Competing risks of RRT and death in CKD patients with a differential GFR annual decline rate followed within the PIRP project

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OBJECTIVES

In the framework of the Prevention of Progressive Renal Insufficiency Project (PIRP), seven groups of CKD stage 1-5 patients were identified using Classification Tree Analysis (CTA).[1] These groups had specific clinical characteristics that were associated with a differential GFR annual decline rate (Table 1).

To determine the predictive validity of CTA classification with respect to the CKD major endpoints, we followed up the same cohort for 2.5 years to assess their risk of RRT or death.

Table 1. Characteristics of the study groups as a function of annual GFR decline (mL/min/1.73 m²)

High risk (ΔGFR < -2)	Medium risk (ΔGFR from -2 to -1)	Low risk (ΔGFR > -1)
Group 1 (n=230, 10.2%): proteinuric, GFR > 33.65 mL/min/1.73m²	Group 3 (n=378, 16.7%): proteinuric, GFR<=33.65 mL/min/1.73m², PO_4 <= 4.3 mg/dL	Group 6 (n=741, 32.7%): non-proteinuric, age > 67.75, male
Group 2 (n=90, 4.0%): non-proteinuric, age <= 67.75, diabetic	Group 5 (n=264, 11.7%): non-proteinuric, age <= 67.75, non-diabetic	Group 7 (n=410, 18.1%): non-proteinuric, age > 67.75, female
Group 4 (n=152, 6.7%): proteinuric, GFR<= 33.65 mL/min/1.73m², PO_4 > 4.3 mg/dL		

Figure 1. Cumulative Hazard function

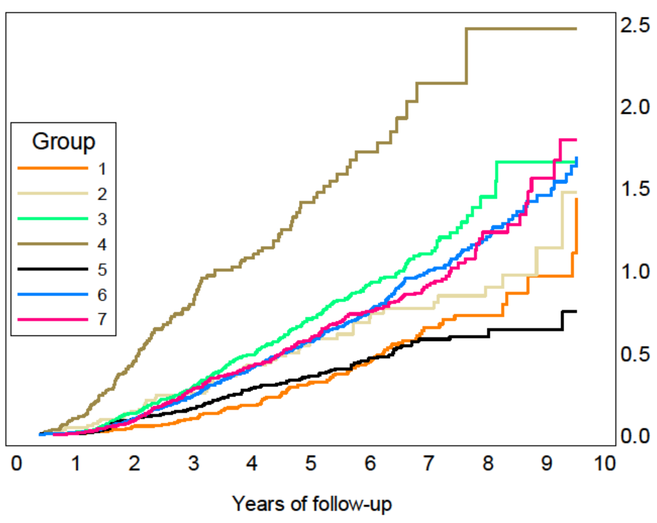
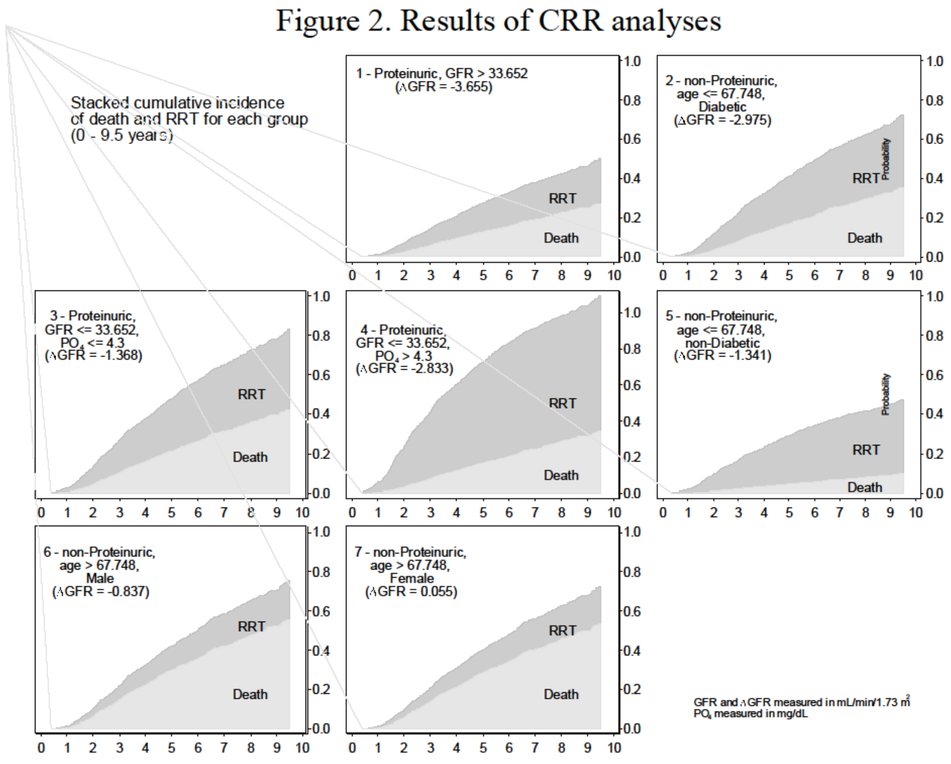


