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Original Article

Reaching Target Hemoglobin Level and Having a Functioning Arteriovenous Fistula Significantly Improve One Year Survival in Twice Weekly Hemodialysis

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Abstract

Introduction: This is a prospective study of a cohort of 1011 patients maintained on regular hemodialysis (HD) in Khartoum, Sudan, studied in the year 2009 and re-evaluated one year later. Their survival rates in November 2010 were related to their baseline characteristics.

Methods: Demographic and clinical data of studied patients was collected by direct patient interviews and dialysis records revision. Survival rates were calculated using the Kaplan Meier method.

Results: Patients had a median age of 45 years and a median duration on dialysis of 25 months. Two thirds of patients were males and 4.2% were children. Studied patients had a one-year survival rate of 86%. Most patients (74.8%) received twice weekly HD, and their survival rate was lower than patients receiving thrice weekly HD (85% versus 89%, P = 0.06). The strongest independent predictors of mortality were lack of a documented measure of dialysis adequacy (HR = 2.7, P = 0.00), poor functional capacity (HR = 2.4, P = 0.00), lack of a functioning AV fistula (HR = 2.0, P = 0.00), age ≥ 65 years (HR = 1.6, P = 0.02) and cardiovascular disease (HR = 1.5, P = 0.04). Patients with hemoglobin level < 10 g/dl had significantly lower survival rates (81% versus 92%, P = 0.00) compared to other patients. HD patients' perception of their own general health was also significantly correlated to their survival rates (P = 0.00).

Conclusion: Patients on thrice weekly HD did marginally better than those on twice weekly HD. In the latter group, however, having an AV fistula and a hemoglobin level of > 10 g/dl appeared to have a positive effect on their survival. Twice weekly HD could be acceptable for many patients provided other aspects of renal care are cared for adequately.

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Introduction

In June 2009, we conducted a national survey for end stage renal disease (ESRD) patents maintained on renal replacement therapy (RRT) in Sudan [1]. At that time, there were 41 working hemodialysis (HD) centers in the country serving a total of 2858 patients. The majority of these patients were being dialyzed in Khartoum; where there were 12 governmental HD centers serving 1003 patients and 16 private HD centers serving 1069 patients.

During the ensuing months, restructuring of HD services in Khartoum resulted in the closure of 15 private HD centers and the creation of additional governmental centers. In November 2010, we conducted another survey of the thirteen HD centers from the original cohort that continued to provide HD services in Khartoum. A total of 1011 patients were being dialyzed in these 13 centers in June 2009. This included 968 adult and 43 pediatric ESRD patients who had been established on HD for three months at least. One of the aims of this second survey was to evaluate the survival of this cohort of patients and relate it to their base-line characteristics.

Methods

Data of prevalent HD patients was collected by direct patient interviews and included demographic data, the most probable cause of ESRD, diabetic status, duration on HD, number of HD sessions, vascular access, urine volume and personal history of ischemic heart disease, cerbrovascular disease or peripheral vascular disease. Ischemic heart disease was defined by history of angina, myocardial infarction or coronary intervention. Cerebrovascular disease was defined by history of stroke or transient ischemic attacks. Peripheral

Table 1: Status of the study cohort of prevalent HD patients after one year follow-up (N = 1011)

Status	Number	Proportion
Regular dialysis at the same HD center	676	66.9
Referred to another HD center	81	8
Dead	152	15
Received a kidney transplant	47	4.6
Transferred to peritoneal dialysis	10	1.0
Regained dialysis independence	1	0.1
Lost to follow up	44	4.4
Total	1011	100

vascular disease was defined by history of intermittent claudication, amputation due to ischemia or peripheral revascularization. Patients were asked whether they needed assistance from family members in activities of daily living, and considered to have poor functional capacity if such assistance was required. Patients were also asked to rate their evaluation of their own general health on a Likert-type scale composed of five items; excellent, very good, good, acceptable and poor. Data related to hemoglobin level and measurements of dialysis adequacy within the previous month was collected form patients' medical records. The pre-HD and post-HD blood pressure (BP) measurements of the previous three HD sessions were recorded and their average taken.

Analysis was done using SPSS for windows version 19 (SPSS Inc. Chicago, IL, USA).Unadjusted survival rates were estimated using Kaplan-Meier survival analysis and compared using the log rank test. Patients were censored at the time of transplantation, transfer to another dialysis modality or referral to another HD center. Cox regression analysis was used to estimate the hazard ratio of potential risk factors. Variables with more than 5% missing data were not included in cox regression analysis. Proportions were compared using Chi-square test. P values less than 0.05 were considered statistically significant.

