agonist

Prohic N, Sakic B, Divanovic Slato A, Hadzic A

Abstract: Obesity is increasingly recognized as an independent risk factor for chronic kidney disease and may contribute to glomerular hyperfiltration, podocyte injury, and proteinuria even in the absence of diabetes mellitus. Obesity-related glomerulopathy represents a manifestation of metabolic kidney disease, although evidence regarding targeted pharmacological treatment in non-diabetic patients remains limited. We present a case of obesity-associated proteinuria in a non-diabetic patient treated with a glucagon-like peptide-1 receptor agonist (GLP-1 RA), followed by the addition of a sodium-glucose cotransporter-2 (SGLT2) inhibitor. We present a case of an adult woman with obesity, preserved renal function, and persistent proteinuria in the absence of diabetes mellitus. A comprehensive nephrological evaluation was performed to exclude secondary causes of proteinuria, including immune-mediated, infectious, and structural renal diseases. Following the exclusion of alternative etiologies, obesity-related glomerulopathy was considered the most likely diagnosis. A multidisciplinary metabolic approach was initiated, including a GLP-1 RA and metformin, followed by the addition of an SGLT2

inhibitor for further renal protection. Clinical, metabolic, and renal parameters were monitored during follow-up. At baseline, the patient had significant obesity and proteinuria of 0.915 g/day, with preserved renal function and no evidence of diabetes mellitus. During follow-up, treatment was associated with clinically meaningful weight reduction and a progressive decline in proteinuria. Proteinuria decreased by 49%, from 0.915 g/day to 0.47 g/day. Renal function remained stable throughout the observation period. The reduction in proteinuria occurred despite the absence of diabetes, supporting a potential role of metabolic-targeted therapy in obesity-associated kidney injury. This case highlights obesity as a potential driver of kidney injury and proteinuria independent of diabetes mellitus. The substantial reduction in proteinuria following initiation of GLP-1 RA-based metabolic therapy potential renoprotective effects of metabolic-targeted treatment beyond glycemic control.

FC-08

HyperIgD syndrome and renal amyloidosis

Danilo Radunovic, Ivana Radunovic

Abstract: Mevalonate kinase deficiency (MKD), also known as hyperimmunoglobulinemia D syndrome (HIDS), is a rare autoinflammatory disorder character–rized by recurrent inflammatory episodes and sustained activation of innate immunity. Chronic inflammation may lead to AA amyloidosis, with the kidneys being among the most frequently affected organs. We present a diagnostically challenging case of renal AA amyloidosis in an adult patient with mevalonate kinase deficiency, highlighting the importance of considering autoinflammatory diseases in patients with unexplained systemic inflammation and renal involvement. A 60-year-old woman was evaluated at the Clinic for Nephrology, Clinical Center of Montenegro, following a complex clinical course characterized by recurrent infections and inflammatory manifestations. During the previous two years, she had experienced four hospital-treated episodes of pneumonia, frequently requiring broad-spectrum or reserve antibiotics. Throughout her life, she reported recurrent “cold-like” illnesses and intermittent skin rash, previously investigated as a possible allergic reaction. In February 2025, she was hospitalized with severe febrile neutropenia and agranulocytosis, bilateral pneumonia, respiratory failure, pleural effusions, influenza A infection, edema, hypertension, anemia, and nephrotic-range proteinuria of 5.76 g/24 h. Extensive infectious, immunological, hematological, and malignant disease investigations were performed. Renal biopsy and subsequent systemic evaluation were undertaken to determine the cause of persistent proteinuria and renal dysfunction. Following clinical stabilization, serum creatinine was 114 µmol/L, estimated glomerular fil–tration rate was 46 mL/min/1.73 m², and proteinuria remained approximately 3 g/24 h. Kidney biopsy per–formed in March 2025 demonstrated mesangial accumulation of PAS-positive material and Congo red-positive deposits involving glomeruli and vascular structures. Immunohistochemical analysis confirmed AA amyloid deposition, establishing the diagnosis of AA renal amyloidosis. Serum protein electrophoresis with immunofixation showed no monoclonal component. Additional investigations excluded several potential secondary causes, including chronic infection, malignancy, and systemic autoimmune disease. Fat tissue and rectal mucosal biopsies were negative for amyloid deposition. Cardiac evaluation showed no evidence of restrictive cardiomyopathy. The patient also had bilateral sen–sorineural hearing loss, mild peripheral polyneuropathy, and osteoporosis. Genetic evaluation for hereditary amyloidosis and autoinflammatory disorders supported the diagnosis of mevalonate kinase deficiency/hyper-IgD syndrome. Treatment with the IL-1 inhibitor canakinumab (150 mg monthly) was initiated, together with pneumococcal vaccination. During follow-up, renal function remained stable, with serum creatinine of 111 µmol/L and eGFR of 47 mL/min/1.73 m², while pro–teinuria decreased to 2.27 g/24 h. This case illustrates that mevalonate kinase deficiency may remain unrecog–nized until adulthood and may present with severe systemic inflammatory complications, including AA renal amyloidosis. In patients with unexplained AA amyloidosis and a history suggestive of recurrent inflammatory episodes, autoinflammatory diseases should be actively considered.

