Risk prediction for death and end-stage renal disease does not align with observed outcomes in older patients with advanced chronic kidney disease: a Romanian center experience

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Abstract

Introduction: In 2016, the European Renal Best Practice (ERBP) group published a guideline on the management of older adults with advanced chronic kidney disease (CKD). Two risk scores were highlighted: the Bansal score for mortality, and the Kidney Failure Risk Equation (KFRE) for estimating progression to end-stage kidney disease (ESRD). Our group, as part of the ERBP team, aimed to apply these risk prediction tools in a cohort of older adults with eGFR < 45 ml/min/1.73 m^2.

Material and methods: This retrospective study included adults aged ≥ 65 years with CKD stage 3b-4, evaluated at a Romanian Outpatient Nephrology Department between October 2016 and October 2018. The Bansal score was calculated for all subjects and the KFRE was then used in the low mortality risk group. Outcomes were death or the initiation of dialysis. These outcomes were used to compare the difference between the estimated trajectory and the observed clinical course of patients. Patients were followed up until September 2019.

Results: From the total population (N = 958 patients), more than half ($N1$ = 548, 57.2%) had a high mortality risk. In the remaining group with low mortality risk ($N2$ = 410, 42.8%), 75.4% had a low risk of progression to ESRD. Observed events consisted of 164 deaths and 31 dialysis initiations. We found similar death rates in the two groups (high versus low predicted mortality risk). There was no difference in the rate of dialysis initiation between subjects with a high or low predicted risk of progression to ESRD.

Conclusions: Risk prognostication for death and ESRD did not correspond to the observed clinical course of our older patients with advanced CKD.

Key words: Bansal score, dialysis, Kidney Failure Risk Equation, mortality.

Introduction

The increasing number of adults surviving to older ages has led to an increase in the incidence and prevalence of diseases common among older adults, including chronic kidney disease (CKD) [1, 2]. More importantly, kidney disease in geriatric patients rarely occurs as a sole condition, often coexisting with other diseases that contribute to CKD development, including diabetes or cardiovascular (CV) disease [3, 4]. This becomes

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more problematic in the presence of advanced CKD, corresponding to an estimated glomerular filtration rate (eGFR) below 45 ml/min/1.73 m^2, in which the high burden of comorbidities contributes to frailty [5], decreased functional status, decreased quality of life, and an increased risk of hospitalization or even death [6–8]. Therefore, it is unsurprising that CKD, a growing health concern in older patients, represents a challenge in terms of appropriate management and healthcare costs.

The clinical management of older patients with advanced CKD is often challenged by the competing risks of kidney failure and death before kidney failure develops. Thus, early referral to a nephrologist and preparation for kidney replacement therapy may become unnecessary and potentially harmful for those patients whose risk of death is higher than the risk of progression to kidney failure. Although prior studies suggest that the risk of death is higher than the risk of ESRD, in clinical practice, identifying the risk in individual patients remains difficult due to the scarcity of studies that include older subjects [9].

From this point of view, in 2016, the European Renal Best Practice (ERBP) group published a clinical practice guideline addressing the clinical approach to patients aged > 65 years with an eGFR < 45 ml/min per 1.73 m^2 [10]. The risk stratification concept, which impacts therapeutic decisions, was underlined by this guideline. For example, risk stratification may inform decisions about whether renal replacement therapy (RRT) should be initiated or conservative treatment be maintained. Two risk stratification scores were emphasized: the Bansal score for prognosticating risk of death in the medium term, and the Kidney Failure Risk Equation (KFRE) for estimating progression of from stage 3b or 4 to ESRD, both of which have been validated in the CKD population [11, 12]. The algorithm in the guideline implies that a patient with a high Bansal score, corresponding to high mortality risk, may benefit from a conservative approach to managing ESRD risk, with focus on advanced care planning and without emphasizing the future need for RRT. The same approach is suggested for older patients with low mortality risk, but who are frail. On the other hand, if the patient has low mortality risk, is not frail, and has a high risk for progression to ESRD, the guideline recommends maximized nephroprotection and predialysis counselling, including modality selection.

