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ORIGINAL ARTICLE

Progressive survival improvement of incident dialysis patients in a tertiary center, Ireland

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Abstract

Background The survival of incident dialysis patients' end-stage kidney disease in some European and American has been reported to improve in modern era compared to earlier periods. However, in Ireland, this has not been well documented.

Aim To investigate the survival outcomes of incident end-stage kidney failure dialysis patients in a tertiary center over a 24-year period, 1993–2017.

Methods A retrospective analysis was carried out utilizing the Beaumont Hospital Renal Database. Consecutive adults with incident dialysis were analyzed. Kaplan-Meier methods and the estimated mean survival times were used to evaluate survival at successive 4-year periods of time.

Results In total, 2106 patients were included, of whom 830 underwent subsequent renal transplantation during follow-up. During the study period, from 1993 up to 2017, the mean patients' age increased from 56.3 ± 17.4 in 1993–1996 to 60.6 ± 18.3 in 2014–2017. There was an overall decrement in mortality over successive time intervals which were mirrored by the improvements in median survival after commencement of dialysis treatment from 6.14 years during 1993–1996 to 8.01 years during 2009–2012. Patients' survival has steadily improved, with the 5-year survival has risen over time, by almost 15%. This positive signal persisted and became more pronounced after adjusting Kaplan-Meier curve to age, where the 5-year survival estimates were exceeding 80% in 2014–2017.

Conclusion Survival rates among incident dialysis patients have improved progressively between 1993 and 2017 in Beaumont Hospital in Dublin, Ireland. The factors which led to this improvement are not entirely clear, but likely to be multifactorial.

Keywords Dialysis · End-stage kidney disease · Mortality · Survival analysis

Introduction

Prevalence of chronic kidney disease (CKD) had been reported as 11.6% in adult population in Ireland [1]. CKD may deteriorate into end-stage kidney disease (ESKD), and it has been reported that more than half of those who started on dialysis would die within 5 years [2, 3]. Renal transplantation, for many but not all patients, is considered the modality of choice for renal replacement therapy (RRT) for patients with ESKD as it carries a superior survival, quality of life, and is most cost-effective [4–6]. Nonetheless, many patients will require dialysis to maintain their lives for prolonged periods, either awaiting for a renal transplantation or they are deemed medically unsuitable due to medical or other reasons [7]. Recent data from the United States Renal Data System (USRDS), European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Registry, and UK Renal Registry (UKRR) have showed a survival improvement in patients starting on dialysis compared to earlier eras [3, 8, 9]. We have previously reported the outcome of the National Kidney Transplant Service (NKTS) program in Ireland, which has shown progressive improvement in long-term allograft survival, and so we were interested to determine if this was also the case for patients commencing dialysis in our unit based in Dublin, Ireland [10]. Our objective in this study was

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to determine the survival of incident dialysis patients over the period of 24 years, from 1993 up to 2017.

Material and methodology

Study population and data source

We performed a retrospective analysis of the Beaumont Hospital Renal Database, covering the period January 1st, 1993, to December 31st, 2017, to determine the survival outcomes of consecutive patients presenting with ESKD who were commenced on dialysis. Criteria for inclusion were all ESKD patients aged 18 years or older whom remained on dialysis after 30 days from being diagnosed with renal failure, based on the assessment of the treating nephrologist. Patients with acute kidney injury requiring dialysis and pre-emptive renal transplant recipients were not included. Complete data sets were available for all years except 2013, so 2013 data was not included in this analysis. Patients were treated by in-center and satellite hemodialysis (HD) and peritoneal dialysis (PD) according to standard protocols aiming to achieve 4-h dialysis 3 days a week and aiming a KT/v of 1.3 or above. All patients deemed suitable for renal transplantation were activated on the deceased or living donor waiting list.