FC-09

Targeting residual proteinuria in AL Amyloidosis: the potential role of SGLT2 inhibitors following autologous stem cell transplantation

Danilo Radunovic, Ivana Radunovic

Abstract: Light-chain (AL) amyloidosis is a rare plasma cell disorder characterized by extracellular deposition of monoclonal immunoglobulin light chains, resulting in progressive organ dysfunction. Renal involvement occurs frequently and may lead to severe nephrotic syndrome with massive proteinuria, edema, throm–boembolic complications, and progressive chronic kidney disease. AL amyloidosis may coexist with multiple myeloma (MM), requiring rapid identification of the underlying plasma cell clone and effective clone-directed therapy. Autologous hematopoietic stem cell transplantation (AHSCT) remains an important therapeutic strategy in eligible patients with MM and AL amyloidosis. However, severe proteinuria may persist despite successful hematological treatment and preserved renal function. Sodium-glucose cotransporter-2 inhibitors (SGLT2i) have demonstrated important nephroprotective and cardioprotective effects, while recent studies suggest potential benefits in patients following hematopoietic stem cell transplantation. We

present a young patient with AL renal amyloidosis and MM who underwent successful AHSCT and was subsequently treated with an SGLT2 inhibitor to reduce persistent massive proteinuria. We present the clinical course of a 31-year-old man with nephrotic syndrome and severe proteinuria ranging from 7 to 47 g/24 h, despite preserved renal function with an esti–mated glomerular filtration rate above 90 mL/min. Renal biopsy demonstrated Congo red-positive amyloid deposits in the mesangium and along the glomerular basement membrane. Repeat biopsy confirmed AL amyloidosis, with homogeneous lambda light-chain deposition (3+ by immunofluorescence) and positive amyloid P immunohistochemistry. Bone marrow rebiopsy with immunophenotyping demonstrated plasma cell infiltration compatible with MM. Cardiac magnetic resonance imaging and PET/CT demonstrated additional cardiac involvement. Following treatment with four cycles of daratumumab, cyclophosphamide, bortezomib, and dexamethasone (Dara-CyBorD), the patient underwent uncomplicated AHSCT. Because severe proteinuria persisted following successful hematological treatment, adjunctive therapy with an SGLT2 inhibitor was introduced with the aim of reducing glomerular protein loss and providing additional kidney protection. The patient maintained preserved renal function throughout chemotherapy and transplantation. Despite hematological treatment and AHSCT, nephrotic-range proteinuria remained substantial, approximately 7.5 g/24 h, requiring repeated 20% albumin substitution. Given the per–sistent massive proteinuria, SGLT2 inhibition was introduced as an adjunctive nephroprotective strategy. After two months of therapy proteinuria was reduced to 4 g/24h. This therapeutic decision was supported by emerging evidence demonstrating favorable outcomes of SGLT2i following HSCT, including reduced mortality, hospitalization, heart failure events, and acute kidney injury. This case highlights the challenge of persistent nephrotic proteinuria in AL amyloidosis despite su–ccessful clone-directed therapy and AHSCT. SGLT2 inhibition may represent a promising adjunctive stra–tegy for reducing proteinuria and preserving renal fun–ction in carefully selected patients after transplantation.

FC-10

Lupus nephritis - our experience

Bubic D, Anicic M, Topic G, Mrgud J

Abstract: Lupus nephritis is renal manifestation of systemic lupus erythematosus and is characterized by wide range of histological changes. It represents a serious complication of this disease, contributing to increase mortality and increase in the number of dialysis-dependent patients. It is diagnosed clinically and serologically, by the presence of antibodies. The highest incidence of lupus is in the period between 15-45 years of age, and it is more common in women by 8-15:1. Among lupus nephritis patients, the incidence of male and female is equal, more severe forms occur in male and children. The prognosis of the disease depends on several parameters such as age, gender, race, ethnicity. The aim of this study is to present the experience of our center in the follow-up of patients with lupus nephritis through the analysis of data on 26 patients who underwent kidney biopsy, with a focus on demographic characteristics, classification according to the NIH (National Institutes of Health) and the outcome of treatment after five years of follow-up. In the Clinic for Internal Diseases, Department of Nephrology in University Clinical Center of Republic of Srpska, a retrospective analysis of treatment out–comes of 26 patients whose diagnosis of lupus nephritis was confirmed by kidney biopsy was conducted. The data were collected by searching the registry of biopsied patients, medical history of treated patients and KIS electronic documentation. We analyzed the gender and age distribution of our patients in relation to literature data, the frequency of occurrence according to the NIH classification, and the outcomes after five years from the day of biopsy. Analyzing this sample, we find that more female are represented, but both female and male are on average older than the global average for lupus nephritis. The most common class is class V (membranous LN)-present in 7 patients (26.9%). They are followed by class II (mesangial proliferative) and IV-G/III/IV combinations. A significant number of patients have advanced or combined forms of the disease (classes IV-G, IV-S, IV-G(A/C), III/IV). This study provides insight into our approach to diagnosis, treatment and follow-up of patients with lupus neph–ritis, with the aim of optimizing biopsy time, treatment strategies and prevention of renal complications.

FC-11

Serum Concentration of Sphingosine-1-Phosphate in End-stage Kidney Disease and in Kidney Transplant Recipients is Decreased Compared to Healthy Subjects

Atic A, Sakic Z, Kulic A, Potocki S, Basic-Jukic N

Abstract: Sphingosine-1-phosphate (S1P) is a bioactive lipid signaling molecule with both intracellular and extracellular functions. Serum concentration of S1P is affected by various disease processes, including athe–rosclerotic disease, heart diseases, obesity, and diabe–tes. While there are some studies associating various aspects of S1P and other sphingolipid metabolism disorders with various renal diseases, changes in S1P metabolism due to end-stage kidney disease (ESKD) have not been elucidated. This is a preliminary analysis of a prospective study investigating the changes in serum S1P concentration after kidney transplantation in ESKD patients. The aim of this study was to compare S1P concentration in healthy subjects, kidney transplant recipients (KTR) and in ESKD patients, as well as to investigate factors associated with changes in serum S1P concentrations in dialyzed patients. A total of 268

