Relative survival in patients on renal replacement therapy in Italy: a method to estimate of the prognosis of end stage renal disease

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Objectives:

Relative survival is a method used in cancer epidemiology in which observed survival of a cohort of patients is compared to expected survival drawn out from the life table of general population. In this paper we applied relative survival methodology to patients beginning renal replacement therapy during the period 2000 -2008 in the Italian Dialysis Registry in order to determine the prognosis of ESRD.
Moreover, we tried to identify special subgroups of patients at high risk of death in order to focus researches aimed at ameliorating their prognosis.

Methods:

Our analysis is based on data from the Italian Dialysis Registry of Dialysis and Transplantation. We performed a cohort study by selecting all patients starting hemodialysis or peritoneal dialysis in the period 1/1/2000- 31/12/2008 in Italy and observed until 31/12/2008.
Of each patient were considered date of first treatment, gender, age (split in 5 classes: < 25 year old, 25 – 45, 45 – 65, 65 – 75 and ≥ 75 year old), primary renal disease (grouped in congenital and hereditary disease, diabetes, primary glomerulonephritis, pyelonephritis, systemic diseases, vascular, unknown and others), modality of renal replacement therapy (hemodialysis, peritoneal dialysis and kidney transplantation), main comorbidities (heart disease, heart failure, cerebral vascular disease, peripheral vascular disease, diabetes, chronic lung disease, cancer and hypertension) defined according to (17), death and date of death. The outcome was death for any cause.
For each patient survival was calculated from the first dialysis to death or to 31/12/2008 if alive at the end of follow - up.
Successful kidney transplanted patients and lost patients were censored at the date of the last scheduled dialysis session.
The number of cases in the Italian regions with complete follow-up in the study period determined the sample size.
The observed survival rates from the first treatment to death were calculated according to the life table method. Two other measures were derived: i) relative survival ratio (RSR) (the ratio of the observed survival in the population of interest to the survival that would have been expected if the patients experienced only the age- and period-specific mortality of the general population from which they were drawn) (18); ii) excess mortality rate (the difference between the observed mortality rate and the mortality rate expected in general population). The data relating to general population were obtained from life tables of the Italian Population in the years 2000 – 2008 (19).
Relative survival and excess mortality rate were estimated according to Ederer II method (20), in which the matched individuals are considered to be at risk until the corresponding patient dies or is censored (for a follow – up less than 10 years Ederer II and other estimation methods, such as Hakulinen methods, give similar estimates).
The statistical analysis was performed using Stata version 11 (Statacorp, College Station, Texas, USA).

Fig.1

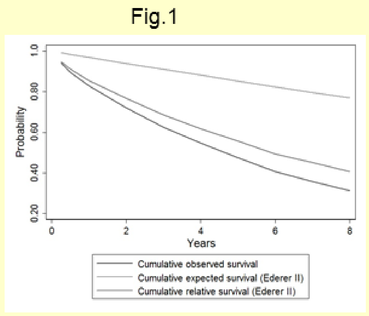


Fig. 2

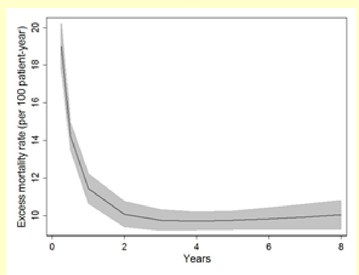


Fig. 3

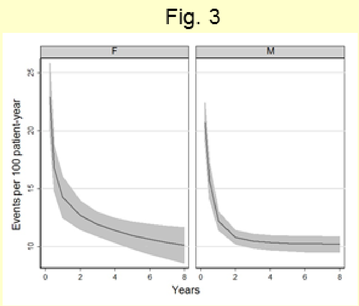


Fig. 4

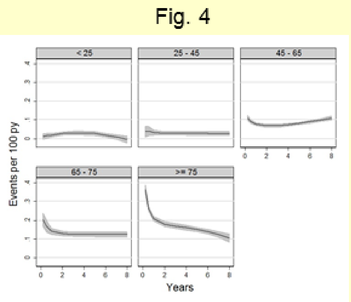
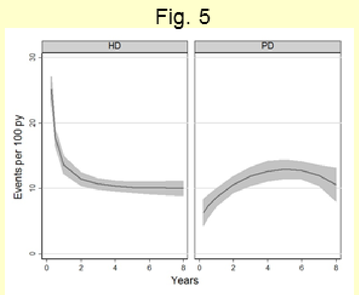


