Short daily haemodialysis: survival in 415 patients treated for 1006 patient-years

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Abstract

Background. Survival statistics for daily haemodialysis are lacking as most centres providing this have treated only a small number of patients for short observation times. We pooled our 23-year, 1006-patient-year, five-centre experience of 415 patients treated by short daily haemodialysis.

Methods. One hundred and fifty patients were treated in-centre, most because of medical complications and 265 by home or self-care haemodialysis. Patients were on daily haemodialysis for 29 ± 31 (0–272) months. Forty-two percent had primary and 31% had secondary renal failure. Treatment time was 136 ± 35 min, frequency 5.8 ± 0.5 times/week and weekly stdKt/V 2.7 ± 0.55.

Results. Eighty-five patients (20%) died; 5-year cumulative survival was 68 ± 4.1% and 10-year survival was 42 ± 9%. Age, secondary renal failure and in-centre dialysis were associated with mortality, while gender, frequency of dialysis (5, 6 or 7 per week), continent, country and blood access were not. Survival was compared with matched patients from the USRDS 2005 Data Report using the standardized mortality ratio and cumulative survival curves. Both comparisons showed that the survival of the daily haemodialysis patients was 2–3 times higher and the predicted 50% survival time 2.3–10.9 years longer than that of the matched US haemodialysis patients. Survival of patients dialyzing daily at home was similar to that of age-matched recipients of deceased donor renal transplants.

Conclusions. Survival of patients on short daily haemodialysis was 2–3 times better than that of matched three times weekly haemodialysis patients reported by the USRDS.

Keywords: daily haemodialysis; mortality rate; short; survival comparisons

Introduction

In 1960, the Quinton–Scribner shunt solved the problem of treating patients with chronic renal failure [1]. Initially, 24 h of haemodialysis was done once weekly after patients developed symptoms of uraemia and fluid overload. To prevent these symptoms the regime soon was changed to twice-weekly dialysis for 16–23 h. This in turn was changed to three times weekly overnight nocturnal dialysis. Each increase in dialysis frequency led to further improvements, and so logic would have indicated proceeding to daily haemodialysis. However, because patients were reasonably well and because of financial problems, no further increase in dialysis frequency was undertaken [2].

In the 1950s, Teschon et al. started daily haemodialysis for acute renal failure [3], and the first study of daily dialysis in patients with end-stage renal disease (ESRD) began four decades ago in 1967 [4]. Since then many have studied daily haemodialysis and reported improvements in biochemistry, cardiovascular physiology, clinical symptoms and quality of life.

Reimbursement problems, the virtual disappearance of home haemodialysis training programs in the USA and other countries, difficult logistics, physician and patient reluctance and conservatism have limited adoption of daily dialysis. Reliable patient survival data for this have not been published, and so we decided to pool our clinical experience with this treatment, analyse survival and make comparisons to other treatments for end-stage renal failure.

Patients were converted to daily dialysis for two reasons. Most were chosen as daily treatment was thought to improve well-being, quality of life and survival. Others were started on daily dialysis because of serious medical complications and/or cardiovascular instability during dialysis. Many of these regularly required a fourth weekend dialysis, and most of these were considered unsuitable for home haemodialysis.
Statistical analysis and comparisons

Patient data were entered on an Excel spreadsheet (Microsoft Inc., WA, USA) and imported to the Staturview 5 (SAS., NC, USA) statistical program for analysis. Data are presented as mean ± SD unless otherwise stated.

Kaplan–Meier and Cox–Mantel log rank analyses were used for comparisons of survival [5]. Error bars on survival graphs are standard error of the mean (SEM).

Backward stepwise Cox proportional hazard analysis was used to study variables influencing survival. The confidence interval (CI) was 95%.

Categorical variables were analysed using the chi square and Fisher’s exact probability tests and continuous variables with one sample and unpaired t-tests. A P-value < 0.05 was used for statistical significance.

Standardized mortality rates (SMRs) were calculated according to the technique described by Wolfe et al. for comparing survival among groups of dialyzed patients [6,7]. Data from the USRDS 2005 Annual Data Report for period prevalent haemodialysis patients [8], matched for age as of 1 January 2003, gender, race and primary diagnosis, were used to calculate an estimated annual mortality rate for each of the 224 short daily haemodialysis patients observed in the same time period.