participants were included (16 healthy, 41 EKSD, 211 KTR). Of the ESKD patients, majority were male (68.3%), on average 53.6 years old (SD 14.1). Most of the patients were on hemodialysis (87.8%) with an average dialysis vintage of 48 months (IQR 34-64), average BMI 26.2 kg/m2. Most frequent comorbidities were T2D (24.4%), 4 patients had a prior myocardial infarction and three had treated malignant disease. S1P concentrations differed significantly between groups (p=0.003), with healthy controls showing the highest levels (313.8±32.9 ng/ml) compared with KTR (255.0 ±98.5 ng/ml) and ESKD patients (264.4±93.1 ng/ml). Post hoc testing confirmed that controls exceeded both the KTR group (mean difference 58.8 ng/ml, 95% CI 32.9-84.7, p<0.001) and the ESKD group (49.4 ng/ml, 95% CI 9.2-89.6, p=0.012), whereas KTR and ESKD did not differ from each other (-9.4 ng/ml, 95% CI -48.0-29.2, p=0.83). Measured S1P concentrations in ESKD were not associated with any of the tested variables (age, sex, dialysis vintage, type of dialysis, comorbidities, blood counts, liver function tests). S1P concentration is lower in ESKD patients than in the healthy population. Factors associated with changes in S1P in other studies have shown no associations in this ESKD cohort. These findings direct future research as they indicate profound changes in S1P metabolism in ESKD patients.

FC-12

Rituximab in therapy of glomerular disease: one-centre experience

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Abstract: Glomerular diseases remain challenging to treat, particularly in patients with persistent proteinuria and an inadequate response to conventional immuno–suppressive therapy. Rituximab has emerged as an important therapeutic option in refractory or relapsing cases. We aimed to evaluate the early clinical response to rituximab in patients with glomerular diseases previously treated with conventional immunosuppressive therapy. We conducted a retrospective observational case series at the Department of Nephrology and Renal Replacement Therapy, Clinical Center University of Sarajevo, over a two-year period. Twelve patients with glomerular diseases treated with rituximab were included. Demographic and clinical characteristics, underlying disease, previous immunosuppressive therapy, proteinuria, serum creatinine, and estimated glomerular filtration rate (eGFR) were analyzed. The primary outcome was the change in proteinuria three months after rituximab treatment. The cohort included 11 men and 1 woman, with a mean age of 47 years (range, 23–68). Membranous nephropathy was the most common diagnosis (58.3%), followed by ANCA-associated vasculitis (16.6%), lupus nephritis, minimal change disease, and thrombotic microangiopathy each accounted for 8.3%. All patients had previously received immu–nosuppressive therapy, most commonly corticosteroids, cyclophosphamide, and calcineurin inhibitors. In 11 patients, rituximab was administered at 375 mg/m² once weekly for four weeks, while one patient received 1 g twice, 14 days apart. Among six patients with paired measurements, mean proteinuria decreased from 9.53 to 0.86 g/day after three months, representing an approximately 91% reduction. Five patients achieved proteinuria <1 g/day. In membranous nephropathy, mean proteinuria decreased from 7.46 to 0.41 g/day (n=4). In lupus nephritis, proteinuria decreased from 18.12 to 0.74 g/day. Among seven patients with available creatinine measurements, mean serum creatinine decreased from 162 to 149 µmol/L. eGFR remained stable in six patients (41.8 vs. 42.4 mL/min/1.73 m²). Rituximab was associated with a marked early reduction in proteinuria without deterioration of renal function in this single-center series of previously treated glomerular diseases. The most pronounced response was observed in membranous nephropathy. Larger studies with longer follow-up are needed to confirm these findings.

FC-13

Open nephrectomy of a polycystic kidney before transplantation – case report

Elvir Mucic

Abstract: Polycystic kidney disease (PKD) is the most common hereditary kidney disorder, characterized by the development of numerous cysts within the renal parenchyma. Besides renal cysts, the disease may also involve cysts in the liver and pancreas, as it affects both sexes and all races worldwide. Approximately 7-8% of all chronic kidney disease patients with end-stage renal failure in Europe suffer from PKD. Diagnosis is based on family history assessment, radiological imaging, and, when indicated, genetic testing. Numerous studies have demonstrated that complication rates do not differ depending on the timing of nephrectomy and that the procedure does not negatively impact graft survival. Conservative treatment of autosomal dominant polycystic kidney disease (ADPKD), before transplantation is challenging. Native nephrectomy remains the gold standard and is performed in those circumstances where it is justified due to high morbidity. It is known that approximately 20-45% of patients undergo neph–rectomy before transplantation, most often due to insufficient space for the renal allograft, as was the case with our patient. Nephrectomy of the polycystic native kidney is one of the recommendations prior to kidney transplantation to create adequate space for the renal graft. In this paper, we present a case of a female patient with end-stage chronic kidney disease on hemodialysis at the Clinical Center of Montenegro, who underwent native nephrectomy of a polycystic

kidney in order to prepare for future kidney transplantation.