Our group, as part of the ERBP team, aimed to evaluate a cohort of older patients with advanced CKD and apply a slightly different framework than the one proposed by the guideline, by assessing the risks of mortality and progression to ESRD concurrently in the same population. After dividing the population into groups according to mortality risk, we described their observed clinical course in terms of death or progression to ESRD. Furthermore, sought to identify a risk threshold for the Bansal score, since the ERBP guideline does not define a threshold for high mortality risk.

Material and methods

Study design and participants

We retrospectively evaluated a cohort of patients aged ≥ 65 years with advanced CKD (eGFR < 45 ml/min/1.73 m^2) followed between October 2016 and October 2018 in the nephrology unit of a tertiary referral hospital in Iași, Romania (Dr C.I. Parhon University Hospital). These patients were considered to be a representative sample for the north-east population of Romania regarding various renal pathology.

Definition of variables

A set of demographic, clinical, and biochemical variables were required to assess patients' risk of mortality and progression to ESRD. These data were collected from the patients' electronic medical records. Glomerular filtration rate was estimated (eGFR) using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula [13] based on serum creatinine values.

Outcomes

After predicting individual risks of mortality and progression to ESRD, the entire cohort was divided into risk groups. The follow-up period was used to assess the first subsequent clinical outcome (death or reaching ESRD), which allowed comparison between the estimated and observed clinical courses.

Risk prediction for mortality and ESRD

Individual risk for mortality was predicted using the Bansal score, a nine-variable model developed in a US cohort of 828 participants aged ≥ 65 years with an eGFR < 60 ml/min per 1.73 m^2, from the Cardiovascular Health Study (CHS) [12]. The Bansal score was validated in an independent cohort of 789 community-living elders with CKD from the Health, Aging and Body Composition Study [14], with the same inclusion criteria regarding age and eGFR.

Each of the 9 variables from the Bansal equation had a corresponding score, and the total score was associated with an estimate of risk. A total score of 7 (associated with a mortality risk of 53.82%) was established as a cutoff value to differentiate between two groups – high mortality risk (Bansal ≥ 7) and low mortality risk (Bansal

< 7) – given the fact that the ERBP guidelines do not define a threshold for high risk with respect to mortality outcome.

For estimating the risk for progression to ESRD at 5 years, we used the 4-variable Kidney Failure Risk Equation (KFRE), according to the algorithm proposed by the ERBP guideline [10]. This was calculated in the low mortality risk group using the KFRE equation, which was initially developed and validated in two Canadian CKD cohorts [11], but it was later validated in 31 multinational cohorts including more than 721,000 participants with GFR < 60 ml/min/1.73 m^2 [15].

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages. For categorical variables, the between-group comparisons were performed using the χ^2 test.

A *p*-value < 0.05 was considered to be statistically significant. All statistical analyses were performed using IBM SPSS Statistics version 21.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 1047 patients who fulfilled the inclusion criteria (age ≥ 65 years and eGFR < 45 ml/min/1.73 m^2) were evaluated during the above-mentioned period. Of these, 89 subjects were excluded because of missing data required for calculation of the risk scores. The final cohort included 958 patients. The mean age was 74.3 ±6.9 years, and the sex distribution was similar (50.6% female vs. 49.4% male). Among the comorbid conditions that were components of the Bansal score, diabetes had the highest prevalence (47.4%) in our older population, followed by heart failure (34%) and stroke (11.2%). Baseline characteristics of study participants by risk scores and by first future outcome (death or dialysis) are reported in Table I.

The predicted trajectory in terms of reaching ESRD/death

After applying the Bansal mortality score, we identified 548 (57.2%) patients with high mortality risk (N1 group) and 410 (42.8%) patients with low mortality risk (N2 group). Patients in the N1 group were more frequently male, older, and had a higher prevalence of comorbidities. Individual risk of progression to ESRD was then estimated in the N2 group, using the 4-variable KFRE. Nearly a quarter of this group (24.6%, 101 patients = N2a subgroup) presented a high risk of progression, with the remaining 309 patients (N2b subgroup) having both predicted low mortality risk and low risk of progression to ESRD.