Results

The median age of prevalent HD patients in this study was 45 years (range: 6-95 years). Fifteen percent of patients were aged ≥ 65 years and 4.2% were children aged ≤ 18 years. Two thirds of patients were males. The median duration on dialysis was 25 months, 22% of patients had been maintained on HD for ≥ 5 years and 3% had been maintained on HD for ≥ 10 years.

The most probable cause of renal failure was undetermined in 41% of patients, hypertension (25%), diabetes mellitus (10%), obstructive uropathy (11%), glomerulonephritis (4%), polycystic kidney disease (3%), and pyelonephritis (3%).

Diabetic patients constituted 12% of the study population. Cardiovascular disease (CVD) was reported by 12.2% of patients at baseline, including 7% patients with history of ischemic heart disease, 4% with history of cerebrovascular disease and 3.7% with history of peripheral vascular disease. Half the patients were anuric. Fifteen percent of patients had poor functional capacity and required assistance from family members in activities of daily living.

The majority of patients (74.8%) received two sessions of HD per week and most patients (82.6%) had a functioning arteriovenous fistula (AVF) at baseline. Both the target pre-dialysis blood pressure (BP) of < 140/90 mmHg and the target post-dialysis BP of < 130/80 mmHg were achieved by 30.2% of patients. Fifty percent of patients had hemoglobin level ≥ 10 g/dl. Eighteen percent of patients had a documented measure of dialysis adequacy (urea reduction ratio).

Table-1 outlines the status of this cohort of prevalent HD patients after one year of follow-up. During the original survey, 226 patients from the study cohort (23%) stated that they were being prepared for live-related kidney transplantation. Of those, only 38 patients (16.8%) received a kidney transplant during the following year.

The one-year survival rate in this group of prevalent HD patients was 86%. In Cox regression analysis, the strongest independent predictors of poor survival were lack of a documented measure of dialysis adequacy, poor functional capacity, lack of a functioning AV fistula, age ≥ 65 years and CVD (Table-2).

Table 2: The mortality hazards associated with various baseline characteristics of the study cohort of prevalent HD patients

Baseline characteristics	HR	95% CI	P value
Age ≥ 65 years	1.6	1.1-2.2	0.02*
Male gender	1.3	1.0-1.8	0.1
Duration on dialysis (months)	1.0	0.9-1.01	0.7
Diabetes mellitus	1.2	0.8-1.9	0.3
Cardiovascular disease	1.5	1.0-2.3	0.04*
Poor functional capacity	2.4	1.7-3.5	0.00*
Lack of a functioning AV fistula	2.0	1.4-2.9	0.00*
No documented measure of dialysis adequacy	2.7	1.6-4.7	0.00*
Twice versus thrice weekly HD	0.9	0.7-1.5	0.9

HR: hazards ratio; CI: confidence interval
* Statistically significant

The one-year survival rate of patients undergoing thrice weekly HD was 89% compared to 85% for patients undergoing twice weekly HD (P = 0.06). More chidren were offered thrice weekly HD compared to adults (63% versus 23%, P = 0.00). There was no difference in age or gender between adult patients receiving thrice or twice weekly HD. Adult patients receiving thrice weekly HD were more likely to be anuric (76.5% versus 41.7%, P=0.00) and to have CVD (17.3% versus 11.1%, P=0.01) compared to patients receiving twice weekly HD. They were also more likely to achieve pre-HD BP targets (61.5% versus 54.5%, P=0.047), to achieve post-HD BP targets (42.8% versus 31.5%, P=0.00), to have a hemoglobin level ≥ 10 g/dl (59.1% versus 46.5%, P=0.01) and to have a documented measure of dialysis adequacy (42.7% versus 10.7%, P=0.00).

The strongest independent predictors of poor survival among patients undergoing twice weekly HD were poor functional capacity (HR = 2.6; P = 0.00), lack of dialysis adequacy monitoring (HR = 2.5, P = 0.01), lack of a functioning AV fistula (HR = 2.0, P = 0.00), age ≥ 65 years (HR = 1.9, P = 0.001) and male gender (HR = 1.6, P = 0.01).

The strongest independent predictors of poor survival among patients undergoing thrice weekly HD were lack of dialysis adequacy monitoring (HR = 3.1, P = 0.01), lack of a functioning AV fistula (HR = 2.8, P = 0.01), poor functional capacity (HR = 2.8, P = 0.02) and CVD (HR = 2.5, P = 0.03). There was no significant difference in survival probability between males and females in this group of patients.