FC-14

Historical Spectrum and Outcome of Biopsy-Proven Glomerular Diseases in Adults: A Single-Center Experience between 2002 and 2010

Leyla Koc, Kubra Kaynar, Sevdegul Mungan, Şukru Ulusoy, Gulsum Ozkan, Muammer Cansiz, Nuray Misir

Abstract: Prior to the 2009 establishment of kidney biopsy registries in Türkiye, the histopathological spec–trum of biopsy-proven kidney diseases in Northeastern Türkiye was not well defined. This study aimed to describe the demographic characteristics, biopsy indications, histopathological findings, and clinical outcomes of adult patients undergoing native kidney biopsy during the pre-registry era. We conducted a retrospective, single-center study of 113 adult patients who underwent percutaneous native kidney biopsy from January 2002 to December 2010. Clinical, laboratory, and histopathological data were extracted from hospital and pathology records. The study protocol was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of Helsinki. Patients (67.2% men) had a mean age of 43.9±15.4 years, with nephrotic syndrome acting as the leading biopsy indication. Primary glomerulonephritis was the predominant histopathological category (n=73). Focal segmental glomerulosclerosis and membranous nephropathy were the most frequent primary glomerular diseases, while amyloidosis was the most common secondary cause. Hypertension was the most frequent comorbidity. Outcome data were missing for 37.1% of patients. Of the evaluated cohort, 28(24.8%) achieved complete remission, and 21(18.6%) progressed to ESKD. Primary glomerulonephritis was the primary histopathological finding in Northeastern Türkiye during the pre-registry era, with focal segmental glomerulosclerosis and membranous nephropathy being the leading causes at that time. Notably, IgA nephron–pathy was less frequent compared to later national registry reports. This cohort provides an important historical baseline for future regional and national comparison.

FC-15

Visceral Leishmaniasis (Kala-Azar) in a Kidney Transplant Recipient

Danilo Radunovic, Ivana Radunovic

Abstract: Visceral leishmaniasis (VL), or kala-azar, is a potentially life-threatening opportunistic infection in immunocompromised patients. Its diagnosis may be challenging in kidney transplant recipients because clinical manifestations can overlap with other infectious, hematological, and transplant-related complications. We present a case of VL in a kidney transplant reci–pient with advanced chronic graft dysfunction, high–lighting the importance of bone marrow examination and coordinated multidisciplinary management. A 53-year-old woman with end-stage kidney disease secondary to bilateral vesicoureteral reflux had undergone two kidney transplantations, in 2001 and 2011. Chronic graft dysfunction had been present since 2023. She was hospitalized because of progressive weakness, fatigue, dyspnea, and generalized edema. She had previously been admitted for bilateral pneumonia, during which hematological evaluation raised suspicion of malignancy. Bone marrow biopsy subsequently demonstrated numerous small particles morphologically consistent with Leishmania, leading to the diagnosis of visceral leishmaniasis. The biopsy showed no mor–phological evidence of lymphoproliferative or myelo–proliferative disease. On admission, laboratory findings included severe anemia, leukopenia, thrombocytopenia, elevated inflammatory markers, and marked renal dysfunction. Abdominal ultrasound revealed spleno–megaly, ascites, and a transplanted kidney without structural abnormalities. Anti-Leishmania donovani IgG serology was negative. Treatment with liposomal amphotericin B was initiated according to an extended regimen recommended for immunocompromised patients: 4 mg/kg intravenously daily for five days, followed by doses on days 10, 17, 24, 31, and 38. The patient also required hemodialysis because of severe renal dysfunction and hypervolemia. During hospitalization, inflammatory markers and blood counts improved, while serum creatinine decreased from 479 to 187 µmol/L before rising again to 296 µmol/L at dis–charge. The patient remained dependent on chronic hemodialysis, but primarily because of hypervolemia and reduced cardiac function. This case illustrates that visceral leishmaniasis should be considered in kidney transplant recipients with unexplained systemic sym–ptoms and cytopenias, even in the absence of fever or positive serology. Bone marrow examination was decisive for diagnosis. Extended liposomal amphotericin B therapy and close nephrological and infectious disease monitoring are essential in this high-risk population.

FC-16

Preoperative Evaluation of a High-Risk Recipient for Living-Related Kidney Transplantation: Immunological, Oncological, and Vascular Aspects

Masnic Fahrudin, Rebic Damir, Grosa Emir, Coric Aida, Ajanovic Selma, Mutevelic-Turkovic Alma, Osmanovic-Aganovic Nadira

Abstract: Preparation of candidates with complex comorbidities for living-related kidney transplantation requires an integrated assessment of oncological risk, vascular anatomy, and donor-specific antibody (DSA) reactivity. A borderline-positive crossmatch in the presence of low DSA titers represents a particular diagnostic challenge, as it requires distinguishing true sensitization from a testing-platform-related artifact. We present a 62-year-old male patient on hemodialysis

for five years due to end-stage renal disease, evaluated for living-related kidney transplantation from his sister as donor (ABO-compatible pair: O RhD- into O RhD+). In May 2023, the patient underwent radical prostatectomy for prostate adenocarcinoma (pT3a pN0 R1), without subsequent adjuvant radiotherapy. Oncological re-evaluation, performed 33 months after surgery, included pelvic MRI (no evidence of local recurrence or significant lymphadenopathy) and laboratory work-up (total PSA 0.04 ng/mL, with a normal panel of additional tumor markers), thereby ruling out an oncological contraindication to immunosuppressive therapy. CT angiography demonstrated extensive aortic and iliac artery calcifications without hemodynamically significant stenosis, confirming the technical feasibility of vascular anastomosis. Immunological work-up revealed isolated low- to moderate-intensity DSA (HLA-DQA101:03, MFI 939; DQB106:03), with a negative panel-reactive antibody (PRA) class I and II, but a weakly positive complement-dependent cytotoxicity (CDC) crossmatch (microlymphocytotoxicity test, MLCT)-a finding inconsistent with the low MFI values. A desensitization protocol was performed, comprising five cycles of therapeutic plasmapheresis with human albumin substitution. Re-evaluation of the crossmatch using testing platforms from different manufacturers did not confirm the initial positivity, indicating a methodological artifact rather than true cytotoxic sensitization. This case highlights the need for critical interpretation of borderline-positive CDC crossmatch results in the presence of low DSA MFI values, particularly when inconsistent with other immunological parameters. Re-evaluation across different diagnostic platforms allows avoidance of a false-po–sitive diagnosis of sensitization, while comprehensive oncological and vascular evaluation ensures the safe realization of kidney transplantation in high-risk recipients.

