Improved survival in renal replacement therapy in Europe between 1975 and 1992
An ERA-EDTA Registry study

Carl-Gustaf Elinder, Elizabeth Jones, J. Douglas Briggs, Otto Mehs, Shalom Mendel, Giovanni Piccoli, Sue P. A. Rigden, Jose Pinto dos Santos, Keith Simpson, Dimitris Tsakiris and Yves Vanrenterghem

Department of Renal Medicine, Huddinge University Hospital and Karolinska Institute, Huddinge, Sweden, ERA-EDTA Registry, St Thomas' Hospital, London, UK, Renal Unit, Western Infirmary, Glasgow, UK, Ruprecht Karsl Universität Heidelberg, Germany, Tel Aviv University, Israel, Cattedra de Nefrologia, Ospedale Molinette, Torino, Italy, Paedetric Nephrology, Guy’s Hospital, London, UK, Centro de Hemodiálise do Luminar, Lisbon, Portugal, Renal Unit, Glasgow Royal Infirmary, UK, Renal Unit, Veria General Hospital, Veria, Greece and Department of Nephrology, UZ Gaishuisberg, Leuven, Belgium

Abstract

Background. The prevalence of Renal Replacement Therapy (RRT) is rising steadily, worldwide and in Europe. One reason for this is an increasing number of patients starting RRT, but improving survival on RRT may also be contributing.

Material and Methods. In an ERA-EDTA Registry study we have examined survival of patients with Standard Primary Renal Disease, or Diabetes, aged 20 to 75 years, who started RRT with haemodialysis (HD) or peritoneal dialysis (PD) between 1975 and 1992. Altogether close to a quarter of a million patients were included in the analysis which included conventional survival analysis of comparable subgroups of the whole cohort as well as Cox regression.

Results. After accounting for age, mode of initial treatment, and diagnosis, an improvement in survival of RRT patients was evident. From Cox regression it was calculated the risk for death decreased by about 5% annually during the time period 1975–1992. Patients who started RRT using PD experienced a steady increase in survival during the first year of treatment. Improved survival may also affect the prevalence of RRT as there is a well-known association between prevalence (P), incidence (I) and duration (D) where P = I × D. In the USA a small but steady increase in survival during the first year has been seen in all age and diagnostic groups since 1980 [2]. A possible change in survival over time in RRT in Europe has however not been thoroughly examined. In doing this one has to consider the age distribution and diagnosis of the treated patients, as changing the risk factor distribution of the population entering RRT will influence the long-term survival [3]. We thought that it would be of interest to examine whether survival on RRT has improved in Europe during the last twenty years. Evidence of improved survival on RRT is important to determine as considerable efforts have been made to improve the efficiency and also safety of dialysis treatment. This includes the use of more biocompatible membranes, bicarbonate dialysate, and

Introduction

The prevalence of renal replacement therapy (RRT) is increasing worldwide as well as in Europe. One important reason for this is an increased rate of acceptance of patients with end stage renal disease (ESRD). Patients who were previously considered unsuitable for treatment, for example because of old age, have been treated by RRT in more recent years, and this is the main reason for the increase in incidence, or acceptance rate [1]. Improved survival may also affect the prevalence of RRT as there is a well-known association between prevalence (P), incidence (I) and duration (D) where P = I × D. In the USA a small but steady increase in survival during the first year has been seen in all age and diagnostic groups since 1980 [2]. A possible change in survival over time in RRT in Europe has however not been thoroughly examined.
better peritoneal dialysis practices. Likewise an increased transplantation rate may have a favourable impact on the overall survival.

**Subjects and methods**

This analysis uses data from the ERA-EDTA registry. We decided not to include children and the very old and thus restricted the analysis to those aged between 20 and 75 years when starting RRT between 1975 and 1992. In addition we limited the analysis to two diagnostic groups, the major standard causes of primary renal disease (PRD), which are given EDTA codes 00–49 and diabetes (EDTA codes 80–81). EDTA codes 00–49 include all primary glomerulonephritis, pyelonephritis, interstitial nephritis and polycystic kidneys but not renal failure secondary to vascular or systemic disease.

First treatment was haemodialysis (HD), or peritoneal dialysis (PD), i.e. pre-emptive transplantation patients are not included. Patients who were treated with dialysis when entering RRT but later received renal allografts are included in the survival analysis in the same way as those patients who have remained on dialysis. Censoring took place at the end of the observation period or, for lost to follow-up individuals, at the day after that the patient was confirmed as being alive usually by 31 December each year.