For comparison of projected survival by the Kaplan–Meier technique, we used survival probabilities for incident haemodialysis patients published by the USRDS in 2005 [8]. We compared survival probabilities after 5 years of dialysis for the 1998 cohort reported by the USRDS in 2005, the last cohort contributing 5-year-survival data. The comparison is reported as the relative risk (RR) of death. We also compared the number of years after which 50% of patients were projected to have died for matched patient groups. Finally, we compared projected life expectancy of daily haemodialysis patients to that of patients on conventional haemodialysis, recipients of deceased donor transplants and the US population published by the USRDS [8].

The efficiency of urea removal was calculated from pre- and post-dialysis BUN and used to calculate spKt/V by Daugirdas’ second equation [9] and weekly stdKt/V by the equation of Leypoldt [10].

Results

Patients

The age of patients when they started daily dialysis was 52 ± 15, range 13–89 years. There were 120 females and 295 males. Forty-three percent had primary renal disease (glomerulonephritis, interstitial nephritis and obstructive uropathy) and 30% had secondary renal disease [15% had diabetes, 9% had hypertensive nephrosclerosis and 6% had other secondary diseases (amyloid, myeloma, cholesterol emboli, systemic lupus erythematosus—SLE)] and in 27% the diagnosis was unknown. Patient characteristics are shown in Table 1.

Two hundred and sixty-five of the 415 patients treated themselves at home, and 150 were treated in a centre. The

Table 1. Demographic and clinical data of the 415 patients by country

<table>
<thead>
<tr>
<th>Variable</th>
<th>USA</th>
<th>Italy</th>
<th>France and UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>169</td>
<td>165</td>
<td>81</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>55 ± 15</td>
<td>51 ± 15</td>
<td>45 ± 14</td>
</tr>
<tr>
<td>Female (%)</td>
<td>35</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td>Male (%)</td>
<td>65</td>
<td>74</td>
<td>79</td>
</tr>
<tr>
<td>Home (%)</td>
<td>70</td>
<td>46</td>
<td>88</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>24</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>21</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Secondary RF other (%)</td>
<td>7</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Unknown (%)</td>
<td>7</td>
<td>55</td>
<td>11</td>
</tr>
<tr>
<td>Deaths/patient-years</td>
<td>40/279</td>
<td>37/560</td>
<td>8/167</td>
</tr>
<tr>
<td>Deaths/1000 patient-years</td>
<td>143</td>
<td>66</td>
<td>48</td>
</tr>
</tbody>
</table>

RF = renal failure.

Table 2. Treatment data

<table>
<thead>
<tr>
<th>Factor</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis duration</td>
<td>136 ± 35 min</td>
<td>65–250 min</td>
</tr>
<tr>
<td>Dialysis (h)</td>
<td>13 ± 3</td>
<td>6.5–22</td>
</tr>
<tr>
<td>Dialysate flow</td>
<td>375 ± 46 ml/min</td>
<td>250–500 ml/min</td>
</tr>
<tr>
<td>Dialysate flow</td>
<td>550 ± 170 ml/min</td>
<td>300–800 ml/min</td>
</tr>
<tr>
<td>spKt/V</td>
<td>0.77 ± 0.17</td>
<td>0.38–1.26</td>
</tr>
<tr>
<td>Weekly stdKt/V</td>
<td>2.74 ± 0.44</td>
<td>1.91–4.20</td>
</tr>
</tbody>
</table>

in-centre patients were older, 56 ± 15 versus 49 ± 14 years (P < 0.0001).

Eighty-four patients began daily dialysis between 1982 and 1996 (early era), 103 started between 1997 and 2000 (mid era) and 228 started between 2001 and June 2005 (late era). Over the 23-year observation period, the mean age of all daily dialysis patients increased from 45 ± 12 years (early era) to 53 ± 15 years (mid late era) (P = 0.0004), and the diagnosis of secondary renal failure increased from 20 to 35% (P = 0.014) for the same periods.

Patients had ESRD for 5.0 ± 5.7 (median 2.4, range 0–31) years before starting on daily haemodialysis and 39 (9%) of the patients began their ESRD treatment on this treatment. Patients were on daily dialysis for 2.4 ± 2.6 years (range 0–23 years), for a total observation period of 1006 patient-years. Fifty-four patients were followed over 5 years on daily dialysis and six for > 10 years. The patient who survived longest on daily haemodialysis died aged 72 years after 23 years of short daily dialysis that started in 1982.