Analytical methods

All data was prospectively inputted into a nephrology bespoke database (Renal PROTON, Clinical Computing Ltd., from 1992 to 1999, Clinical Vision 3.4a Version 1.1.34.1, Clinical Computing, Cincinnati, OH, USA, from 1999 to 2015, eMEDRenal Version 3.2.4, Mediqal Health Informatics Ltd., from 2015 to present). Patient characteristics were extracted, such as age, gender, ESKD etiology, and dialysis modality. We evaluated patients' median survival with respective 95% confidence intervals based on the available patients' data with a minimum of 4-year observation time span assuming exponentially distributed survival times. The baseline data for our analysis was selected to extend from 30 days after dialysis initiation until the time of death. We generated Kaplan-Meier curves which were categorized into 4-year brackets to display differences in mortality during 1993–2017, while the number of patients at risk to each interval of time had been censored for missing data. Moreover, we used multivariable Cox proportional hazards models to estimate the survival outcomes associated within the 4-year time bracket of ESKD treatment and which was adjusted to age. We also monitored the total proportion of patients who experienced renal transplantation and the differences between the cumulative numbers who were transplanted during each period of time. STATA SE (version 16 StataCorp, College Station, TX, USA) was used for the data analysis and for the construction of figures and tables. Probability of a type 1 error less than 0.05 was considered to be statistically significant.

Results

Complete data sets were available for all years except 2013, because of a transition in between two in-hospital database software that lead to insufficient data to for this particular year to facilitate accurate evaluation, so excluded from this analysis. In total, 2106 incident ESKD patients were included in this study. There was a declining trend in the gross number of patients per time period: 425 in 1993–1996 and 244 in 2014–2017. It is notable that patients' age progressively increased during the study period from 56.3 (± 17.4) to 60.6 (± 18.3) years, during 1993–1996 and 2014–2017, respectively, $P < 0.001$. Most patients were male (65%); diabetes mellitus and hypertension were the most common cause of ESKD, 23.1%. The incident use of PD accounted for approximately 20% of dialysis treatment modality during the course of each time

Table 1 Patient characteristics at commencement of ESKD in successive 4-year periods

Variable	1993–1996 *N* = 425	1997–2000 *N* = 429	2001–2004 *N* = 393	2005–2008 *N* = 288	2009–2012 *N* = 327	2014–2017 *N* = 244	*P* value
Age at start (years) ESKD (mean (sd))	56.3 (17.4)	58.5 (17.0)	60.3 (18.0)	58.1 (18.8)	60.1 (17.1)	60.6 (18.3)	< 0.-001
Sex (male/female, %)	65/35	59/41	60/40	65/35	68/32	64/36	0.069
Modality ESKD (HD/PD, %)	80/20	80/20	80/20	84/16	74/26	82/18	0.061
Cause of ESKD by %*							
- 1	22	20	24	23	27	24	0.081
- 2	21	16	15	19	11	13	
- 3	8	10	9	5	11	7	
- 4	49	54	52	53	51	56	

*1, hypertension/diabetes/vascular; 2, glomerulonephritis; 3, polycystic disease; 4, other

Table 2 Median survival in successive 4-year periods

Time period	Median survival (years) (95% conf. interval)
1993–1996	6.14 (4.81, 8.31)
1997–2000	6.56 (4.83, 8.70)
2001–2004	5.55 (4.68, 7.44)
2005–2008	8.53 (6.98, 10.24)
2009–2012	8.01 (6.01, 10.02)
2014–2017	Not defined
Overall, 1993–2017	7.19 (6.26, 8.05)

period of the study. Mean follow-up was 7.2 years. Patients' characteristics are displayed in Table 1.