FC-17

Cryptococcal Meningitis in a Kidney Transplant Recipient: A Case Report

Danilo Radunovic, Ivana Radunovic

Abstract: Cryptococcal meningitis (CM) is a severe, opportunistic fungal infection that predominantly affects immunocompromised individuals, including solid organ transplant recipients. Diagnosis is frequently challenging due to insidious and non-specific clinical presentations, which can significantly delay treatment initiation. This abstract reports the successful diagnosis and management of CM in a patient with a functioning kidney allograft. A 51-year-old male with a 29-year history of type 1 diabetes mellitus and arterial hypertension presented with persistent headaches, nausea, vomiting, malaise, and transient low-grade fever. The symptoms occurred nine months following a cadaveric kidney transplantation. Initial laboratory testing revealed severe hyponatremia (serum sodium 116-120 mmol/L) and a stable baseline serum creatinine. Due to the high suspicion of a central nervous system infection, and following fundoscopic exclusion of papilledema, a lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis demon–strated pleocytosis (69 white blood cells/µL, 70% mononuclears) and decreased glucose levels. Molecular diagnostics using a multiplex PCR CNS panel identified Cryptococcus neoformans in the CSF, which was subsequently confirmed by CSF cultures and a positive blood culture for Cryptococcus sp. Targeted induction antifungal therapy was immediately initiated with liposomal amphotericin B and parenteral fluconazole, which was maintained for a total of 8 weeks. To optimize immune status, mycophenolate mofetil (MMF) was permanently discontinued, while tacrolimus and corticosteroids were maintained with close therapeutic drug monitoring. During the hospital course, a transient elevation of serum creatinine up to 250 µmol/L was noted, which later stabilized at a baseline of 188-190 µmol/L (eGFR ~35 mL/min). Repeat follow-up lumbar punctures successfully documented CSF sterilization. The patient was discharged in good clinical condition and remained asymptomatic. He was prescribed a consolidation phase of oral fluconazole (400 mg daily for 8 weeks) followed by lifelong maintenance therapy (100 mg daily for at least 12 months). CM requires a high index of clinical suspicion in renal transplant recipients presenting with persistent neurological complaints and hyponatremia. Prompt, aggressive, and prolonged combination antifungal regimen, coupled with timely reduction of net immunosuppression, is essential to eradicate the fungal pathogen and preserve allograft function.

FC-18

A rare cause of acute kidney injury and rhabdomyolisis, with concomitant infective endocarditis

Kopric Damir, Pjanic Mirha, Jasarevic Amila, Aleckovic Halilovic Mirna

Abstract: This case report highlights the importance of a comprehensive diagnostic evaluation of the underlying causes of AKI and rhabdomyolysis, as well as the crucial role of a detailed medical history and thorough physical examination. A 50-year-old man was admitted with acute kidney injury (AKI) (serum creatinine 120 µmol/L), muscle stiffness, and tenderness. Laboratory investigations revealed markedly elevated creatine kinase (8,269 U/L) and lactate dehydrogenase (686 U/L), consistent with rhabdomyolysis. A com–prehensive diagnostic work-up was initiated to deter–mine the underlying etiology of AKI and rhabdomyolysis. The patient worked in a coal mine and sought medical attention only a few hours after completing a night shift. Because of the patient's occupational exposure to rodents in a coal mine and contact with cattle, sheep, cats, and dogs, the evaluation included potential

zoonotic infections. Simultaneously, investigations for non-exertional rhabdomyolysis were performed. La–boratory testing demonstrated severe autoimmune hypothyroidism with markedly elevated thyroid-stimulating hormone (139.24 mIU/L), decreased free triiodothyronine and free thyroxine levels, and strongly positive anti-thyroglobulin (>1000 IU/mL) and anti-thyroid peroxidase (>400 IU/mL) antibodies. The patient responded well to the conservative treat–ment for suspected heme pigment nephropathy second–dary to rhabdomyolysis and did not require dialysis. Following endocrinology consultation, levothyroxine replacement therapy was initiated and titrated, re–sulting in improvement of muscle complaints and muscle enzyme levels. After discharge, microbiological inves–tigations returned positive for Coxiella burnetii IgG, IgA, and IgM antibodies. Transthoracic and transeso–phageal echocardiography confirmed infective endo–carditis involving the tricuspid valve. The patient was readmitted, treated with doxycycline and rifampicin, and subsequently underwent mechanical tricuspid valve replacement because of severe valvular involvement. Persistent hypothyroidism required increasing levo–thyroxine to 175 μg/day, and the patient remains under endocrinological follow-up. Our comprehensive approach resulted in the timely initiation of appropriate the–rapeutic interventions, including the management of complications such as severe rhabdomyolysis and bacterial endocarditis.

FC-19

COPD and CKD - Relatives or Just Neighbors?

