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Original Article

Attainment of Clinical Guideline Targets is Associated with Improved Survival in Prevalent Hemodialysis Patients

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Abstract

Introduction. The development and implementation of clinical guidelines aims at delivering better healthcare by means of quality improvement. In a single-centre, retrospective cohort study we examined the association between achievement of guideline targets and clinical outcomes of prevalent hemodialysis patients..

Methods. Forty-seven stable, prevalent, end-stage renal disease patients treated with thrice weekly, in-centre hemodialysis were included in the analysis. The guideline targets examined at the initiation of the study were: 1) use of an arteriovenous (AV) fistula as vascular access or not, 2) haemoglobin ≥ 11 g/dl, and 3) serum albumin ≥ 3,8 g/dl. Mean follow-up time was 11,2±2,0 months.

Results. At baseline, 78,7% of patients had an AV fistula as vascular access, 72,3% of patients had haemoglobin ≥11 g/dl, 76,6% of patients had serum albumin ≥3,8 g/dl, whereas 17,0%,31,9%,48,9% of patients met any one, two or all three guideline targets, respectively. The largest survival benefit was found for the use of an AV fistula (unadjusted mortality hazard ratio: 0,11, p=0,002). The simultaneous attainment of more than one guideline target was also associated, in a graded manner, with lower mortality over the study period (unadjusted mortality hazard ratio: 0,10 and 0,07 for any two or all three guideline targets met, respectively, p<0,05).

Conclusions. The attainment of clinical guideline targets, especially the use of an AV fistula as vascular access, is related to improved mid-term survival in prevalent hemodialysis patients in a single centre and possibly contributes to the so-called centre effect.

Keywords: guidelines, hemodialysis, arteriovenous fistula, haemoglobin, albumin

Introduction

The evolution of modern medical practice over the last decades has relied heavily upon evidence-based data from clinical trials. Alongside this trend, large professional societies have developed and published clinical guidelines based on hard evidence whenever possible and alternatively on expert opinion. These clinical guidelines aim at defining the standard of care and at reducing discrepancies in practice patterns without compromising the role of physician judgement and individualization of patient care. KDIGO (Kidney Disease Improving Global Outcomes) and KDOQI (Kidney Disease Outcomes Quality Initiative) are premier examples of guideline developing organizations of interest to the nephrology community.

In an era of global financial restraints and stringent control over health expenditures, the notion of 'pay for performance' has gained special attention and has incurporated the use of clinical guidelines targets. These act as performance measures and their attainment by the healthcare provider serves as a financial incentive. For example, KDOQI clinical guidelines for vascular access [1], anemia [2] and dialysis adequacy [1] in end-stage renal disease (ESRD) patients are officially endorsed in the United States by a quality improvement program [3] and attaining the specified targets leads to compensation of in-centre dialysis facilities [4].

Several studies have examined the association between achievement of KDOQI parameters, either separately or grouped, and clinical outcomes [5-7]. Decreased mortality and morbidity, lower rates of hospitalizations and lower health costs have been reported for patients satisfying the target values. Among KDOQI parameters, serum albumin, a marker of nutrition and inflammatory status, is considered a strong predictor of mortality in ESRD and, thus, it has been extensively studied [8,9]. Data from Southeastern Europe on the issue of guideline targets attainment in hemodialysis are sparse. We evaluated the relation between achievement of guideline targets and clinical outcomes of prevalent hemodialysis patients in a single-centre study from Greece.

Subjects and methods

Study design and participants

This study is designed as a retrospective cohort analysis. Forty-seven Caucasian prevalent end-stage renal disease patients who underwent thrice weekly chronic hemodia-

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lysis (HD) in a single centre were enrolled. The eligibility criteria were: age more than 18 years and receiving chronic HD for more than 3 months. Exclusion criteria were: scheduled living donor renal transplantation and severe comorbidities (active malignancy, active infection, end-stage organ disease namely cardiac, pulmonary or hepatic failure). Residual renal function was negligible in all patients.