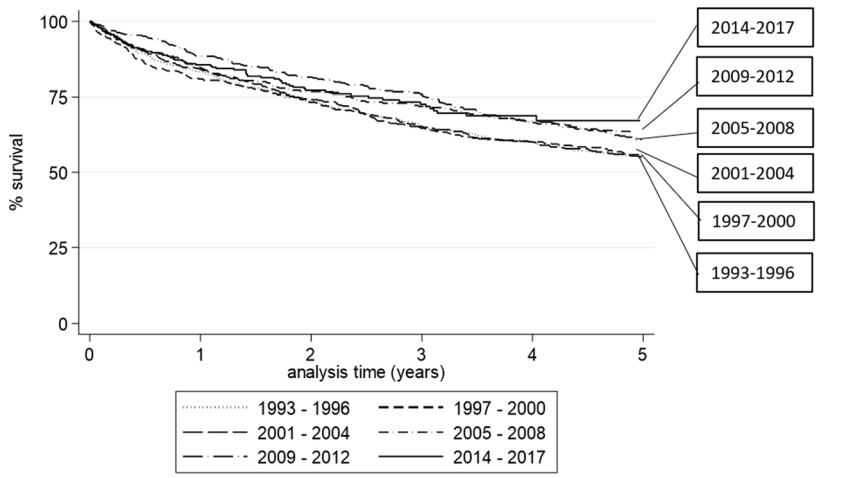
Table 2 shows patient survival over the study period. With initial median survival of 6.14 years for 1993–1996, all other time periods showed a progressive decrease in mortality over time, with median survival increased to 8.53 years (CI 6.98–10.24) and 8.01 years (CI 6.01–10.02) during 2005–2008 and 2009–2012, respectively, except for period of 2001–2004. Survival progression was not captured for period of 2014–2017 partly due to improvements in survival but is mainly down to a lack of follow-up time. Overall, the annual survival, expressed as a percentage, improved progressively between 1993 and 2017. Although 1-year and 2-year survival probability remained almost constant with mean percentage of 85% and 75%, respectively, the 5-year survival has risen steadily over time, by almost 15% between 1993–1996 and 2014–2017 as shown by the Kaplan-Meier curves for the unadjusted data (Fig. 1). After adjustment for age, the survival outcome of incident ESKD patients has persisted, where the 5-year survival estimates were more than 80% in 2014–2017 (Fig. 2). In a multivariable Cox regression model, time period (HR 0.88; 95% CI 0.84–0.92; $P = 0.000$), age at start of renal replacement therapy (RRT) (HR 1.06; 95% CI 1.06–1.07; $P < 0.001$), and the primary cause of ESKD were significant predictors for life expectancy (Table 3). Sex and difference in dialysis modalities were not significantly associated with survival.

We examined the trend of patients who have had renal transplantation after being initiated on RRT during the time periods, and whether variation of the trend would have a link to the survival outcome for each period of time. Eight hundred and thirty patients underwent renal transplantation from 1993 to 2017, accounting for 39.4% of the total cohort, with more than 60% of them transplanted within the first half of the study period. The rate of transplantation was similar across the 6 time periods ($P = 0.219$) with overall cumulative transplant rates at 1, 3, and 5 years of 8%, 31%, and 42%, respectively (Fig. 3).

Discussion

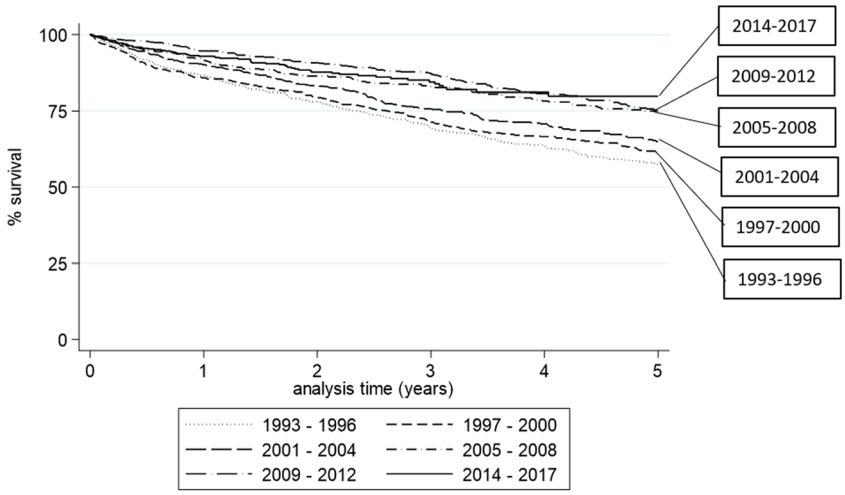
This retrospective study demonstrated that survival following dialysis commencement at our tertiary center has progressively improved from 1993 to 2017. While this concurs with reports from regional and international programs, which showed a decline in mortality risk in dialysis populations across different age groups, our study has demonstrated similar improvements in a large cohort and a long period of time; 24 years[3, 8, 11].