Reporting to the ERA-EDTA Registry became much less complete during the mid-1990s. This is illustrated in Figure 1. The percentage of lost-to-follow-up (LTFU) patients increases with time of follow-up in all subgroups of patients i.e. those starting in 1975, 1980, 1985 and 1990. In particular for patients who started RRT in 1990 there was already a high percentage of lost-to-follow-up by 3 years, i.e. more than 20%. A small number of lost-to-follow-up patients is acceptable but when the rate increase above 10–15% it is not possible to make any analysis or interpretations with accuracy. As the returns of data after 1992 are less good we decided to end the analysis at this year. Table 1 shows the total number of patients included in this analysis, altogether close to a quarter of a million. In order to get a more homogenous population we have in a few of the analyses restricted the data used to European Union (EU) countries only.

All data analysis was performed using the features of the SPSS statistical package. This program provides a straightforward analysis of survival by Life Tables. The Wilcoxon (Gehan) test was used to analyse survival of the subgroups. The Cox regression analysis that enables adjustments to be made for covariates such as age and diagnosis when comparing sub-groups within the cohort was also used. However, Cox regression can be invalid, in particular when analysing covariates that are not linear or constant over time [4]. Therefore we have presented the survival analysis in two ways, as conventional actuarial survival curves for certain strata of the examined cohort and also as relative hazard risks as calculated by Cox regression.

**Results**

Figure 2 shows the actuarial survival of patients with standard PRD aged 40–49 years, starting HD during two time periods, 1975–1979 (n=8833) and 1985–1989 (n=11484). There is an improvement in survival, from 67 to 77% at 5 years when the later cohort (1985–1989) is compared to the former (1975–1979). For patients with the same age (40–49) and diagnosis (standard PRD) who started PD, survival during the same time periods (1975–1979, n=1186 and 1985–1989, n=1523) increased from 60 to 77% respectively, i.e. to the same level as with HD (Figure 3).

Figure 4 shows a comparison of the survival of

---

**Table 1.** The total number of patients with standard PRD or diabetes, aged between 20 and 75 years, starting RRT with haemodialysis or peritoneal dialysis between 1975 and 1992

<table>
<thead>
<tr>
<th>Patients</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>243167</td>
</tr>
<tr>
<td>HD standard PRD</td>
<td>177742</td>
</tr>
<tr>
<td>HD diabetes</td>
<td>26602</td>
</tr>
<tr>
<td>PD standard PRD</td>
<td>29872</td>
</tr>
<tr>
<td>PD diabetes</td>
<td>9551</td>
</tr>
</tbody>
</table>

---

**Fig. 1.** The percentage of lost to follow up (LTFU) among patients who started RRT in 1975, 1980, 1985 and 1990 after 1–6-year follow-up.

**Fig. 2.** Survival of patients with standard PRD, aged 40–49 years, starting RRT with haemodialysis between 1975 and 1979 or 1985 and 1989.
Fig. 3. Survival of patients with standard PRD, aged 40–49 years, starting RRT with peritoneal dialysis between 1975 and 1979 or 1985 and 1989.

Fig. 4. Survival of patients with standard PRD, aged 60–69 years, starting RRT with haemodialysis or peritoneal dialysis 1985–1989.

Fig. 5. Survival of patients with diabetes, aged 60–69 years, starting RRT with haemodialysis or peritoneal dialysis between 1985 and 1989.

Fig. 6. The overall 5-year survival in different groups of patients starting RRT with haemodialysis or peritoneal dialysis between 1975 and 1992.

patients aged 60–69 years, with standard PRD who started RRT between 1985 and 1989 with HD (n = 14 438) or PD (n = 2789). Patients who started with HD have a higher 5-year survival of 53% than those commencing with PD (44%). For patients of the same age group (60–69 years) with diabetes who started with HD (n = 3513) between 1985 and 1989 the 5-year survival was again somewhat better than for those who started with PD (n = 996), namely 24% and 15% for HD and PD respectively (Figure 5). Figure 6 summarizes the 5-year survival of all patients starting treatment with HD and with PD who had standard PRD or diabetes in two age groups namely 20–75 years and 60–69 years, for the whole period of analysis from 1975 to 1992. For all the patient groups with the exception of those with diabetes aged 20–75 years, those starting treatment with HD have a better survival than those starting with PD.