Hemodialysis prescription

All patients were dialyzed for a minimum of 4 hours per session. Extended HD duration was applied whenever clinically indicated. Blood flow rate ranged between 250-300 ml/min and dialysate flow rate was fixed at 500 ml/min as per centre`s protocols. Dialysate composition was individualized according to each patient`s clinical needs. Dialysate sodium ranged from 138 to 142 mmol/l, dialysate calcium ranged from 1,5 to 1,75 mmol/l and dialysate potassium ranged from 2 to 3 mmol/l; rest of the dialysate ingredients were the same among all patients. Sodium or ultrafiltration modeling was not applied. The dialysis monitors in use were the same for all patients (AK 200™ S, Gambro AB, Lund, Sweden). Two types of dialyzers were used during the study period: a high-flux membrane dialyzer (Toraysulfone® TS 2.1, Toray Industries, Inc., Tokyo, Japan) and a low-flux membrane one (Filtryzer® B3 2,0, Polymethylmethacrylate-PMMA membrane, Toray Industries, Inc., Tokyo, Japan).

Study variables

At study initiation the following parameters were categorized as to whether they satisfied the respective KDOQI guideline targets or not: 1) use of an AV fistula as vascular access, 2) haemoglobin ≥11 g/dl, and 3) serum albumin ≥3,8 g/dl (lower normal limit for the reference range of our laboratory). Follow-up clinical assessment was performed monthly during the study period. In addition, biochemical tests were also performed on a monthly basis and the time-averaged values of the latter two independent variables were calculated. All blood samples were analyzed at the same, central, certified laboratory (Medisyn SA). Primary outcome variable was all-cause mortality. Follow-up time was continued until death, kidney transplantation, switch to peritoneal dialysis or loss to follow-up.

Statistical analysis

Descriptive data were expressed as mean ± standard deviation (SD) and percentages of the total. The comparison between baseline and time-averaged values was done using the paired Student's t-test, where appropriate; chi-square test was used for categorical data. We used the Cox proportional hazards model for estimating the association between guideline targets attained and mortality. Model results were summarized by the use of hazard ratio (HR) and 95% confidence intervals (CI). The level of statistical significance was set at $p<0,05$. All analyses were performed using SPSS software, version 17.0 (SPSS Inc, Chicago, IL).

Results

Baseline patient data are displayed in Table 1. Mean patient age was 69,4±15.4 years. Mean time on dialysis was 1,8±1,1 years. 25,5% of the patients were diabetics whereas 50% had cardiovascular disease. Mean follow-up time was 11,2±2,0 months. No patients were switched to peritoneal dialysis, transferred to another HD unit or underwent kidney transplantation during the study period; as such, no losses to follow-up were recorded.

Table 1. Baseline demographic, clinical, laboratory data. URR, urea reduction ratio

Age (years)	69,7	±15,4
Sex: Males (%)	74,5	
Females (%)	25,5	
Diabetes (%)	23,4	
HD burden (years)	1,8	±1,1
AV access: AV fistula (%)	78,7	
AV graft (%)	6,4	
Catheter (%)	14,9	
Causes of ESRD:		
Diabetic nephropathy (%)	18,2	
Glomerulonephritis (%)	13,6	
Hypertension (%)	18,2	
Other/unknown (%)	50,0	
Cardiovascular disease (%)	50,0	
URR (%)	72,5	±5,7
Haemoglobin (g/dl)	11,3	±1,2
Albumin (mg/dl)	3,9	±0,3