Previous reports from Tassin, France, examined 20-year survival for 445 hemodialysis patients and reported that



ERA	Number at Risk (*number censored)					
1993-1996	425	352	311	274	251	230
1997-2000	429	344	311	273	245	221
2001-2004	393	323	274	230	209	189
2005-2008	288	237	213	198	183	174
2009-2012	327	278	253	232	204	183
2014-2017	244	209*	146*	98*	46*	4*

Fig. 1 Unadjusted patient survival curve



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survival had improved with higher urea clearance (Kt/V > 1.6) and better control of blood pressure [12]. However, the Haemodialysis (HEMO) Study reported that the risk of death from any cause was similar between high versus standard dialysis dose [12–14]. With regard to peritoneal dialysis, the Canada and the United States (CANUSA) study and Adequacy of Peritoneal Dialysis in Mexico (ADEMEX) trial found that survival was not related to peritoneal clearance dose rather than residual kidney function (RKF) and patient health-related quality of life (HRQOL) factors, respectively [15, 16]. Some studies have reported a positive correlation between home-hemodialysis (HHD) and survival rates, while others do not [17–20]. Nevertheless, improvement in the survival of dialysis patients has been reported by many national and regional registries. Methvena et al. recently reported UK Renal Registry (UKRR) data where they analyzed 7251 adult incident ESKD patients initiated on renal replacement therapy (RRT) between 1998 and 2014. Overall, patients had experienced improvement in the long-term survival irrespective of their age, for instance, the 5-year survival had improved for patients aged under 65 years compared to those aged 65 years and above, from 64.1 to 72.8% and from 20 to 32.5%, in 1998 and 2010, respectively. For uncertain reasons, these improvements were more pronounced in patients aged 65 and older, with 1-year survival had incremented, from the 1998 to 2014, by just above 16% [9].

Because of the higher prevalence of co-morbidities, the elderly might experience a shorter life expectancy [21]. We observed an incremental increase in the age of incident ESKD patients from 1993 to 2017, which probably reflects changes in referral practices and clinical practice as well as the natural aging trend in the population of Ireland (https://www.cso.ie/en/index.html). Nevertheless, the magnitude in survival trended up after adjustment to the age. In fact, we cannot rule out that improvement in survival of general population over this period of time might have an effect on the examined cohort. Studying the trend of excess mortality, Boenink et al. assessed the European Renal Association-European Dialysis

Table 3 Multivariable Cox proportional hazards model of survival after starting dialysis

Variable	Hazard ratio (95% conf. interval)	*P* value
Time period	0.888 (0.843 0.922)	< 0.001
Age at start ESKD (mean (sd))	1.067 (1.061 1.072)	< 0.001
Sex % male/female	0.989 (0.867 1.128)	0.869
Modality ESKD % HD/PD	0.958 (0.809 1.134)	0.616
Diagnosis % ESKD other causes	1.000	
HTN/diabetes	1.073 (0.926 1.243)	0.348
Glomerulonephritis	0.777 (0.632 0.957)	0.017
Polycystic kidney	0.627 (0.473 0.829)	0.001

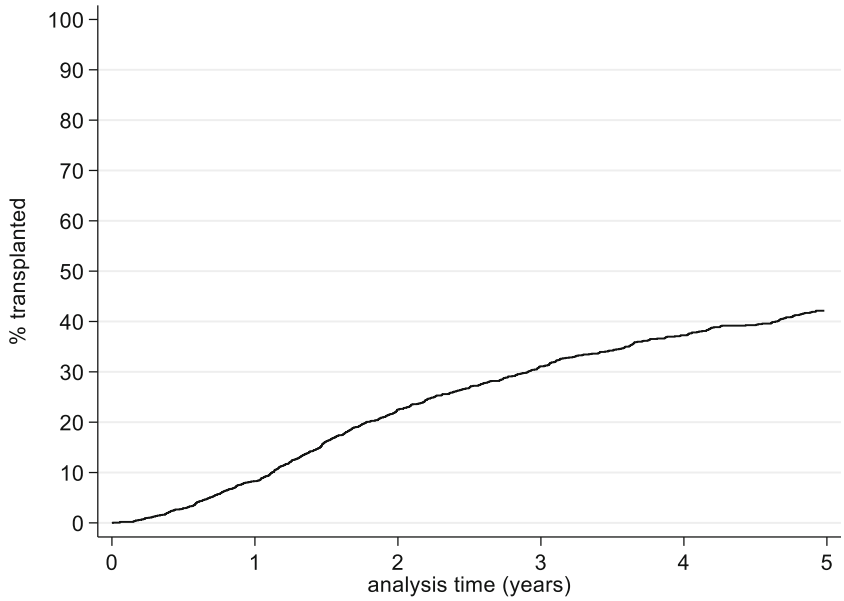

Fig. 3 Time to transplant for 1993–2017 patient cohort

and Transplant Association (ERA-EDTA) Registry, where 280,075 European end-stage kidney disease (ESKD) adults had started on RRT [11]. In patients on dialysis, those over 65 years had a greater reduction in mortality compare to younger age groups. In contrast, another study analyzing USRDS registry data found that younger age groups on dialysis had experienced larger improvement in excess mortality, although the absolute mortality improvement was largest in the older group [8]. The factors behind this were unclear.