Data related to hemoglobin level, urine output and blood pressure readings were missing for 47%, 16% and 16% of patients respectively, hence these three variables were not included in the cox regression model. However, patients with hemoglobin level < 10 g/dl had a significantly higher mortality hazard compared to patients with hemoglobin level ≥10 g/dl (HR = 2.1, CI 1.4-3.1, P = 0.00). Patients with a baseline pre-HD BP ≥ 140/90 mmHg also had a significantly higher mortality hazard compared to patients with pre-HD BP < 140/90 mmHg (HR = 1.4, CI 1.0-1.9, P = 0.02).

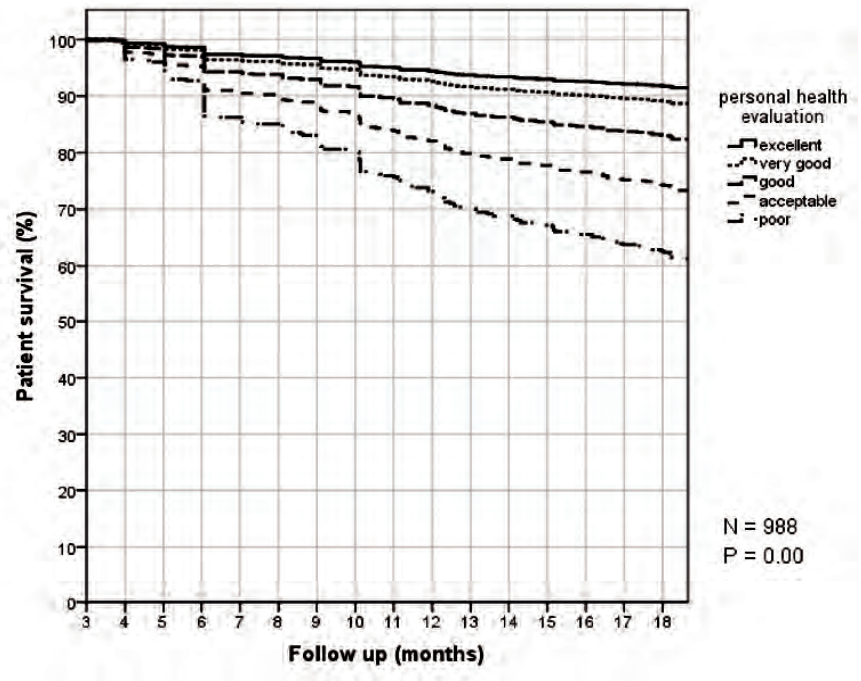
During the original survey, prevalent HD patients were asked to rate their evaluation of their own health on a Likert-type scale. Patients who thought their general health was “excellent”, “very good”, “good”, “acceptable” and “poor” constituted 3.8%, 15.6%, 48.7%, 25.9% and 6% of the study population respectively. This evaluation was closely reflected on those patients’ survival probabilities (Figure-1).

Discussion

The cohort of patients of this study represents 37% of patients who were maintained on regular dialysis in Sudan in 2009. Their baseline characteristics closely reflect the characteristics of the Sudanese dialysis population as described in a previous report [1]. We believe that the findings of this study provide reasonable estimates of the outcomes of dialysis services at the national level.

The one-year survival rate for prevalent adult dialysis patients in this study (86%) is similar to the reported survival rate of prevalent adult dialysis patients in UK in 2009 (86.2%) [2]. However, it must be noted that dialysis patients in UK have a higher median age and a heavier comorbidity burden than the current study population. On the other hand, life expectancy at birth among UK general population is 78 years for males and 82 years for females compared to 59 years for males and females

Figure 1: Survival curves of prevalent HD patients according to their rating of their own general health at baseline (N=988, P=0.00)



in Sudan [3]. Such differences in patient and population characteristics make direct comparison of survival rates inappropriate.

In Sudan, most patients are offered twice weekly HD for economic reasons. Earlier K-DOQI guidelines set thrice weekly sessions as the minimum frequency level of adequate HD. This standpoint changed in response to an important cross-sectional study from the USA that reported lower mortality risk (RR = 0.76, P = 0.02) for twice weekly HD compared to thrice weekly HD among prevalent patients. The authors attributed this survival advantage to patient selection and greater residual kidney function (RKF) among patients maintained on twice weekly HD [5]. The most recent K-DOQI guidelines recommend two to six HD sessions per week, provided that the HD schedule is tailored to achieve a minimum standard Kt/V of 2.0 per week [4]. In the absence of RKF, it is not possible to reach this target using a twice-weekly schedule. Thus, twice-weeklydialysis is only permissible in a few patients with RKF greater than 2 ml/min/1.73m^2 who have stable function and do not have excessive fluid gains [4].