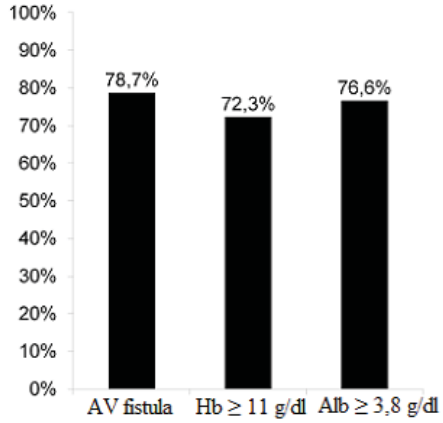

Fig. 1. Percentage of patients with functioning AV fistula, haemoglobin ≥ 11 g/dl and serum albumin ≥ 3,8 g/dl

The percentage of patients with a functioning AV fistula at baseline was 78,7% (Figure 1). Likewise, 72,3% of patients had haemoglobin ≥11 g/dl and 76,6% of patients had serum albumin ≥3,8 g/dl. Time-averaged values of haemoglobin and serum albumin were kept constant over the course of the study and did not differ significantly from baseline. The percentage of patients who simultaneously attained any one, two or three guideline targets was 17,0%, 31,9% and 48,9%, respectively (Figure 2). Of the patient subset who achieved only one target, the majority (62,5%) had achieved the target of haemoglobin ≥ 11 g/dl.

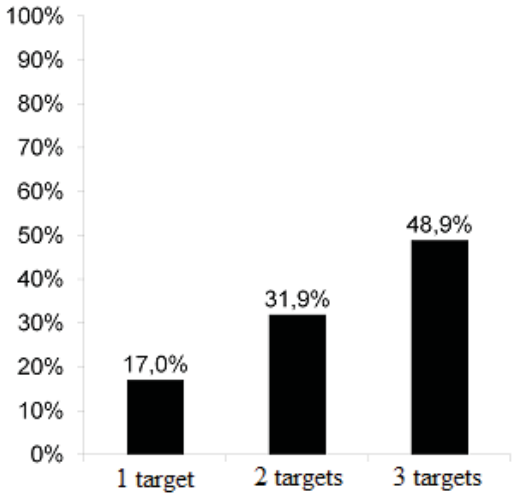

Fig. 2. Percentage of simultaneously attained guideline targets

Seven patients (14,9%) deceased during the follow-up period. Three patients died from cardiovascular causes (abdominal aortic aneurysm rupture, thoracic aortic dissection and ischemic cerebrovascular accident) and three patients from infectious complications. One of them had satisfied one guideline target, four had satisfied two guideline targets simultaneously and the remaining one had satisfied all three guideline targets simultaneously. The unadjusted all-cause mortality hazard ratio for use of a functioning AV fistula was 0,11 (95% CI: 0,02-0,59) (Table 2). Satisfying each individual guideline for haemoglobin ≥11 g/dl and serum albumin ≥3,8 g/dl was also correlated with decreased mortality, albeit it did not reach statistical significance. The simultaneous attainment of more than one guideline targets was also associated with a robust survival benefit. Unadjusted mortality hazard ratio for satisfying any two guideline targets simultaneously was 0,10 and unadjusted mortality hazard ratio for satisfying all three guideline targets was 0,07 ($p<0,05$).

Table 2. Hazard ratio (HR) for mortality associated with guideline targets attained

Guideline target	Frequency (%)	HR (95% CI)
None	2,1	1
AV fistula	78,7	0,11 (0,02-0,59)
Haemoglobin ≥ 11 g/dl	72,3	0,81 (0,15-4,43)
Albumin ≥ 3,8 g/dl	76,6	0,25 (0,05-1,25)