Dialysis

Treatment data are given in Table 2. European patients dialyzed fewer minutes per dialysis (106 ± 28 versus 143 ± 36, P < 0.0001) but with a higher frequency per week (5.9 ± 0.4 versus 5.6 ± 0.5, P < 0.0001). There was no difference in spKt/V, but US patients had a higher mean weekly stdKt/V (2.9 ± 0.6 versus 2.6 ± 0.5, P = 0.0001).

Clinical course

One hundred and sixty-nine (41%) of the patients continued short daily dialysis, 75 (18%) had a renal transplant, 85 (20%) died, 78 (19%) returned to conventional in-centre haemodialysis and in 8 (2%) patients the continued
Short daily haemodialysis

Fig. 1. Survival of all 415 short daily haemodialysis patients, upper panel. The 5-year survival is 65% and 50% have died at 9 years. Comparison of survival of the daily haemodialysis patients by site of dialysis and to the USRDS survival data, lower panel. The 5-year mortality of daily haemodialysis patients treating at home is one-third and of those treated in centre ~2/3 of that of the patients on conventional three times per week haemodialysis.

Factors influencing survival

In a Cox proportional hazards analysis including all 415 patients, three factors were independently associated with mortality—secondary renal disease (HR 2.72, CI 1.76–4.20, \( P < 0.0001 \)), age more than the mean of 52 years (HR 2.39, CI 1.49–3.83, \( P = 0.0003 \)) and in-centre dialysis (HR 2.42, CI 1.54–3.79, \( P = 0.0001 \)). Gender, vascular access, duration of renal failure treatment before start of daily dialysis, centre, year of starting daily dialysis, era, country or continent were not associated with mortality. The European patients were younger, had less secondary disease and less often dialyzed at home and had a lower incidence of deaths per 1000 patient-years. (Table 1). When age, diagnosis and place of dialysis were included in Cox proportional hazards analysis, there was no difference in mortality between the countries or continents. (Table 3). The similarity of mortality rate between countries and continents remained the same even when including differences in dialysis frequency, \( Kt/V \) or time on dialysis (data not shown).

We had data on the duration of each dialysis in 259 patients and repeated \( Kt/V \) determinations in 139 patients. Backward stepwise Cox proportional hazard analyses were done using age, dialysis place, secondary/primary renal disease, individual dialysis duration, weekly dialysis hours, frequency per week of dialysis, \( spKt/V \) and weekly std\( Kt/V \) as covariates. Three factors were independently associated with survival in this analysis: weekly dialysis hours (HR 0.72, CI 0.58–0.89, \( P = 0.002 \)), secondary renal disease (HR 3.23, CI 1.39–7.52, \( P = 0.007 \)) and weekly std\( Kt/V \) (HR 0.43, CI 0.19–0.98, \( P = 0.045 \)).

Comparison to dialyzed patients in the USRDS

We did three comparisons to survival as reported in the USRDS 2005 Annual Data Report matching the patients by age, diagnosis and place of dialysis.

At 5 years, the RR of mortality of daily haemodialysis patients was 0.35–0.83 of that of the matched USRDS haemodialysis patients, Table 4, upper panel.

The time to 50% mortality was more than double for the short daily haemodialysis patients. The daily haemodialysis patients have a 50% survival 2.5–10.9 years longer than in matched USRDS haemodialysis patients, (Table 4, lower panel). As daily home dialysis patients had a better outcome than in-centre daily dialysis patients, we also compared the daily dialysis patients treated in-centre to all USRDS patients. More than 99% of US haemodialysis patients are treated in a centre. The in-centre daily dialysis patients had a much better survival than the USRDS patients—Figure 1 and Table 4. Cumulative survival curves comparing the patients on short daily haemodialysis to survival of patients in the USRDS matched for age are shown in Figure 2 and matched for diagnosis in Figure 3.