This conventional survival analysis of age strata, diagnosis and time-periods of starting RRT of the whole cohort show that age, mode of renal replacement therapy (MOT), year of starting treatment, and cause of renal disease influence survival. These factors thus constitute alternative determinants and may act as confounders. We therefore proceeded with a proportional hazard analysis, i.e. Cox regression [4]. The following variables were included in the hazard analysis: gender, age, treatment modality, year of starting RRT and diagnosis (standard PRD or diabetes). In order to get a more homogenous sample a separate analysis was also made for EU countries only.

Figure 7 presents the relative risk (RR) for mortality for one determinant while the other ones are adjusted and controlled for. The RR for PD compared to HD is higher at 1.25 (95% CI: 1.23–1.27), i.e. it indicates a 25% higher risk of death for patients who started treatment with PD compared with HD. Likewise the RR of 1.045 (95% CI: 1.044–1.046) for age means that the relative risk of death increases by 5% for each 1-year increase in age. Woman have a slightly (5%) higher mortality than men, RR 1.046 (95% CI: 1.040–1.053), i.e. a 5% increase in risk. Patients with diabetes have a considerably higher mortality than those with standard PRD with a RR of 2.46 (95% CI: 2.42–2.50) (not shown in Figure 7). The RR of 0.958 (95% CI: 0.957–0.960) for the year of starting RRT is the most interesting finding, indicating that mortality
Fig. 7. The adjusted relative risk (RR) of death in patients starting RRT with the following variables: peritoneal dialysis compared to haemodialysis, increasing age by annual increments, women compared with men, and calendar year of starting treatment.

Fig. 8. The adjusted relative risk (RR) of death in different groups of patients starting RRT related to increasing age by annual increments and calendar year of starting treatment.

Fig. 9. The adjusted relative risk (RR) of death in patients from EU countries, starting RRT between 1975 and 1983 or 1984 and 1992 with the following variables: peritoneal dialysis compared to haemodialysis, increasing age by annual increments, women compared to men, and calendar year of starting treatment.

has decreased by about 4% with each calendar year of starting RRT.

The effect of age within the range of 20–75 years at the start of RRT and of calendar year (1975–1992) were analysed separately for different subsets of patients, namely all patients, those with standard PRD receiving HD and PD and those with diabetes receiving these two types of treatment (Figure 8). The impact of age and year of starting RRT is similar in all subsets of the patients. The RR for age at starting treatment ranged from 1.025 to 1.050 and year of starting treatment from 0.93–0.96. An increase in age of 1 year at start of RRT increased the relative risk of death by 2.5–5%. On the contrary a more recent calendar year of starting RRT decreased the relative risk of death by 4–7% each year. Finally we have divided the period of commencing RRT into two groups, 1975–1983 and 1984–1992, and restricted the analysis to countries currently in the EU (Figure 9). A similar pattern is evident in that patients who started with PD experienced a higher mortality compared to those who started with HD. Likewise, age increased the relative risk, whereas a more recent year of starting treatment appeared to be beneficial. It is worth noting that the difference between PD and HD is less prominent in the later part of the observation period. For patients starting RRT during 1975–1983 the RR of death for PD compared with HD was 1.32 (95% CI; 1.28–1.34) and for 1984–1992 it was 1.18 (95% CI; 1.16–1.21).

Discussion

The most important finding is the reassuring observation that, although mortality on RRT is still high, it appears to be slowly decreasing. Patients starting RRT with HD or PD in the 1990s have a better prognosis than those who started in the 1970s with an improvement of about 5% annually. Agodoa and Eggers [2] have reported on the 1-year survival of patients starting RRT in the United States in different age and diagnostic groups since 1980. In age groups 20–44 years and 45–65 years the 1-year survival during the first year on dialysis increased from 78 to 90% and from 78 to 82% respectively during the years 1980–1990. This corresponds to an annual improvement in survival of the order of 1–5%, similar to what we report here. The 5-year survival for patients aged 40–49 years or 60–69 years with standard PRD or diabetes (Figures 2–5) is very similar to what has previously been reported from the ERA-EDTA Registry [1] and is higher than that reported from the US Renal Data System although lower than the figures reported from Japan. Five-year survival of all patients starting RRT during 1982–1987 in the USA was 40%, in Europe 59%, and in Japan 61%. For non-diabetic patients aged 45–54 years in these three geographical areas, the 5-year survival was 58, 66, and 72% respectively [5]. The higher mortality among RRT patients in the USA as compared to Europe can probably be explained to a considerable extent, if not entirely, by a higher prevalence of co-morbidities in the US dialysis population [6]. Relatively large differences in the survival of
dialysis patients have on the other hand also been documented within Europe after the influence of age, primary renal disease and co-morbidity have been taken into account [7].