Discussion

The results of this study confirm previous trials that achievement of guideline targets in ESRD patients is associated with reductions in mortality [6,7]. Although patient characteristics of this specific case mix, such as mean age of 69,7 years, mean HD burden of 1,8 years and 50% prevalence of cardiovascular disease, a high risk cohort in terms of morbidity and a potential survivor bias, the proportion of achieved targets may as well reflect the time and efforts consumed by the medical and nursing staff to reach and preserve a survival benefit. An overall 80,8% of the patients had achieved simultaneously two or more of the targets studied, whereas over 70% of them had achieved each of the targets separately. Moreover, the consistency of time-averaged values over follow-up time secures a stable effect during the study period and adds to the strength of the observed outcome. The selection of clinical guideline targets to be studied requires further attention. According to the U.S. ESRD Clinical Performance Measures Project [3] the parameters used for the 'pay per performance' schema of in-centre dialysis facilities are urea reduction ratio (URR) ≥65%, haemoglobin ≥11 g/dl and the use of AV fistula as vascular access. However, differences in clinical practice between U.S. and the rest of the world limit the comparison of URR as a guideline target across different populations. Even in large, multicenter trials [10], mean dialysis session duration in U.S. hardly reaches four hours, which is the minimum accepted norm in Europe and Japan. Consequently, U.S. dialysis units strive to achieve the URR target within these time limitations. By contrast, almost all our patients had URR ≥ 65% and we chose not to use this guideline target because of the obvious bias. Instead, we selected the use of serum albumin, a KDOQI guideline target [11] and a powerful risk marker in ESRD [12], which is influenced by poor nutrition and persistent inflammation. Malnutrition, inflammation and atherosclerosis (MIA) syndrome is rather common in ESRD and, hence, renders the normalization of serum albumin levels a difficult task for the attending nephrologist. The correlation of serum albumin ≥ 3,8 g/dl with mortality failed to reach statistical significance in our study but the simultaneous attainment of this target alongside the other two targets did relate to reduced mortality. The importance of AV fistula as the vascular access of choice in ESRD patients is indispensable. Its use has demonstrated longer access survival half-life and has been associated with fewer complications. Furthermore, timely creation of an AV fistula and avoidance of a central venous catheter has been argued recently to be the principal determinant of superior survival in incident hemodialysis patients, which equals that of incident peritoneal dialysis patient and thus ceasing effectively the controversy over dialysis modality choice for this population [13,14]. Fistula First initiative [15] in the U.S. has been developed solely for the purpose of increasing the rates of native AV fistula use. The utility of haemoglobin as a clinical guideline target is even more plausible partly because it is easily modifiable by the use of erythropoiesis stimula-

ting agents (ESAs). However, caution should be exercised regarding the targeted upper limit of haemoglobin in fear of severe cardiovascular complications [16,17]. In our study, mean haemoglobin was 11,3±1,2 g/dl, whereas in seven patients on ESAs it was over the cutoff of 12 g/dl, ranging from 12,1 to 12,7 g/dl.

The financial implications of guideline targeting reveal a large cost benefit [18]. According to Plantinga, *et al*. [6], attainment of each target resulted in a decrease in annual Medicare hospital payments of approximately $762 per patient-year. Vice versa, every 0,1 decrease in Kt/V was independently associated with an additional $940 of Medicare inpatient expenditures in another study [19]. Moreover, the benefits of reduced hospitalizations on overstressed healthcare systems and on health related quality of life of patients must also be taken into account. Although our study did not address specifically the issue of expenditures and hospitalizations, there is ample evidence that guideline targeting is cost effective.

We feel that certain possible limitations to this study deserve to be mentioned. First of all, the small sample size of a single centre study may attenuate the robustness of our results. On the other hand, there exists a homogeneous approach by the healthcare providers in the same clinical setting that reduces variability in practice and prevents suboptimal performance. Secondly, the retrospecttive, observational nature of this study demonstrates associations among the study variables and outcomes but it cannot prove causality. Residual confounding due to unknown variables cannot be excluded with certainty.

In conclusion, the attainment of clinical guideline targets represents a therapeutic challenge requiring strenuous efforts and vigilance by the healthcare team. Nevertheless, the potential benefits are becoming more and more tangible. Our study adds to the existing literature that improved survival is a feasible outcome together with reduced morbidity and expenditure costs.

Conflict of interest statement. None declared.

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