With the SMR technique, the number of expected deaths over the 2 years was 50.5, and the number of actual deaths was 17. The SMR was 0.34 (CI 0.20–0.54). The chi square test was statistically significant (\( P = 0.0003 \)).
Table 4. Matched comparisons to the 2005 USRDS incident haemodialysis patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Percent</th>
<th>USRDS Daily haemodialysis</th>
<th>Category</th>
<th>Percent ± SEM</th>
<th>RR ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Percent surviving 5 years of haemodialysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>31</td>
<td>In-centre</td>
<td>50 ± 6</td>
<td>0.73 (0.69–0.81)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>27</td>
<td>Diabetes</td>
<td>38 ± 16</td>
<td>0.83 (0.59–1.06)</td>
<td></td>
</tr>
<tr>
<td>Glomeruloneph.</td>
<td>49</td>
<td>Primary RF</td>
<td>74 ± 5</td>
<td>0.52 (0.42–0.61)</td>
<td></td>
</tr>
<tr>
<td>Age 20–44</td>
<td>58</td>
<td>Age 20–44</td>
<td>82 ± 7</td>
<td>0.35 (0.26–0.51)</td>
<td></td>
</tr>
<tr>
<td>Age 45–64</td>
<td>41</td>
<td>Age 45–64</td>
<td>71 ± 5</td>
<td>0.49 (0.41–0.58)</td>
<td></td>
</tr>
<tr>
<td>Category</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(B) Years until 50% mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>2.8</td>
<td>In-centre</td>
<td>5.1 ± 0.8</td>
<td>2.3 (1.3–3.1)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.1</td>
<td>Diabetes</td>
<td>4.6 ± 0.6</td>
<td>2.5 (1.9–3.1)</td>
<td></td>
</tr>
<tr>
<td>Glomeruloneph.</td>
<td>4.8</td>
<td>Primary RF</td>
<td>10.5 ± 2.2</td>
<td>5.9 (3.7–8.1)</td>
<td></td>
</tr>
<tr>
<td>Age 20–44</td>
<td>6.5</td>
<td>Age 20–44</td>
<td>17.4 ± 6.1</td>
<td>10.9 (4.8–17.0)</td>
<td></td>
</tr>
<tr>
<td>Age 45–64</td>
<td>4.0</td>
<td>Age 45–64</td>
<td>9.8 ± 0.7</td>
<td>5.8 (5.1–6.5)</td>
<td></td>
</tr>
</tbody>
</table>

Glomeruloneph = Glomerulonephritis, RF = renal failure, RR = percent surviving at 5 years, USRDS = patients divided by daily haemodialysis patients.

**Life expectancy and comparison to transplanted patients in the USRDS**

We also compared survival of all the daily home haemodialysis patients to that of US patients receiving a deceased donor transplant. The mean age of US patients receiving a transplant was similar to that of the daily home dialysis patients, 50 versus 49 years (P = 0.280). Survival curves of patients on home daily dialysis are almost identical to those of recipients of cadaveric kidney transplants, Figure 4.

The estimated life expectancies of the daily haemodialysis dialysis patients, patients on conventional dialysis, recipients of deceased donor transplants and the US population are shown in Figure 5. The life expectancies are 9–15 years longer than those of the age-matched US haemodialysis patients and the same as in deceased donor recipients in the USRDS.

**Discussion**

The survival of these 415 patients strongly suggests that short daily dialysis offers much longer survival than conventional three times weekly haemodialysis. Survival of any group of patients is much influenced by selection. However, one-third of the daily dialysis patients were selected because of serious complications or serious co-morbidities and a poor prognosis and often needed a fourth dialysis for congestive heart failure or dangerous metabolic derangements developing over the weekend. The increasing age and numbers with secondary renal disease over time among these daily dialysis patients also paralleled that of all dialysis patients. As a result, these 415 patients represent a wide spectrum of chronic dialysis patients and are a representative group for survival comparisons using techniques similar to those used in comparisons of different groups of dialyzed and transplanted patients [5–7].

We used three methods to compare survival. First, we matched patients by age and diagnosis and compared projected survival curves to those of comparable haemodialyzed patients from the USRDS 2005 Annual Data Report.
Second, we compared patients by the standardized mortality rate technique. With both methods, survival was 2–3 times higher than that of patients dialyzing three times weekly. The time to 50% mortality was prolonged by 2.3–10.9 years in the daily dialysis patients. Third, we compared survival with that of transplanted patients. Dialysis patients are carefully selected before acceptance to a transplant waiting list, and selected again when a kidney becomes available for transplant. Currently, <15% of patients starting dialysis receive a transplant. Dialysis patients on a transplant waiting list have an RR of ~0.5 compared to those not on the list, and the RR of those finally selected for a transplant is only 0.5 of those on the waiting list but who are not selected for a transplant [8,11,12]. Survival of daily haemodialysis patients was similar to that of transplanted patients of comparable age receiving a deceased donor transplant who have been shown to have a mortality of only one-third that of matched patients on conventional three-times-weekly dialysis [11].