We found that patients with underlying glomerulonephritis (GN) (HR 0.76; 95% CI 0.62–0.94; $P = 0.01$) and polycystic kidney disease (PKD) (HR 0.63; 95% CI 0.48–0.84; $P = 0.001$) experienced lower mortality rates which was not detected among the other causes including diabetes mellitus. This agrees with previous reports which showed that 5-year survival among dialysis patients was worse in diabetes compared to GN and PKD. Data from the ERA-EDTA Registry found that survival of PKD patients had improved markedly and justified by the reduction in the cardiovascular mortality [22].

However, it is a matter of debate to conclude if an improvement of a single intervention like management of hypertension or anemia control would be translated into a survival advantage. The impact of adherence to the recommendations of the guidelines has been assessed by Liabeuf et al. They assessed the effect of attaining guideline objectives in five parameters of hypertension, anemia, and mineral bone disease on all-cause mortality across seven European countries between 2009 and 2011 [23]. This perspective study found that failure to achieve the recommended parameters has been associated with worse survival outcomes, and hence providing a good evidence that attainment of the guidelines is associated with better survival outcomes [24, 25].

Earlier, Kaballo et al. reported the survival outcomes of 3597 incident ESKD patients in Ireland, comparing the annual risk of death among three groups, kidney transplant recipients (KTRs), patients listed for transplant, and patients continued on dialysis [7]. They confirmed the superior survival advantages for KTRs and similarly demonstrated that patients continued on dialysis were exposed to seven times higher annual death rates than the group of patients on the waiting list. Looking at the current data, while the rate of transplantation was similar across the 6 time periods ($P = 0.219$), more than one-third of our cohort had undergone renal transplantation, which is associated with a superior survival advantage [6]. However, 1276 patients had continued on dialysis, which expose them to a higher risk of mortality. In spite of that, the improvement in survival persisted, which agreed with studies reported elsewhere [8, 9, 11]. The factors behind this is uncertain, but acknowledging the complexity of a condition such as ESKD, where many risk factors and co-morbidities interplay together, we assume that this improvement is a "multifaceted" advancement, as a single "game-changer" is quite unlikely.

In a global setting, higher socioeconomic status (SES) is associated with improved survival [26]. Our group has published an age-adjusted analysis on the negative influence of lower SES on patient survival, which has been addressed by other studies too, highlighting the negative impact of lower socioeconomic status and income disparity on survival of dialysis [27]. Of note, ESKD patients in Ireland are not accountable for any direct expenses in relation to provision of in-center hemodialysis or home-therapies which include home-hemodialysis and PD. A number of tax reliefs are available which include personal expenses for travel or utilities relating to the undertaking of renal replacement therapy. Meanwhile, national reports have shown 9.8% incremental rise in disposable income per person in Ireland accompanied by a drop in the deprivation rate by almost half, 15.7% in 2018 compared

to 30.5% in 2013 (https://www.cso.ie/en/index.html). Taking these together, perhaps these improvements in SES parameters have been echoed by patient survival improvements. An additional analysis focusing on SES and survival of dialysis patients may be of merit.

Our study validates recent reports about progressive improvement in dialysis patient survival in a large cohort of incident ESKD patients. However, it should be interpreted in the context of the acknowledged limitations. Firstly, because of its retrospective nature with no matching comparator group used in the analysis, no causal relationships can be ascertained. Secondly, as we initiated our analysis 30 days after incident ESKD, this might has contributed potentially to lead-time bias where sicker patient may have died prior to inclusion. Thirdly, we should recognize that recall bias cannot be ruled out, especially when 2013 data was not included which may lead to uncaptured residual confounding bias. Lastly, we did not examine, in a much detailed model, the correlation between the progress in practice and intervention of our unit and the associated survival improvement.

Conclusion

In summary, these data demonstrate that incident ESKD patient who starts on dialysis experiences progressive survival advantage over time. Our findings are based on the experiences of a large cohort of incident ESKD patients over 24 years. Although these findings agree with other studies, the reasons for them are unclear but likely represent multifaceted advances in the care of ESKD population.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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