Fig. 5



Age Category (years)	Observed survival	Expected survival	Relative survival (95% CI)	Excess mortality rate (%py)
< 25	0.87	0.998	0.87 (0.80 – 0.92)	3.9
25 – 45	0.87	0.994	0.88 (0.86 – 0.90)	2.8
45 – 65	0.66	0.964	0.65 (0.67 – 0.70)	8.4
65 – 75	0.46	0.881	0.52 (0.50 – 0.54)	12.0
≥ 75	0.27	0.670	0.40 (0.38 – 0.41)	17.5

Table I

Results:

In the period January 2000 – December 2008, 45,427 subjects started either hemodialysis or peritoneal dialysis. Since 8 over 17 regions were able to provide a complete follow – up, only the 27,642 patients belonging to these regions were considered. They comprised 61% of the full dataset. The mean coverage in these eight regions was 91%.
The median age was 70.0 years (interquartile range: 58.7-77.7), 64% of the patients were male. During the follow-up, 22,756 patients (82.3%) were treated only with hemodialysis, 3,265 (11.8%) only with peritoneal dialysis and 1,621 (5.9%) both with hemodialysis and peritoneal dialysis. 11,616 deaths occurred in 74,104 years at risk, determining a crude mortality rate during the study period of 15.68 per 100 patient-year (95% confidence interval: 15.39 – 15.96).
Five-years observed and expected survival was respectively 47.4% and 85.0%, yielding a relative survival estimate of 55.6% (95% CI: 54.7 – 56.5%), i.e. the survival was less than expected for the general population by 44.4% (Fig.1).
The five-year relative survival was 56.8 % (95%CI: 55.6 – 57.9 %) in males, and 53.5% (95%CI: 52.1 – 55.0%) in females. Figure 2 shows relative survival stratified by gender.
As reported in Tab. I relative survival largely differed according to age category, declining especially in the two oldest groups.
Five-year relative survival was 55% (95%CI: 54 – 56%) in hemodialysis patients and 58% (95% CI: 56 – 60%) in peritoneal dialysis patients.
The excess mortality rate did not stay constant over the time period elapsed since dialysis start. In fact, as shown in Fig 3, the excess mortality rate shows a peak at 3 months (21 per 100 patient-years), then it declines to 16 per 100 patient-years at 6 months and at last it becomes almost constant after 1 year, remaining constantly around 10 per 100 patient-years.
The subsequent decline of excess mortality rate was similar for male and female (Fig. 4), suggesting that the first year excess of deaths is independent from gender.
In Fig 5 the behavior of the mortality rate excess by age category is shown, it remains stable over time in patients younger than 65 years, while it shows a fall in the first six months in patients older than 65 years.
The excess mortality rate, stratified by primary renal disease, in the earliest period after commencing dialysis was observed mainly in two diagnostic categories: systemic disease and miscellaneous category.

Conclusions:

1. This study confirms the utility of methods based on relative survivorship in ESRD patients.
2. By using this methodology, we were able to estimate the prognosis of ESRD patients on RRT, showing that they experience a survival of 55% at 5 year in comparison with general population. To our knowledge, this is the first time that ESRD prognosis is measured by determining its relationship with background survival.
3. The 5-year relative survival of ESRD patients is lower than that reported for regional breast cancer (84%), regional colon cancer (69.5%), regional kidney cancer (62.7%), but higher than that for chronic heart failure (35%) and regional lung cancer (24%). It is possible to rank the severity of different chronic diseases and to compare their prognosis. From this perspective, ESRD appears a disease deserving at least as much attention as cancer from health authorities and public opinion.
4. The excess mortality rate seems a suitable measure to describe the trend of mortality in dialysis population in a much more sensitive and informative way than that provided by the simple assessment of proportion of the survivors.

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