Hristova D, Borisova E, Borisov B

Abstract: COPD was diagnosed in approximately 400 million patients in 2019 and is projected to cause the deaths of about 5.4 million people annually by 2060. In 2017, approximately 700 million people met the criteria for chronic kidney disease (CKD), corresponding to a prevalence of about 10%. Both diseases become more common with advancing age and share similar comorbidities. The aim of our study was to investigate the significance of renal involvement in patients with COPD regarding changes in key clinical, laboratory, and immunological parameters. The study was conducted over a two-year period involving 210 outpatients with established COPD, 63 of whom were women. The mean age of the patients was 67.7±7.45 years. Longi–tudinal monitoring was performed for parameters including complete blood count, creatinine, urea, CRP, IL-6, IL-8, and vitamin D. Chronic kidney disease (CKD) was defined as abnormalities in kidney structure or function present for at least 3 months, in accordance with the KDIGO 2024 Clinical Practice Guideline. Patients were divided into two groups for the analysis of results: those under 65 years of age and those aged 65 and older. We identified criteria for CKD in 35% of our patients with known COPD; this condition was more frequent in patients over 65 years of age (p= 0.05), and creatinine levels increased significantly with age (p=0.007, Pearson correlation). Among patients over 65 with an eGFR<60 mL/min/1.73 m², 58.1% were women and 4% were men (χ^2=5.725; df=1, p=0.017). CKD in the context of COPD was more common in women over 65 (OR 2.6807; 95% CI 1.5107–4.7567; p=0.0008). We found no statistically significant diffe–rence between the two groups (COPD vs. COPD with CKD) regarding COPD severity as assessed by functional respiratory parameters (χ^2=0.310, df=3, p=0.958). In the group with eGFR<60 mL/min/1.73 m², 38.3% of patients had cardiovascular disease (χ^2 5.749, df 1, p=0.016), and the presence of such disease was a factor in the development of CKD in patients with COPD (OR 2.9294, 95% CI 1.5470-5.7884, p= 0.0011). Hypertensive heart disease, as a comorbidity, was a factor in the development of CKD in patients with COPD (OR 3.8361, 95% CI 1.9940–7.3803, p=0.0001). We found that patients with COPD who were overweight or obese were more likely to have CKD (OR 2.0396, 95% CI 1.1272-3.6905, p=0.02). Elevated uric acid levels were more common in patients with CKD and COPD (OR 3.3052, 95% CI 1.8512-5.9013, p=0.0001), but increased during the cold months only in patients with isolated COPD (p=0.003). Vitamin D levels also showed seasonal variations, independent of renal function (t=11.86, df=77, p<0.01). In our study, we found that the prevalence of CKD in patients with COPD increases with age, female gender, and the presence of overweight, arterial hypertension, and cardiovascular diseases. CKD does not significantly affect the severity of COPD or changes in markers reflecting immune and inflammatory status.

FC-20

When renoprotection becomes a metabolic risk: SGLT2 inhibitor-associated euglycemic ketoacidosis in a patient with an atypical diabetes phenotype

Prohic N, Sakic B, Krdzovic E, Divanovic Slato A, Hadzic A

Abstract: Sodium-glucose cotransporter 2 (SGLT2) inhibitors provide well-established renal and cardio–vascular benefits but may precipitate euglycemic diabetic ketoacidosis (euDKA). We present a case of severe SGLT2 inhibitor-associated euDKA in a young patient with an atypical diabetes phenotype, highlighting the need to balance established cardiorenal benefits against individual metabolic risk. We present a case of a 31-year-old woman with diabetes who developed severe euDKA shortly after initiation of dapagliflozin. Diabetes was diagnosed at 25 years of age and was initially treated with oral glucose-lowering therapy, later requiring basal insulin. Fifteen days before admission, semaglutide and dapagliflozin 10 mg daily were initiated. Subsequently, severe nausea and recurrent vomiting

developed, leading to markedly reduced oral intake and probable dehydration. At presentation, the patient was tachycardic and dyspneic, with a capillary blood glucose of 9.9 mmol/L. Laboratory evaluation revealed severe metabolic acidosis (pH 7.10, bicarbonate 5 mmol/L), potassium of 5.34 mmol/L, and an increase in serum creatinine to 115 μmol/L. Marked glucosuria and 3+ ketonuria supported the diagnosis of SGLT2 inhibitor-associated euDKA. HbA1c before hospitali–zation was 11.6%. C-peptide was preserved at 2.8 ng/mL, with a negative autoimmune diabetes antibody panel. Despite an overweight phenotype (BMI 28.7 kg/m2), the young age at diabetes onset prompted consideration of alternative diabetes subtypes. The MODY probability calculator yielded a probability of 21%; however, genetic testing was not performed. At follow-up, HbA1c remained elevated at 11.4% despite treatment with insulin, a glucagon-like peptide-1 receptor agonist, and metformin. Kidney function fully recovered, with serum creatinine of 70 μmol/L and an eGFR of 117 mL/min/1.73 m2. Urinary albumin was undetectable, with no current evidence of albuminuric kidney disease. Given the previous severe SGLT2 inhibitor-associated euDKA, re-exposure to this drug class would generally be avoided because of the potential risk of recurrence. This case illustrates the metabolic complexity of SGLT2 inhibitor therapy in a young patient with an atypical diabetes phenotype. Severe euDKA may occur despite only modest elevation of blood glucose, particularly in the setting of reduced oral intake, vomiting, and dehydration. Patient education regarding sick-day rules and temporary discontinuation of SGLT2 inhibitors during acute illness or markedly reduced oral intake is essential for risk mitigation.

