Geriatric comorbidities, such as falls, confer an independent mortality risk to elderly dialysis patients

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Abstract

Background. As the number of patients aged ≥65 years starting haemodialysis (HD) continues to increase, more patients are at risk of falls, functional decline and cognitive impairment. In an earlier prospective cohort study, we showed that 44% of elderly HD patients had more than one fall within a 1-year period. The objective of this study was to assess whether falls remained predictive of increased mortality risk even after controlling for age, comorbidity, dialysis vintage and laboratory variables.

Methods. Using a prospective, cohort study design, patients aged ≥65 years and on chronic HD during the period April 2002–2003 were recruited. Patients were followed biweekly, and falls occurring within the first year were recorded. Outcome data were collected until death, study end (30 December 2006), transplantation or transfer to another dialysis centre.

Results. A total of 162 patients were followed for a median of 32.7 months (quartiles 14–57). In a univariate Cox model with a time-dependent variable for falls status, survival was worse amongst fallers compared to non-fallers (HR 2.13, 95% CI 1.32–3.45; P = 0.002). After adjustment for age, dialysis vintage, comorbidity and laboratory variables, falls were a significant predictor of mortality (HR 1.78, 95% CI 1.07–2.98, P = 0.03). Exclusion of falls associated with concurrent illnesses did not alter the results (HR 1.63, CI 1.02–2.28 P = 0.05).

Conclusions. We conclude that the occurrence of more than one accidental fall in a community-dwelling HD patient aged ≥65 years is associated with an independent increased risk of death. As fall interventions are effective, screening HD patients for falls may be a simple measure of clinical importance.

Keywords: accidental falls; geriatric nephrology; haemodialysis; mortality; predictive model

Introduction

The absolute number of patients aged over 65 years starting dialysis continues to increase internationally [1–4]. Survival rates are modest, with administrative data suggesting higher mortality in those with poor mobility [5,6]. Factors associated with high mortality include increased comorbidity, age, low haemoglobin levels, malnutrition and inflammation, and disorders of mineral metabolism (notably high calcium and phosphate levels). As a result of ageing, many patients on chronic haemodialysis (HD) are at risk of problems such as accidental falls and functional and cognitive impairment. In the general geriatric population, accidental falls are common, particularly in those with chronic debilitating diseases [7–11]. Falls have been shown to result in increased hospitalizations, the need for long-term care and increased mortality [12–15].

Within the chronic HD population, the high degree of comorbidity, rapid shifts in volume status occurring as a direct result of dialysis ultrafiltration and polypharmacy are some factors that place patients at an increased hypothetical risk of falls [16,17]. In a prospective cohort study, we reported that 44% of HD patients had one or more falls over a 1-year period [18]. Of these patients, more than half had multiple falls [average number of falls 2.8 (95% CI 1.8–3.8)] with injuries being common. Many patients reported cuts, bruises or other minor injuries and 19% of patients who had a fall sought medical attention as a direct result of their fall. We hypothesized that the occurrence of accidental falls is an easily identifiable marker that places HD patients at an increased risk of death. The objective of this study was to assess whether falls independently predicted death in a population of chronic HD patients aged 65 years or more, after controlling for age, comorbidity, dialysis vintage, haemoglobin, albumin and mineral metabolism.

Subjects and methods

Using a prospective cohort study design, all end-stage renal disease patients ≥65 years undergoing HD treatment...
at the outpatient dialysis unit of the University Health Network during the period 9 April 2002 to 9 April 2003 were approached to participate in the study [18]. Both patients newly starting on HD (incident cases) and patients chronically on HD (prevalent cases) were eligible. Patients were excluded if they were unable or unwilling to provide informed consent. Patients who lived in a long-term institutional setting were excluded. Baseline assessments were conducted by a research study nurse using standardized protocols. These protocols have been previously reported in detail [18]. In brief, the medical history, including cause of end-stage renal disease and comorbid conditions, was abstracted from the clinical and electronic chart records. The Charlson Comorbidity Index was used to summarize medical comorbidity based on previous studies validating its use in dialysis patients [19]. A full medication history, dialysis history and laboratory history (haemoglobin, serum albumin, serum calcium and serum phosphate levels) was recorded for each subject. Three consecutive values of each laboratory test, taken at 1-month intervals, were averaged. Falls were recorded prospectively using a standardized method [20]. A fall was defined as an event, which resulted in a person coming to rest inadvertently on the ground or other lower level [20].