The real-life trajectory in terms of reaching ESRD/death

The end date for follow-up was September 1, 2019. In the entire cohort, 31 (3.23%) patients started RRT and 164 (17.11%) patients died as their first clinical event.

When comparing the two groups (deaths vs. dialysis) according to the baseline prevalence of comorbidities, patients who ultimately died had a higher prevalence of diabetes (47% vs. 41.9%, approximately half of the patients in each group) and a similar prevalence of heart failure (28.1% vs. 29.1%, approximately one third of patients in each group). Stroke prevalence at baseline was higher in patients who subsequently initiated chronic dialysis than in those who died (19.3 vs. 10.3%).

The RRT initiation rate was higher in the N1 group than in the N2 group, but it did not reach statistical significance (3.6% vs. 2.7%, $p = 0.46$). Furthermore, when only patients with low mortality risk were analyzed, there was no difference in the rate of RRT initiation between subjects with a high or low risk of progression to ESRD (N2a group – 5.0% vs. N2b group – 1.9%, $p = 0.15$). The mortality rate was not significantly different between the N1 and N2 groups (15.5% vs. 19.3%, re-

Table I. Baseline characteristics of study participants

Parameter	Total population (*N* = 958)	The predicted trajectory in terms of reaching ESRD/death				The real-life trajectory in terms of reaching ESRD/death	
		High mortality risk (N1 = 548)	Low mortality risk (N2 = 410)	High risk of progression (N2a = 101)	Low risk of progression (N2b = 309)	Deaths (164)	Dialysis (31)
Age [years]	74.3 ±6.9	76.4 ±7.3	71.5 ±5.2	69.4 ±4	72.1 ±5.4	73.7 ±6.5	75.3 ±7.2
Male, *n* (%)	473 (49.4%)	327 (59.7%)	146 (35.6%)	43 (42.6%)	103 (33.3%)	91 (55.5%)	15 (48.4%)
DM, *n* (%)	454 (47.4%)	293 (53.5%)	161 (39.3%)	43 (42.5%)	118 (38.2%)	77 (47%)	13 (41.9%)
HF, *n* (%)	326 (34%)	281 (51.3%)	45 (11%)	4 (4%)	41 (13.3%)	46 (28.1%)	9 (29.1%)
Stroke, *n* (%)	108 (11.2%)	85 (15.5%)	23 (5.6%)	5 (5%)	18 (5.8%)	17 (10.3%)	6 (19.3%)

ESRD – end-stage renal disease, DM – diabetes mellitus, HF – heart failure. Data are mean (± SD), frequencies (or percentages).

spectively, $p = 0.14$). Similarly, when only patients with a Bansal score below 7 were analyzed, there was no significant difference in the mortality rates between subjects with a high or low risk of progression to ESRD (N2a group – 18.8% vs. N2b group – 19.4%, $p = 1.00$).

Figure 1 depicts the observed clinical course of the study population in terms of dialysis initiation or death.

Discussion

This is the first study seeking to examine how the two risk prediction scores for mortality and progression to ESRD proposed by the ERBP guideline were implemented in a large population of older patients with advanced CKD from Eastern Europe and whether the predicted risks overlapped with real-life outcomes. One of the major findings was that more than half of our older subjects had an estimated 5-year mortality risk that exceeded 50%. This finding draws attention to a growing population of older patients with substantial comorbidity, because such a high estimated risk of death is often associated with an accumulation of diseases like diabetes, heart failure or stroke, according to the Bansal score. For this segment of multimorbid older patients with a relatively short life expectancy, efforts should be made to maximize functional status and quality of life. After all, maintaining independence is ranked as a top health outcome priority from the older patient's point of view, and is valued more highly than the wish to stay alive, as a recent study shows [16].