FC-21

AKI–AKD–CKD Continuum in Cancer Patients: A Proposed Practical Onconephrology Algorithm

Prohic N, Hasanbegovic B, Beslija S, Ceric T, Nesimi E, Campara E, Zubovic D, Kovacevic A

Abstract: Acute kidney injury (AKI) is a frequent complication in patients with cancer and may result from patient-related factors, the malignancy itself, or anticancer treatment. AKI does not necessarily represent an isolated and reversible event but may constitute the starting point of a continuum toward acute kidney disease (AKD) and chronic kidney disease (CKD). Despite this, the period between acute kidney injury and established CKD remains insufficiently structured in the routine follow-up of cancer patients. To summarize current evidence on the AKI-AKD-CKD continuum in patients with cancer and to propose a practical algo–rithm for renal risk assessment, kidney recovery eva–luation, and post-AKI follow-up. A targeted narrative review of contemporary literature addressing onco–nephrology, AKI, AKD, CKD, and anticancer treatment-related nephrotoxicity was performed. Particular attention was given to factors associated with incomplete kidney recovery and principles of post-AKI surveillance. Based on the available evidence, a structured clinical algorithm incorporating proposed 0-7-30-90-day follow-up checkpoints was developed. The proposed algorithm begins with pre-AKI baseline renal risk assessment, including serum creatinine/eGFR, albuminuria/proteinuria, urinalysis, previous AKI or CKD, relevant comor–bidities, and exposure to potentially nephrotoxic anti–cancer therapies. Day 0, corresponding to AKI recog–nition, includes severity assessment and systematic evaluation of patient-related, cancer-related, and treat–ment-related causes, with prompt identification of potentially reversible factors. Day 7 focuses on early kidney recovery and identification of persistent kidney dysfunction. Day 30 represents an intermediate assessment during the AKD period, with particular attention to patients with incomplete renal recovery, persistent albuminuria/proteinuria, recurrent AKI, pre-existing CKD, or ongoing nephrotoxic exposure. Day 90 represents the key reassessment point for identifying persistent kidney dysfunction and transition toward CKD. Patients with incomplete recovery or persistent kidney abnormalities at any stage are considered candidates for intensified onconephrology surveillance. AKI in patients with cancer should be considered a potential entry point into the AKI-AKD-CKD continuum rather than solely an acute complication. A structured 0-7-30-90-day onconephrology pathway may facilitate earlier recognition of incomplete kidney recovery and patients at risk of CKD, enable timely nephrology intervention, and help preserve eligibility for optimal anticancer treatment.

FC-22

Medical Outreach Campaign – An Effective Strategy for Chronic Kidney Disease Detection and Renal Risk Assessment in an Underserved Community

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Abstract: Chronic kidney disease (CKD) is frequently underdiagnosed in underserved communities. The aim of this study was to assess kidney impairment and the risk of CKD progression during a medical outreach campaign conducted in Anina, Caraș-Severin County, Romania. This observational study included 119 adults, 19.3% of whom were residents of a residential care center for older adults. The assessment included clinical examination, renal ultrasonography, and laboratory investigations performed using a point-of-care analyzer. Serum creatinine and urinary albumin-to-creatinine ratio (UACR) were measured in all participants. The risk of kidney disease progression was assessed using estimated glomerular filtration rate (eGFR) and UACR. The mean age was 66 years. Hypertension was identified in 75.6% of participants and diabetes mellitus

in 20.2%. Only 16% had a previously known diagnosis of CKD, and some had not undergone nephrology evaluation during the previous year. Kidney function was assessed in 74 participants, of whom 24.3% had an eGFR <60 mL/min/1.73 m². Among 38 participants with complete assessment (eGFR and UACR), 39.5% had a low risk of kidney disease progression, 34.2% moderate risk, 23.7% high risk, and 2.6% very high risk. Renal ultrasonography revealed findings suggestive of CKD, characterized by reduced kidney size and increased parenchymal echogenicity, in 28.6% of participants. Notably, such imaging abnormalities were present in 24.6% of participants with an eGFR >60 mL/min/1.73 m². The medical outreach campaign identified patients with previously undiagnosed or unmonitored CKD and enabled stratification of kidney disease progression risk. Combining eGFR, UACR, and renal ultrasonography may increase screening sensitivity, demonstrating that structural kidney abnormalities may be present even in individuals with normal serum creatinine levels.

FC-23

Lower is not always better: the non-linear effect of individualized dialysate sodium on volume, thirst and cardiac remodeling

Eftimovska-Otovikj N, Nakovska M, Poposka E, Ristovski O, Krstaveska T, Zlatevska K, Nikolova E, Ilioska S

Abstract: Individualized dialysate sodium (iDNa), prescribed according to predialysis serum sodium, is considered a physiological approach to sodium and volume management in hemodialysis. However, whether progressively lower iDNa provides additional clinical benefit remains uncertain. We investigated the relation–ship between iDNa and volume status, thirst, blood pressure and cardiac remodeling. Seventy-seven stable, non-diabetic maintenance hemodialysis patients re–ceiving iDNa based on predialysis serum sodium were stratified into three groups: 134-136 mmol/L (n=39), 137-138 mmol/L (n=33), and >139 mmol/L (n=5). Interdialytic weight gain (IDWG), blood pressure, thirst assessed by the Dialysis Thirst Inventory (DTI), and echocardiographic parameters were compared across sodium strata. Mean IDWG was 1.97±0.58, 1.88±0.73 and 1.98±0.21 kg in the 134-136, 137-138 and >139 mmol/L groups, respectively, with no significant between-group difference. Thirst also showed no dose-dependent relationship with iDNa (Kruskal-Wallis p=0.774), with DTI scores of 10.55±3.25, 10.72±3.41 and 12.20±4.81, respectively. Left ventricular diastolic and systolic diameters tended to be lower in the 134-136 mmol/L group compared with 137–138 mmol/L (44.61±7.41 vs. 48.34±7.34 mm, p=0.060; 30.34±6.48 vs. 34.07±7.24 mm, p=0.074). Left ven–tricular mass and mass index were comparable. Notably, relative wall thickness was significantly higher in the lowest sodium group (0.49±0.08 vs. 0.42±0.06, p= 0.002). The effects of individualized dialysate sodium were not linearly dose-dependent. Lower iDNa was not associated with significantly lower IDWG or thirst, while cardiac geometry showed potentially relevant differences. These findings suggest that sodium matching to the individual patient may be more important than simply prescribing lower dialysate sodium concentrations.