Patients were monitored for accidental falls using biweekly interviews in the HD unit [18]. Subjects were considered to be fallers if they sustained one or more falls during the fall observation period. Patient outcome was followed until death or until study end (31 December 2006). Subjects were censored if they were transferred to another dialysis facility, underwent kidney transplantation, had renal recovery or were lost to follow-up. Death, kidney transplantation and facility transfer dates were confirmed using data from the local Toronto Area Dialysis Registry. This is a prospectively maintained dialysis registry for all patients on renal replacement therapy within the Toronto region.

Acute illnesses occurring within a 2-week period of the fall (1 week before or 1 week after the fall) were noted. Such illnesses were defined as any illness requiring a visit to the emergency room, admission to hospital, symptoms precipitating further investigation with non-routine blood tests, radiological or cardiac investigations or referral to a specialist. Fractures, cuts or bruising occurring directly as a result of the fall were not included as an acute illness.

Ethics approval was granted by the University Health Network Research Ethics Board.

Statistical methods

Demographic data were summarized using the mean and standard deviation (SD) or median and quartiles for continuous variables and percentages for categorical data. Survival analysis techniques were used to assess patient survival.

Survival was defined as the time from start of study to death, end of the follow-up or transplantation. For the purposes of the analysis, we assumed that all patients were non-fallers at the start of the study. Once a subject fell, he or she switched groups to become a faller, thus fulfilling the criteria as a time-dependent variable. Among subjects who fell, the time at risk prior to a fall is allocated to the non-faller group and the time at risk after the fall is allocated to the faller group. A graphical presentation of the survival of fallers versus non-fallers was made using an adaptation of the Kaplan–Meier product-limit estimator [21]. A Cox proportional hazards model was used to fit a time-dependent variable for fall status in a univariate model as well as in a multivariable model that adjusted for other known risk factors for death in this population. These risk factors were comorbidity, dialysis vintage, age at the time of study entry, mean haemoglobin, mean serum albumin, mean serum calcium–phosphate product and dialysis adequacy as measured by the percent reduction of urea (PRU). The proportionality of hazards over time was assessed for all variables [22].

In a secondary analysis, all falls occurring in relation to an acute illness, as defined above, were excluded. Univariate and multivariable analyses were performed as described above.

All survival analyses were performed using the survival package in the R statistical software (R-Core Development Group, R Foundation of Vienna, Austria, 2004, v 2.0.1). A significance level of 0.05 was used in all analyses.

Results

Of 182 potential participants, 162 (89%) agreed to participate. Patients had a mean age of 74.7 years and were on dialysis for a median of 2.3 years at the time of study entry (Table 1). Forty-five percent were diabetic [18]. Over the fall follow-up period, a total of 305 falls occurred in 76 patients. Forty-three percent of those who fell had only one observed fall. The remaining 57% of patients had between 2 and 48 falls (median 2.0 falls) [18].

Patients who had falls were more likely to be older, have a higher number of comorbid illnesses and have diabetes. In addition, patients who had initiated renal replacement therapy more recently had an increased risk of falling. Baseline clinical laboratory results appeared to be similar in both faller and non-faller groups (Table 1).

Two-year survival was estimated at 63% (CI 55–70%). One hundred and one patients died during the follow-up period (median time to death 17.6 months, quartiles 10.1–32.7 months). Data for 17 patients were censored prior to the study end (5 transplant, 1 renal recovery and 11 transferred to another HD centre). Of those who died, 48 had no falls during the 1-year monitoring period for falls. In the univariate Cox regression, mortality was significantly increased by falls (HR 2.13; 95% CI 1.32–3.45, P = 0.002) (Figure 1). After adjustment for known predictors of dialysis mortality, falls were a significant predictor of death (HR 1.78; 95% CI, 1.07–2.98, Table 2). In a separate analysis where a separate HR was fitted for each of the four time intervals after a first fall, the risk of death after a fall did not appear to consistently increase or decrease with time since the first fall [HR 1.9 (0.9–3.8) within 0–6 months, 2.1 (1.1–4.1) within 6–12 months, 1.6 (0.6–4.2) within 12–18 months and 3.8 (1.5–9.9) for >18 months]. All tests
Table 1. Table showing patient demographics at the start of the study [18]