The use of both equations proposed by the ERBP guideline was already validated in a cohort study of older Norwegians with advanced CKD, both having overall good performance, with higher diagnostic accuracy for KFRE as compared to the Bansal score [17, 18]. When quantifying how the risk of death and ESRD compare to one another, the authors found that mortality risk was much higher than ESRD risk (10 : 1), with only a small proportion of individuals (2.6%) having a predicted risk of ESRD higher than their risk of death over 5 years.

In contrast, in our study, we went a step forward by proposing a threshold of 7 for the mortality score that corresponds to an estimated risk of 53.82% and then calculating the risk of progression to ESRD only in those with low mortality risk. The observed mortality rate was approximately five times greater than the rate of dialysis initiation, supporting the idea that in the older population, the risk of death exceeds the risk of progression to ESRD, even among those with severe reductions in eGFR (e.g. < 30 ml/min/1.73 m^2) [19]. When we used the Bansal score to estimate mortality risk, we found that more than half of the population had a high risk. Nevertheless, the

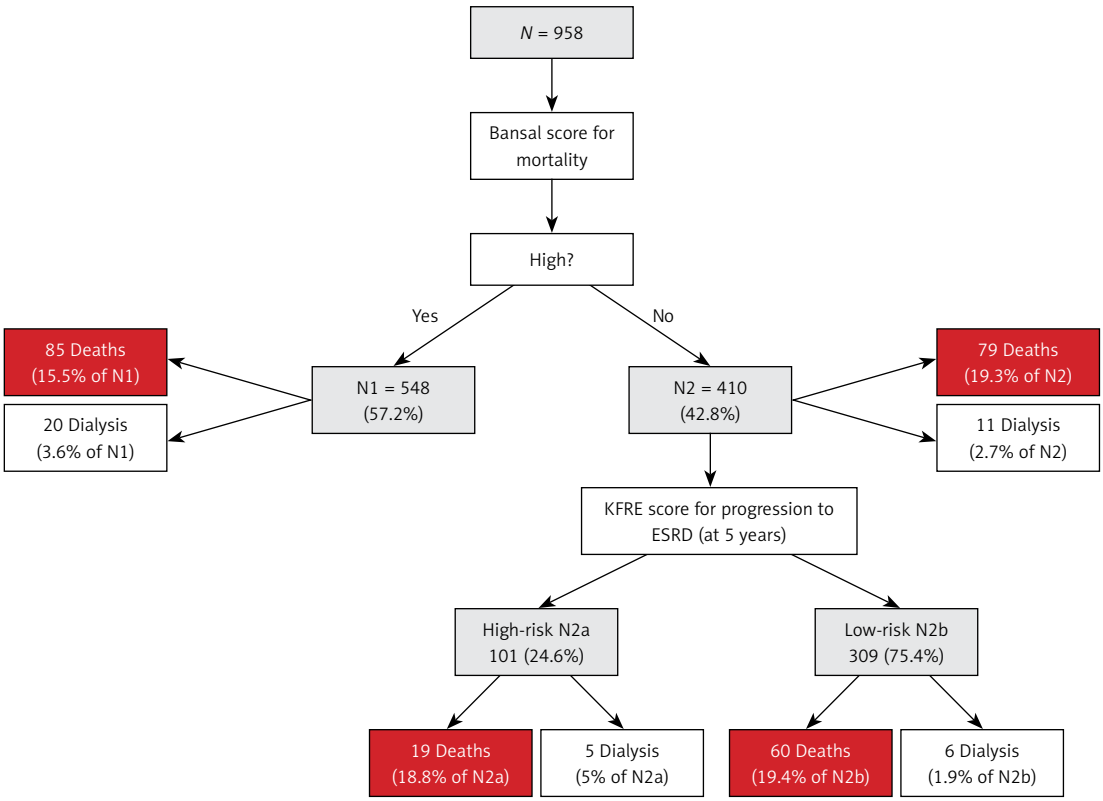

Figure 1. The real-life trajectory of the study population in terms of reaching dialysis/death

interesting finding was that the observed mortality rates were similar in the two groups (N1 with a high mortality risk versus N2 with low mortality risk), suggesting the discrepancy between predicted mortality risks and observed mortality in the two groups.