This study has several limitations. It is difficult to compare survival among different patient groups when the patients are from different countries with different selection criteria and practice patterns [12,13]. However, both the Cox proportional hazards analysis and the SMR comparison indicated there was no difference in the outcome of daily dialysis between European and the US patients once age, diagnosis and site of treatment had been considered. It would also have been better if co-morbidities had been considered, but these details were not available for all of our patients. However, in survival comparisons among haemodialysis patients it has been shown that once age and diagnosis are considered, including co-morbidity adds only little additional information [14]. Based on the similar results of all three comparisons, each using a different methodology to normalize survival, we conclude that the improved survival is a result of the short daily haemodialysis modality itself, and not of patient selection.

We found, as have others, that patients on home haemodialysis survived better than patients dialyzing in centre [14–16]. The RR of death of our patients dialyzed daily at home, compared to the in-centre daily dialysis patients, was 0.44 when correcting for differences in age and diagnosis. A high percentage of our patients were on home haemodialysis, 64% compared to the 0.7% of US haemodialysis patients, but this difference by itself does not explain the better survival in the daily dialysis patients, as those treated by daily dialysis in-centre also had a much better survival than all USRDS patients.

More hours of dialysis weekly were associated with longer survival, and thus, the higher frequency of dialysis, the positive influence of dialyzing at home and the longer hours the patient could spend on dialysis, apparently, all contribute to the much lower mortality of patients on short daily haemodialysis when compared to three times weekly haemodialysis patients.

There are a number of reasons why daily haemodialysis might improve patient survival. It minimizes the oscillations in body chemistry and fluid volumes seen with three times weekly dialysis [17,18]. The dangers of three times a week haemodialysis are shown by the 2–3 times increase in sudden and cardiac deaths on Mondays and Tuesdays after the long weekend interval without dialysis compared with deaths on the other weekdays [19,20].

Several abnormal physiological parameters associated with a high mortality are improved by daily dialysis. Fluid
overload quickly decreases to 50% of that on three times weekly haemodialysis patients; blood pressure normalizes and antihypertensive drugs can be decreased or discontinued in most patients [18]. Left ventricular hypertrophy, an important predictor of mortality, regresses; levels of brain natriuretic peptide normalize; pulmonary fluid overload disappears and cardiac output increases [4,18,21–31].

Many metabolic markers that are associated with mortality also improve in patients on daily dialysis. These include hyperhomocysteinaemia, dyslipidaemia, malnutrition and hypoalbuminaemia and hormonal abnormalities. The need for erythropoietin may decline, vascular calcification is reduced and baroreceptor function is normalized [4,18,29–36].

Quality of life has uniformly been reported to improve as painful and dangerous complications during dialysis markedly decrease, the profound fatigue between dialyses disappears and appetite and physical strength return [4,18,21,23,25,26,33,34,37,38].

Both standardized mortality rate and actuarial comparisons with matched patients allow survival comparison among different patient groups, but the gold standard is the prospective randomized clinical trial. The National Institutes of Health is conducting such a study to compare short daily in-centre haemodialysis and long nightly home haemodialysis patients to patients on three times weekly in-centre haemodialysis. It will be several years before the results of this study are known. While this randomized study will be a valuable contribution, even such studies are affected by unanticipated problems. A recent comparison of the predictive value of randomized prospective studies and carefully conducted clinical analyses found no superiority of large-scale randomization over clinical analyses [39].

More than 300 publications of clinical observations spanning over four decades have shown much better metabolic and physiologic parameters and quality of life measures with short daily dialysis when compared to three times weekly haemodialysis. Our pooled data suggest that the survival of short daily dialysis patients is also much superior to that of conventional haemodialysis patients. Logistical problems, conservatism by physicians and nurses, worries about expenses by government, businessmen and administrators, the decline in training of physicians and nurses and training units for home haemodialysis, unavailability of haemodialysis machines suitable for the use at home and patient worries have made the introduction of daily haemodialysis slow and difficult.

We believe that daily haemodialysis presently is the best dialysis modality for patients willing to undertake this and should be considered the gold standard of dialysis to which other dialysis methods should now be compared.

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Conflict of interest statement. Some of these data have been published in abstract form and presented at the Annual Dialysis Conference, Tampa Florida, February 2005, at the annual meeting of the American Society of Nephrology in Philadelphia, PA, November 2005, and at the Annual Dialysis Conference in San Francisco, February 2006, and in Denver, CO, February 2007. Carl M. Kjellstrand is a freelance consultant to
References

1. Sibai-Galland have no conflict of interest.


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