<table>
<thead>
<tr>
<th></th>
<th>Final study participants</th>
<th>Fallers (≥1 fall during 1 year f/u)</th>
<th>Non-fallers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 162</td>
<td>n = 76</td>
<td>n = 86</td>
</tr>
<tr>
<td>Mean age, in years, at time of RRT start (SD)*</td>
<td>74.7 (6.1)</td>
<td>75.8 (6.3)</td>
<td>73.9 (5.4)</td>
</tr>
<tr>
<td>Median duration, in years, on RRT at study start (range)</td>
<td>2.3 (0–26)</td>
<td>2.4 (0–26)</td>
<td>3.4 (0–24)</td>
</tr>
<tr>
<td>Number of incident patients (%)</td>
<td>20 (11.9%)</td>
<td>5.1%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Male%*</td>
<td>57%</td>
<td>66%</td>
<td>48%</td>
</tr>
<tr>
<td>Primary renal disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>27%</td>
<td>34%</td>
<td>20%</td>
</tr>
<tr>
<td>Renovascular or hypertensive</td>
<td>28%</td>
<td>29%</td>
<td>27%</td>
</tr>
<tr>
<td>Glomerulonephritis, systemic disease/collagen vascular disease</td>
<td>12%</td>
<td>8%</td>
<td>16%</td>
</tr>
<tr>
<td>Other</td>
<td>28%</td>
<td>26%</td>
<td>30%</td>
</tr>
<tr>
<td>Unknown</td>
<td>5%</td>
<td>3%</td>
<td>7%</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean systolic BP post–HD</td>
<td>139 ± 20</td>
<td>137 ± 21</td>
<td>141 ± 20</td>
</tr>
<tr>
<td>Mean diastolic BP post–HD</td>
<td>71 ± 10</td>
<td>70 ± 10</td>
<td>71 ± 10</td>
</tr>
<tr>
<td>Mean Charlson score (SD)*</td>
<td>8.7 (1.8)</td>
<td>9.6 (1.7)</td>
<td>8.4 (1.4)</td>
</tr>
<tr>
<td>Lab values</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean haemoglobin g/L (SD)</td>
<td>117 (12)</td>
<td>115 (13)</td>
<td>118 (11)</td>
</tr>
<tr>
<td>Mean creatinine µmol/L (SD)</td>
<td>723 (188)</td>
<td>704 (165)</td>
<td>743 (203)</td>
</tr>
<tr>
<td>Mean albumin g/L (SD)</td>
<td>37 (3)</td>
<td>37 (3)</td>
<td>38 (3)</td>
</tr>
<tr>
<td>Mean calcium mmol/L (SD)</td>
<td>2.4 (0.2)</td>
<td>2.4 (0.2)</td>
<td>2.4 (0.2)</td>
</tr>
<tr>
<td>Mean phosphate mmol/L (SD)</td>
<td>1.5 (0.4)</td>
<td>1.5 (0.5)</td>
<td>1.5 (0.4)</td>
</tr>
<tr>
<td>Intact PTH τ pmol/L (median &amp; quartiles)</td>
<td>18 (6–36)</td>
<td>16 (7–29)</td>
<td>19 (6–47)</td>
</tr>
<tr>
<td>Mean PRU% (SD)</td>
<td>75.0 (6.6)</td>
<td>73.3 (3.3)</td>
<td>76.3 (6.2)</td>
</tr>
</tbody>
</table>

*P < 0.05 between fallers and non-fallers.

Fig. 1. Survival of patients who had one or more falls during the follow-up period (grey line) compared with those who had no falls (black line). Survival probability was calculated using a time-dependent regression model where all patients were defined as being non-fallers at the start of the study. Once a subject fell, he or she switched groups to become a fal ler. Among subjects who fell, the time at risk prior to a fall was allocated to the non-faller group and the time at risk after the fall was allocated to the fal ler group.

for the proportional hazards assumption gave P > 0.1; the global test had P = 0.85 and the fall variable had P = 0.8.

Sixty-three falls were associated temporally with an acute illness, and were thus excluded in a secondary analysis. Twenty-two falls were excluded because they occurred within 1 week of admission to, or discharge from, hospital. Of those not associated with an admission, falls were excluded because they were associated with cardiac symptoms, deep venous thrombosis, infection, syncope, foot ulceration or lower limb ischaemia, or a gastrointestinal bleed. A further 11 falls were excluded because patients had non-specific symptoms, were seen by an MD and had additional investigations performed although no diagnosis was made. After exclusion of these falls, 69 patients had 242 falls over the follow-up period. Univariate Cox regression results remained similar with a falls HR of 1.9 (95% CI 1.2–3.1, P = 0.006) (Figure 2). After adjustment for known predictors of dialysis mortality, falls remained a significant predictor of death (HR 1.63; 95% CI, 1.02–2.28). All tests for the proportional hazards assumption gave P > 0.1; the global test had P = 0.9 and the fall variable had P = 0.9.

Discussion

This is the first report to show an association between accidental falls and increased mortality in the older HD
population. On univariate analysis, falls were associated with doubling of the risk of death. On multivariable analysis, after correction for commonly recognized predictors of mortality in HD patients, the risk of death in those who experienced a fall was still 1.8 times that of individuals who had no fall. In our analysis, the risk of death associated with a fall was higher than the risk of death associated with a 1-year increase in dialysis vintage, a 1-year increase in age or with changes in haemoglobin, serum albumin and the calcium–phosphate product.