Another interesting observation is the higher mortality of patients who start RRT with PD as compared to HD. A relative risk of 1.25 is not as high as, for example, the risk from diabetes, which in this study gave a RR around 2.5, or age that gave a RR of about 1.05 per increment of 1 year. For a RR of 1.05, on a yearly basis, it can be deduced that an increase in age of 10 years would increase risk by the order of 1.6. This difference between PD and HD is worth commenting on as the long-term efficacy of these two treatment modalities has been discussed and compared on many occasions [8,9]. In general our observations agree with those in other analyses when it has not been possible to fully adjust for case mix and co-morbidities [10,11,12]. Bloembergen et al. [13] compared mortality between prevalent patients treated with HD and PD in the USA. The age-adjusted mortality was higher in prevalent PD patients compared with HD patients during 1987–1989, the RR being 1.11 for all primary renal diseases excluding diabetes and 1.38 for diabetes. On the other hand Fenton et al. [14] from Canada, in an extensive follow-up of more than ten thousand patients who began RRT with PD or HD, found no significant difference in survival between PD and HD, although with a trend towards better survival with PD. Likewise no difference in the survival of PD and HD treated patients was found in an Italian study where 102 HD and PD patients were followed prospectively for 3 years [15]. Furthermore, in a more recent reassessment of survival among incident patients entering RRT with PD or HD after 1989 in the USA, no significant differences were seen between the treatment modalities [16].

It is likely that if we had been able to study patients who commenced PD and HD since 1990, we would have found a higher proportion of PD patients and a further decrease in the difference in survival between those on PD and HD [15]. The data presented here are to some extent ‘historical’ as the follow-up was terminated in 1992 and most of the data comes from the 1980s. In addition we have shown that the observed differences in survival between PD and HD decreased with time. It should also be remembered that this analysis does not represent a randomized study and that the difference in survival between HD and PD patients well may also be due to case-mix and confounders not possible to explore in this retrospective analysis. Thus we do not believe that our current findings should be used as an argument against PD treatment.

One aspect that has not been examined at all in this study is the influence of kidney transplantation. As pointed out in Subjects and methods all patients who started RRT with HD or PD have been included, irrespective of whether they later had a transplant or changed their type of dialysis. One reason for analysing the data in this way is that there are omissions in reporting to the Registry of changes in the mode of treatment, in particular if there have been several changes for the same patient. If transplanted RRT patients were censored at the date of transplantation that would most probably decrease the overall survival as transplanted patients demonstrate a superior survival, at least in the long term [17]. We would be left with a selection of RRT patients waiting for a renal transplant, not accepted for transplantation, and a few not interested to become transplanted. This would give a more than appropriately gloomy outlook for a typical patient entering RRT with dialysis, where transplantation is a possibility. We have examined the annual rate of transplantation in our cohort and it is very low at around 1–2%, and this rate did not change much over the observation period (1975–1992). Thus an increased rate of transplantation cannot account for the improvement we have observed in the survival of RRT patients, which is the most important message from this study.

Differences in transplantation rates may, however, be part of the explanation for differences in survival of patients who started PD or HD, and we have not been able to examine this. Likewise the unexpected slightly better survival of men versus women may perhaps be explained by a higher transplantation rate for men.

The objective of this study has not been primarily to compare different modes of RRT but rather to examine the prognosis of a patient with end-stage renal disease who presented to a nephrologist in the late 1970s as compared to the early 1990s, irrespective of what mode of RRT treatment was available and was provided. Whatever statistical method we use, whether conventional survival analysis with survival curves related to age, diagnosis and time-period of the cohort (Figures 2–5) or the Cox hazard regression model (Figures 6–9) the results are in agreement, showing that survival on RRT in Europe has improved between 1975 and 1992. It would be interesting to know what has happened to patient survival since 1992, and future studies will hopefully investigate this issue based on up-dated Registry data of good quality.

References
replacement therapy in Europe: is there a 'centre effect'? *Nephrol Dial Transplant* 1996; 11: 300–307

Received for publication: 24.9.98
Accepted in revised form: 21.12.98