Invited lectures

IL-01 What do we know about renal functional reserve in adult living kidney donors?

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Introduction. Living kidney donors are an important source of kidneys given the shortage of organs required for transplantation. Good short-term outcomes in living kidney donation has led to more recent acceptance of "borderline" donors (with hypertension, obesity, older age), although recent studies have pointed to increased long term risk in some donor subgroups. The long-term impact of donation on hemodynamics and function of the remaining kidney is less well understood. The capacity of a kidney to increase its glomerular filtration rate (GFR) in response to a higher functional requirement is known as the renal functional reserve (RFR). The change and relevance of RFR after donation in living donors is insufficiently clarified.

Methods. A systematic literature review was performed of studies that assessed RFR in donors pre- and/or post-donation. Web of science, PubMed and EBSCO were searched using the following terms: kidney function, glomerular filtration rate, renal functional reserve capacity, renal blood flow and kidney donor.

Results. 3250 studies published between 1956 and 2019 were identified. Sixteen studies met final inclusion criteria. RFR measurements are not standardized. A trend towards loss of some RFR was observed after donation, although RFR in young donors with no risk factors is largely preserved. Donors with hypertension, obesity or older age had a lower RFR after kidney donation.

Conclusion. RFR testing is rarely done in clinical evaluation of potential living kidney donors. Given the increasing acceptance of borderline donors, better understanding of the relevance of RFR may complement donor assessment and inform long-term risk estimation.

IL-02 UP-TO-date in diagnosis and treatment of membranous glomerulonephritis

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Membranous glomerulonephritis (MGN) is the most common cause of non-diabetic nephrotic syndrome in adults. It may be associated with a secondary cause in 25-30% of the cases. Although the majority of patients present with signs and symptoms of nephrotic syndrome, microscopic hematuria and hypertension and, asymptomatic proteinuria may be seen at presentation. Urinary sediment generally appears benign.

The definitive diagnosis is made by renal biopsy. The main histopathological findings are thickening of the glomerular basement membrane on light microscopy, which should be distinguished from that seen in diabetic nephropathy and renal amyloidosis. The deposition of IgG and C3 across the entire basement membrane on immunofluorescence staining and subepithelial electron-dense immune deposition on electron microscopy are other histopathological features. It is not possible to distinguish between primary and secondary MGN by histopathology.

In the clinical course of MGN spontaneous remission occurs in approximately one-third of patients with nephrotic syndrome. Some clinical, laboratory and histopathological findings are considered as indicators of poor prognosis. Thrombotic complications are most commonly reported in MGN among glomerulonephritis. Therefore, prophylactic anticoagulation is frequently recommended in nephrotic MGN patients.

Recently, 50-80% of idiopathic MGNs were found to have antibodies against M-type phospholipase A2 receptor (PLA2R) in the serum, and in later publications, it was found that this antibody might be present in secondary MGN. This antibody is not detected in any disease other than MGN; hence it is very specific to MGN. Moreover, PLA2R antibody can be found on biopsy tissue at a higher rate (85%). For these reasons, there is strong evidence that MGN can be diagnosed in the presence of PLA2R antibody in patients who cannot undergo renal biopsy (e.g. due to use of anticoagulants, solitary kidney, etc.).

Conservative treatment is recommended to all patients in MGN treatment. The patients can be followed clinically with conservative treatment as there is the possibility of spontaneous remission for 3-6 months. Immunosuppressive therapy should be commenced in patients whose proteinuria do not regress at the end of this period, or earlier in patients who develop complications of nephrotic syndrome or patients who develop rapid renal dysfunction.

The main immunosuppressive therapies used as initial therapy in MGN treatment are; cyclic corticosteroid-alkylating agent (Cyclophosphamide or Chlorambucil), calcineurin inhibitor (cyclosporin-A or Tacrolimus) or Rituximab treatments. Patients can be switched from one treatment to another in case of contraindication, non-response or relapse. GFR and proteinuria are used

in the follow-up. Changes in serum anti-PLA2R levels may also be used in PLA2R positive patients.
In addition to diagnostic utility, anti-PLA2R can also be used as a predictor of response or relapse. Recent studies have highlighted the role of Rituximab in treatment of MGN.

IL-03 Challenges in diagnosis and management of aa amyloidosis

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Amyloidosis constitutes a group of disorders that are characterized by extracellular deposition of amyloid fibrils which are composed of misfolded protein precursors. Amyloidosis is classified according to the protein precursors that form amyloid fibrils. Diagnosis and typing depends on histopathological evaluation. New methods like electron microscopy, mass spectrometry are identified for typing. One of the most common forms of systemic amyloidosis is AA amyloidosis in which amyloid fibrils are derived from serum amyloid A (SAA) protein. AA amyloidosis is a complication of chronic inflammatory diseases. Inflammatory arthritides are the most common underlying diseases, however in some countries, Familial Mediterranean Fever is the most common cause. Renal involvement is a major cause of morbidity and mortality. Identification of genetic factors that regulate susceptibility to deposition of SAA is important for detection of high risk patients. Surrogate biomarkers predicting effectiveness of treatment have been investigated. Management primarily depends on reduction of serum amyloid A production by treating underlying inflammatory condition. Biologic agents may reduce the risk of development of AA amyloidosis as well as treating existing amyloidosis. Drugs that inhibit AA fibrillogenesis and destabilize AA fibrils have recently been employed. It was shown that eprodisate reduced the progression of renal disease by inhibiting polymerization and deposition of fibrils. A novel bis (proline) compound (CPHPC) binds to serum amyloid P component of amyloid fibrils, resulting in rapid clearance.
Significant improvements have been made in understanding pathogenesis, diagnosis and clinical treatment of chronic inflammatory diseases. But AA amyloidosis is still a significant complication that is difficult to prevent and treat. Identification of patients with poor prognosis and detection of effectiveness of treatment modalities by the help of biomarkers are important challenges in prevention and treatment of systemic AA amyloidosis. In recent years, new drugs that control inflammation improved the management of chronic inflammatory conditions and also systemic AA amyloidosis. Novel treatment modalities that inhibit new fibril formation and target deposited fibrils are expected to be further treatment options for patients with AA amyloidosis.

IL-04 Factors influencing the progression in autosomal dominant polycystic kidney disease

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Autosomal-dominant polycystic kidney disease is the most common hereditary kidney disease and it is the fourth leading cause for end stage renal disease in adults. PKD1 and PKD2 are expressed in most organs and tissues of the human body. The proteins that are encoded by PKD1 and PKD2, polycystin1 and polycystin2, seem to function together to regulate the morphologic configuration of epithelial cells. Many factors contribute for progression of the disease. In order to evaluate the factors influencing the progression in adult polycystic kidney disease, we have analyzed the results of several clinical studies of other Nephrology departments, comparing with the results in our department. It is well known that renal cysts contribute to morbidity and can impair the quality of life early in the course of the disease. The size of the cysts formations and the number of the cysts, influence the progression of the disease, but in our study there is not statistical significance for the progression of the renal failure. Younger age at diagnosis and male gender are important in the course of the disease, with earlier progression to renal failure. Arterial hypertension is the most important factor for progression of the kidney diseases which is conformed in our results, especially together with proteinuria in these patients. Urinary tract infections, also infections of the cysts, are important for the progression of the disease. In conclusion we can say that among the other factors influencing the progression, most important are the PKDI gene, gender, age of the patients, hypertension, gross hematuria, urinary tract infections and renal size expressed as renal volume.