FC-24

Structural and functional severity of peripheral neuropathy across CKD stages, including hemodialysis: An ultrasonographic, electrophysiological, and clinical correlation study

Cule E

Abstract: Peripheral neuropathy is the most common and frequently underestimated complication of chronic kidney disease (CKD). As kidney function declines, structural and functional nerve damage erodes mobility, sensation, and quality of life in CKD patients. High-resolution ultrasound (HRUS) of the tibial nerve is a non-invasive tool for detecting neuropathy. Still, the relationship between structural (ultrasonographic) and functional/clinical severity across CKD stages, including hemodialysis (HD), remains unclear. We prospectively studied 125 CKD patients (stages 3a–5 and HD) and 28 healthy controls. We measured tibial nerve cross-sectional area (CSA) by HRUS, and findings were correlated with electromyography (ENMG), the Michigan Neuropathy Screening Instrument (MNSI), the Total Clinical Neuropathy Score (TNS), and a structured symptom questionnaire. We also analysed associations with renal function, electrolytes, parathyroid hormone (PTH), and dietary compliance. Tibial CSA was significantly larger in CKD patients than in controls (median 13 vs 10 mm², p<0.001). CSA showed good diagnostic accuracy for ENMG-confirmed neuropathy (AUC 0.85; optimal cutoff ≥13 mm², sensitivity 84%, specificity 75%), with similar performance in diabetic (AUC 0.88) and non-diabetic (AUC 0.85) subgroups. CSA increased progressively from stage 3a to stage 5 (mean 10.7 to 15.7 mm², p<0.001) but plateaued in HD patients (13.0 mm²). In contrast, clinical and electrophysiological severity (MNSI, TNS, symptom score) continued to worsen progressively into the HD stage (all p<0.001). CSA correlated significantly with MNSI (ρ=0.61), eGFR (ρ=−0.58), creatinine (ρ=0.51), potassium (ρ=0.39), and PTH (ρ=0.29) (all p<0.05). Dietary non-compliance was associated with higher potassium, larger CSA, and higher MNSI scores (all p<0.05). In the HD subgroup, dialysis vintage correlated significantly with neuropathy severity (MNSI ρ=0.48, p<0.001; CSA ρ=0.30, p=0.017; median vintage 7 vs 3 years in ENMG-positive vs -negative patients, p<0.001). Tibial nerve HRUS reliably detects CKD-associated neuropathy across all disease stages, with strong diag–nostic accuracy against ENMG. However, structural

nerve enlargement plateaus at advanced pre-dialysis stages, while clinical and electrophysiological severity continues to progress on hemodialysis, suggesting that functional deterioration in HD patients may outpace detectable structural change.

FC-25

Catheter-Related Bloodstream Infections in Haemodialysis: A Nine-Centre Study of Microbiology, Antimicrobial Resistance and Vascular Access

Roglev B, Mitrova E, Taseva E, Kulibrk-Nedelkovska M, Postolovska B, Draskaceva N, Mijakova M, Ilievski S, Cvetkova S, Anakieva M, Nedelkoska M, Misovska N

Abstract: Catheter-related bloodstream infection (CRBSI) remains a major cause of morbidity in haemodialysis patients, particularly in those dependent on central venous catheters. We analysed vascular access distribution, microbiological characteristics, antimicrobial resistance and clinical outcomes of CRBSI across nine dialysis centres in North Macedonia. We retrospectively analysed culture-confirmed CRBSI episodes across nine dialysis centres in North Mace–donia between 1 November 2023 and 31 October 2024 using Centers for Disease Control and Prevention criteria. Catheter colonisation and episodes with missing outcome data were excluded. Microbiological records were reviewed to identify unique clinically significant isolates, with probable contaminants ex–cluded from analysis. Polymicrobial CRBSI required at least two distinct clinically relevant organisms. MDR was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial cate–gories. We included 121 CRBSI episodes in 85 pa–tients; 23 patients experienced recurrent episodes. Male patients accounted for 76 episodes (63%) and those aged 61-80 years for 71 (59%). Non-tunnelled catheters accounted for 87 episodes (72%), predomi–nantly non-tunnelled femoral catheters (78, 64%). Without catheter-day denominators, these data represent episode distribution rather than access-specific infection rates. Microbiological analysis identified 127 unique clinically significant isolates, comprising 87 Gram-positive (69%) and 40 Gram-negative (31%) organisms. Gram-positive isolates were predominantly staphylococci, particularly coagulase-negative staphylococci including Staphylococcus epidermidis and Staphylococcus aureus. Gram-negative isolates were predominantly Escherichia coli, followed by Enterobacter species and Pseudomonas aeruginosa. Six episodes (5.0%) were polymicrobial. Susceptibility data were available for 120 episodes; 67 (56%) were classified as MDR, mainly methicillin-resistant staphylococci. MDR infections had a nume–rically higher rate of complicated clinical course than non-MDR infections (30% vs 19%; p=0.21). Vancomycin was the most frequently prescribed antimicrobial. Death during a CRBSI episode occurred in 5 of 85 patients (5.9%). Complications were not mutually exclusive and included sepsis in 17 episodes (14.0%), catheter thrombosis or occlusion in 8 (6.6%), and metastatic infection in 4(3.3%). In this multicentre cohort, CRBSI episodes predominantly occurred in patients with non-tunnelled femoral catheters and were mainly caused by Gram-positive organisms, with methicillin-resistant staphylococci representing the predominant resistant pathogens. These findings support strategies to minimise non-tunnelled femoral catheter use, strengthen antimicrobial stewardship and facilitate timely definitive vascular access.

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