Accidental falls may be precipitated by concurrent acute medical illnesses such as stroke or arrhythmia, which themselves may be associated with an increased mortality risk. Thus, we hypothesized that the observed effect of falls on mortality may in some instances be related to acute illnesses that precipitated the falls. To overcome this potential confounder, we identified all acute medical illnesses occurring around the time of a fall, and made the assumption that any fall occurring during this period was precipitated by the illness. We used strict criteria to identify falls that should be excluded in the secondary analysis. By excluding falls that resulted in hospitalization, we may have excluded some falls that resulted in hospitalization to facilitate investigation for a cause of the fall and thus have led to an underestimation of the impact of falls on mortality. The observation that our results remained unchanged after exclusion of all falls associated with acute illness, however, suggest that the association between falls and increased mortality is robust.

To adjust for the survival effect of including both prevalent and incident HD patients, we included dialysis vintage as an explanatory variable in the regression model. After correcting for dialysis vintage, falls remained highly predictive of death. Since one of the strongest predictors of a fall is a past history of falls, we explored the effect of having reported a fall prior to study enrolment by including previous falls as a risk factor. A large number of patients who previously reported a fall fell again during the monitoring period, and the inclusion of a past history of falls as a variable in the model did not alter the results.

An association between increased mortality and falls has previously been recognized in older individuals without end-stage renal disease. Complications related to falls, such as fractures or head injuries, are the leading cause of death from injury in the general population over the age of 65 years [23]. Falls are the sixth most common cause of death in older individuals [10,23,24]. Deaths directly attributable to falls are estimated to occur in 2 per 1000 community-dwelling individuals aged over 65 years [13,14,24,25].

Although fall-related injuries are the sixth most common cause of death in the elderly, most fall events in this study did not directly lead to death. Rather, we believe that falls are a marker of frailty in the HD population, and are consistent with the observation that HD patients who cannot walk have higher mortality rates [5]. Frailty is a syndrome of impaired homeostasis and resistance to stresses that leads to an individual’s increased vulnerability and risk of adverse outcomes including disease progression, falls, disability and premature death [26]. While an exact definition is still debated, characteristics of a frailty phenotype have been identified including weakness, poor endurance, reduced physical activity, slow gait speed and unintentional weight loss [27]. Frailty is associated with increased hospitalization, loss of functional independence, the need for long-term care and death [15,27–31]. Numerous interventions have been shown to reduce fall rates and/or prevent the injury associated with falls. These include multifactorial assessment and intervention, exercise strengthening and balance programmes and the use of hip protectors in institutionalized populations (which serve to reduce the injury resulting from falls rather than limiting the number of falls) [32–34]. Vitamin D supplementation, in the form of ergocalciferol or cholecalciferol, has been shown to prevent falls and fall-related fractures [35]. During the study timeframe, 25-vitamin D levels were not routinely monitored in dialysis patients, and the use of products containing vitamin D were discouraged. Nevertheless, many patients (43%) were prescribed activated vitamin D analogues for renal bone metabolism problems. We did not attempt to adjust for the use of 1,25-vitamin D analogues, since a simple statistical adjustment would not adequately reflect the complex story of bone mineralization, adynamic bone disease or vascular calcification in dialysis patients. We did collect data on serum parathormone levels, and serum calcium and phosphate levels, and have reported those in the baseline data.

Levels were not statistically different in fallers compared with non-fallers; however, we acknowledge that most physicians within our practice do follow the Kidney Disease Outcomes Quality Initiative guidelines, and thus there was little variability in the mean levels. The variable ‘calcium–phosphate product’ was included in our regression model, as we feel that it reflects the increased mortality risk associated with both bone disease and vascular calcification.

In conclusion, we report a significant association between falls and increased mortality in older dialysis patients. Studies are needed to assess whether the identification and referral, of dialysis patients who fall, for a specialized interdisciplinary geriatric assessment may improve
survival and quality of life, as well as reduce health care resource utilization.

Acknowledgements. The authors would like to thank the patients and staff who participated in this project, in particular Dimitra Jovanovich for her diligent and thorough work. This project was funded by the Physicians’ Services Incorporated Foundation.

Conflict of interest statement. S. V. Jassal has no conflict of interest with respect to this article but is currently acting as a consultant for Amgen Canada and has held investigator-led grant funding from OrthoBiotec. She has received speaker fees from Pfizer, Amgen, OrthoBiotec and Bristol Myers Squibb in the past 5 years. This article was presented in abstract form at the American Society of Nephrology Meeting in San Diego, 2006. Other authors have nothing to declare.

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Received for publication: 8.8.07
Accepted in revised form: 4.10.07