Intermittent dialysis has reduced efficiency when compared to continuous dialysis; efficiency defined as the effect of lowering solute concentration achieved for a given level of dialysis dose. Intermittent dialysis is also less likely to achieve adequate volume control in anuric patients. In a representative sample of the US dialysis population undergoing thrice weekly HD, mortality and cardiovascular event rates were significantly higher on the day after the long (2-day) interdialytic interval compared to other days [6]. Patients undergoing twice weekly HD are required to tolerate an even longer interdialytic interval of three days. The higher mortality observed in patients undergoing twice weekly HD in this study is not unexpected, bearing in mind that 42% of them had no significant RKF.

The quality of delivered HD is of no less importance than the number of weekly HD sessions. In this study, lack of a documented measure of dialysis adequacy was consistently associated with increased mortality, even among patients receiving three sessions of HD per week. Lower survival rates achieved by males compared to females on twice weekly HD are likely to be due to under-dialysis. Males generally have a larger muscle bulk and are less likely to achieve adequate dialysis on a twice weekly regimen.

More than 80% of HD patients in this study were dialyzed through an arteriovenous fistula (AVF), in accordance with published guidelines. Dialysis via a central venous

catheter (CVC) doubled the one-year mortality hazard compared to a functioning AVF. Moreover, there was no difference in mortality hazard between cuffed and non-cuffed HD catheters. The significantly increased mortality of patients undergoing dialysis through a CVC is well documented in the literature [7-10]. Data from the USRD system reveals that vascular access complications account for 16-25% of hospital admissions of HD patients. The relative mortality risk was higher for patients with CVC compared to AVF (RR = 1.5, P < 0.002). Cause-specific analysis found higher infection-related deaths for CVC compared with AVF in both DM (RR = 2.3, P < 0.06) and non-DM patients (RR = 1.8, P < 0.04). Deaths due to cardiac causes were also significantly higher in CVC than AVF for both DM (RR = 1.5, P < 0.05) and non-DM patients (RR = 1.3, P < 0.05) [8]. In an analysis of the UK Renal Registry, the mean percentage of prevalent HD patients using definitive access (AVF or AVG) in a center was 69.8% in 2005. There was a small but significant positive association between the percentage of HD patients using an AVF or AVG in a center and one-year uncensored survival. The type of access in use was able to explain 6% of the variation in center level survival [9]. In fact; a recent study attributed the survival advantage of PD compared to HD in the first 1-2 years to the higher rates of CVC use at the initiation of HD. After analyzing data of 40,526 incident dialysis patients from the Canadian Organ Replacement Register, the authors found that the one-year mortality of HD-AVF/AVG patients was similar to PD patients while HD-CVC patients had an 80% higher mortality [10].

HD patients perceptions of their own health in this study were closely reflected on their survival rates. Illness perceptions have been shown to be important determinants of functional and psychosocial outcomes, including quality of life and treatment adherence in patients with chronic diseases. In a small prospective study in UK, 223 HD patients completed the Revised Illness Perception Questionnaire. Treatment control perceptions demonstrated a significant association with mortality (HR = 0.9, P = 0.03) independently of other survival risk factors including comorbidity [11].

In our opinion, the most important aspect of this study was demonstrating the impact of vascular access and hemoglobin level on patient survival. These two factors appear to have a greater effect on patient survival than the mere number of weekly HD sessions. It is estimated that a non-diabetic patient aged 19-64 years who is maintained on twice weekly HD would have a one-year survival probability of 97% if he had a functioning AV fistula and hemoglobin level ≥10 g/dl at baseline. The same patient would have a one-year survival probability of 72% if he was being dialyzed through a central venous catheter and had hemoglobin level <10 g/dl at baseline. Economic barriers prevent the provision of thrice weekly HD for the majority of patients in our setting. Nevertheless, we believe that improving other aspects of patient care would still have a significanst impact on outcomes.

Conclusion

Treatment outcomes of HD services in Sudan are acceptable despite the economic limitations. There are deficiencies in several aspects of HD patient care, including quality assurance of delivered dialysis dose and management of anemia. Lack of a documented measure of dialysis adequacy and lack of a functioning AV fistula were two of the strongest independent predictors of poor survival among prevalent HD patients.

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