Figure 2. Results of CRR analyses



METHODS

The study cohort included 2265 patients enrolled in PIRP between 1 July 2004 and 30 June 2010, in which the annual GFR decline was determined using at least four serum creatinine measurements. Patients were classified in three groups with differential risk according to their average annual GFR decline: high risk (ΔGFR < - 2 mL/min/1.73m²), medium risk (ΔGFR from - 2 to -1 mL/min/1.73m²) and low risk (ΔGFR > - 1 mL/min/1.73m²).

Outcomes were evaluated until 31 December 2013 and were obtained through a deterministic linkage with the Emilia-Romagna Region administrative databases.

Kaplan-Meier (KM) survival analysis was used to estimate the cumulative hazard of the composite outcome (death or RRT). Competing risks regression (CRR) was used to assess the risk of RRT, with death as a competing risk, for each group of patients.[2]

RESULTS

RRT was reached by 541 (23.9%) patients, of which 538 underwent dialysis and 3 kidney transplant. Patients who died were 675 (29.8%).

Figure 1 depicts the cumulative hazard of the composite outcome for each study group. KM analysis highlighted that group 4 (corresponding to patients who had proteinuria, low GFR and high phosphates) was by far the one at highest risk. Group 5 (younger, non-proteinuric and non-diabetic) was at a low risk through the entire follow-up, while risk for group 1 (proteinuric with higher GFR) was low for the first 7 years then it abruptly increased.

The panels of fig.2 show the stacked cumulative incidence of death (light-grey area) and RRT (dark-grey area) obtained with CRR for each group. Larger areas indicate a higher risk. The sum of the two areas defines the composite risk at each timepoint. CRR results confirmed the findings on composite endpoint obtained from KM analysis, furthermore showing the RRT and death risks breakdown.

Point estimates obtained by CRR, using group 1 as reference, showed that group 4 was at greatest risk of RRT (HR=5.28, p<0.001). The risk of RRT and death was also higher for groups 3 (HR=2.03, p<0.001), 5 (HR=1.82, p=0.001) and 2 (HR=1.77, p=0.020). On the contrary, death was more likely to occur than RRT among male and female elderly (groups 6 and 7, with HR=2.45, p<0.001 and HR=2.31, p<0.001 respectively).

CONCLUSIONS

In conclusion, the groups defined by CTA proved to have good predictive validity. Patient groups at higher risk based on their GFR decline and clinical characteristics were those who experienced the higher probability of RRT and of the composite endpoint, with the exception of group 1. Given that the GFR average starting value of group 1 was the highest, the effect of GFR decline on renal endpoints for this group would probably be apparent with a longer follow-up, as is already suggested by KM analysis.

The CTA classification, which is obtained from usually available demographic and clinical information, can be used to stratify patients at differential risk of poor renal outcomes.

REFERENCES

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