Mortality attributable to chronic kidney disease: a cohort study based on the Italian PIRP registry

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OBJECTIVES

Patients with chronic kidney disease (CKD) experience poorer outcomes compared with the general population.

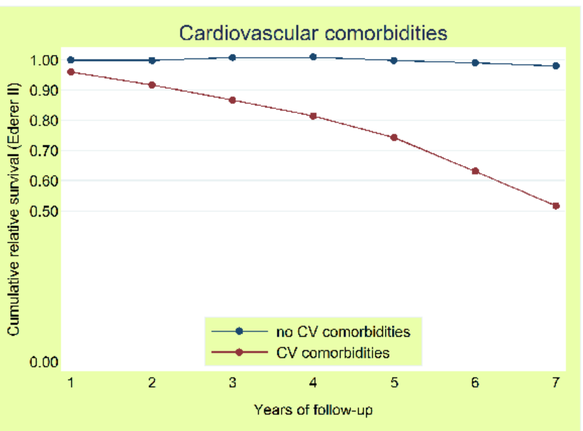
However, mortality attributable to a specific disease is often estimated from cause of death recordings, that may be incomplete or inaccurate. Relative survival (RS) is a method that allows to address these difficulties by estimating attributable mortality without relying on the recorded causes of death.[1] It provides an estimate of the excess mortality (EM) attributable to CKD. While relative survival is the standard method in cancer studies and epidemiological findings are available for kidney transplant[2] and dialysis data,[3] evidence on mortality attributable to CKD using relative survival is still lacking.

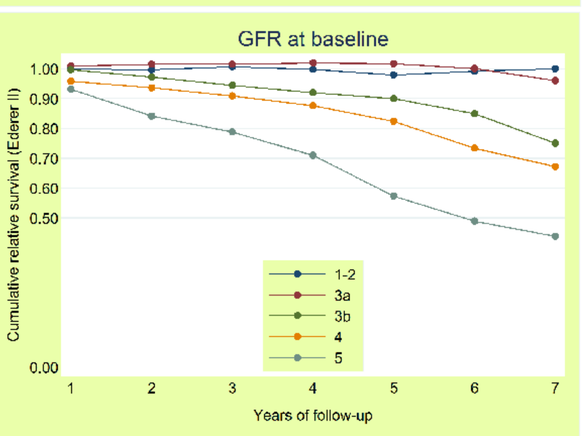
METHODS

Patients who entered the Prevention of Progressive Renal Insufficiency (PIRP) project between 2006 and 2011 were followed up for at least one year until 2012 or death. The PIRP registry collects clinical data on CKD patients living in Emilia-Romagna, a North Eastern Italian region with about 4.3 million inhabitants, who received an individualized pharmacological and dietary treatment aimed to reduce CKD progression.

Relative survival is the ratio of patients' observed survival to the general population expected survival, obtained from a matched population life table. ISTAT mortality tables of the Emilia-Romagna region were used to match CKD patients with the general population by calendar year, gender and age for the years 2006-2011. Estimates of excess mortality were then modeled using multiple flexible parametric survival analysis.[4] Analyses were carried out on the subset of eligible patients who had complete data at baseline on all the predictors of interest. Missing data at baseline were replaced with data from the first available follow-up visit within 6 months, if any. Exclusion criteria were: age less than 18 years, rare types of nephropathy (myeloma or amyloidosis, transplant-related IRC, inherited IRC, congenital malformative IRC), wrong data on clinical variables or on event dates. Dialysis was used as a time-varying covariate to adjust for the timing of entry into dialysis for patients who underwent this procedure.

RELATIVE SURVIVAL ON SUBGROUPS OF CKD PATIENTS





MULTIPLE FLEXIBLE SURVIVAL ANALYSIS ON EXCESS MORTALITY

Covariates	EMRR	Std. Err.	z	P>z	[95% Conf.Interval]	
AGE at baseline (ref. 70-79)						
<50	0.148	0.082	-3.43	0.001	0.049	0.441
50-59	0.370	0.118	-3.12	0.002	0.198	0.690
60-69	0.567	0.116	-2.77	0.006	0.380	0.847
>=80	1.484	0.270	2.17	0.030	1.039	2.119
BMI at baseline (ref. 18.5-24.99)						
<18.5	3.517	1.210	3.66	<0.001	1.792	6.902
25-29.99	0.636	0.111	-2.59	0.010	0.452	0.896
>=30	0.772	0.154	-1.29	0.196	0.522	1.142
GFR STAGE at baseline (ref. 3a)						
1-2	0.000	0.007	-0.02	0.981	0.000.	
3b	3.598	2.394	1.92	0.054	0.977	13.258
4	3.666	2.418	1.97	0.049	1.006	13.352
5	7.449	5.043	2.97	0.003	1.976	28.080
NEPHROPATHY (ref. Glomerulonephritis)						
diabetic nephropathy	1.341	0.542	0.73	0.467	0.608	2.960
hypertensive nephropathy	1.095	0.412	0.24	0.809	0.524	2.287
pyelonephritis	1.194	0.535	0.40	0.692	0.496	2.876
policistic kidney	1.024	0.661	0.04	0.970	0.289	3.630
unknown cause CKD	1.709	0.665	1.38	0.168	0.797	3.664
CV previous events	4.324	1.222	5.18	<0.001	2.486	7.523
females	1.010	0.153	0.07	0.947	0.751	1.359
diabetes	1.737	0.303	3.16	0.002	1.233	2.446
dialysis	0.258	0.081	-4.33	<0.001	0.140	0.476
hemoglobin	0.870	0.046	-2.61	0.009	0.784	0.966
proteinuria	2.334	0.514	3.85	<0.001	1.516	3.594
phosphate	1.461	0.126	4.41	<0.001	1.235	1.730

RESULTS

The study population consisted of 12,293 subjects meeting the time-window inclusion criteria and 12,074 with no exclusion criteria. Patients with complete data were 2,179 (18.1% of those eligible). The relative survival estimate at 7 years was 0.712, indicating a 28.8% mortality increase attributable to CKD disease. Patients without previous CV events had a 7-year survival comparable to that of the matched population's survival, but almost double compared with patients with CV diseases (RS=0.516); patients in stage 5 survival was very low (RS=0.439), like malnourished patients; diabetic CKD was the nephropathy with the lowest survival. Multivariate analysis showed that *dialysis treatment* reduced EM by 74.2%. An increased EM risk was associated with: *older age*; *BMI under 18.5;* baseline *GFR higher values*; *cardiovascular comorbidity; diabetes, proteinuria*, *higher phosphate levels* and *lower hemoglobin*.

Type of nephropathy and gender were not significantly related to excess mortality.

CONCLUSIONS

Relative survival is a useful method to monitor mortality in a large CKD population-based cohort, due to the chronic nature of the disease. Our findings further underline that CKD patients are a particularly frail population; at each stage of the disease and even at older ages they have an excess of mortality compared with the general population. Because the large majority of patients are in CKD stages 3 and 4, our results provide additional useful information for primary care physicians and nephrologists about factors to be monitored to decrease the risk of death from the onset of the disease onwards.

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H) Clinical Nephrology, CKD. H1) Lab methods, progression & risk factors for CKD 1-5, nutrition in CKD, renal diseases (except GNs and cystic diseases).
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