Of the 31 patients who ultimately entered a chronic dialysis program, 20 (64.51%) subjects had a high mortality risk at baseline, as estimated by the Bansal score, which incorporates comorbidities such as diabetes, heart failure, and stroke. The large proportion of multimorbid patients with a high mortality risk who entered dialysis is inconsistent with the ERBP guideline against promoting dialysis solely on the basis of kidney function in this context, highlighting the difficulty of applying the guideline in real-life settings. Also, the similar dialysis initiation rates irrespective of predicted kidney failure risk suggest that risk prognostication for ESRD did not parallel the real-life trajectory of our older patients with advanced CKD.

Estimating the risk of death and progression to ESRD in older adults is important because it may help guide decisions about whether to start dialysis or to choose a conservative approach. In a first clinical scenario, a patient with a high risk of developing ESRD needs an early referral to a nephrologist, preparation for dialysis (modality selection, placement of an arteriovenous fistula) or transplant evaluation. The second scenario involves an older patient who has a greater risk of dying than of experiencing ESRD, in which case planning dialysis may entail financial, psychological and physical costs that are unnecessary, making conservative care a more suitable option. Although conservative management provides reasonable symptom control and is likely to improve quality of life in older patients with CKD [20], only about one-third of nephrologists discuss this approach with them, mainly due to the common view of conservative care as "no care" [21].

For the nephrologists, presenting conservative management as an option is challenging because this approach may be considered passive rather than active, although it encompasses a whole spectrum of services available to patients, including nutrition, psychology, social work, and palliative care. The conservative approach is part of end-of-life care for older adults with advanced CKD, and is an important component of patient-centered care.

In our study, metabolic and cardiovascular comorbidities were common, with almost half of the subjects having diabetes and approximately one third having heart failure. This finding underlines the high burden of comorbidities in this Eastern European older cohort with advanced CKD, compared to other European populations; for example, these conditions were less prevalent in Hallan's recent Norwegian analysis of 1,188 subjects with same inclusion criteria regarding age and eGFR [17].

Our study has several strengths. We implemented the risk stratification tools from the ERBP guideline for the first time in a large sample of older patients with advanced CKD from Eastern Europe. We also defined a threshold for the mortality score, since the ERBP guideline does not specify what constitutes high mortality risk. Comparing the estimated trajectory of our older patients (mortality risk, risk of progression to ESRD) with real-life events is another important aspect, since the vulnerability of geriatric patients may contribute to outcomes that are difficult to predict.

The fact that frailty could not be evaluated due to the retrospective design of the study is a limitation of our analysis. However, formal frailty scores are so heterogeneous that results based on different scoring systems cannot be compared or pooled [22]. We also studied only subjects who were evaluated at the Outpatient Department of Nephrology, which may limit the generalizability of our results. Another important issue is the limited power of the study, reflected in the small number of certain events. For example, there were 31 events of initiation of RRT (11 in the N2 group with low mortality risk, distributed as follows: 5 in the N2a subgroup with high risk of progression and 6 in the N2b subgroup with low risk of progression to ESRD; Figure 1). These events were observed in a follow-up period of up to 3 years, while the Bansal score and KFRE estimate mortality and progression to ESRD over 5 years; this difference in time horizons could explain the incongruence between predicted outcomes and real-life outcomes in our population.

In conclusion, although the two prediction scores proposed by the ERBP guideline to estimate mortality and progression to ESRD are well validated in previous studies, the predicted risks did not correspond closely to the observed outcomes in our older patients with advanced CKD. Another possible explanation may be the different clinical profile of our older subjects, characterized by a high burden of comorbidities, which highlights the need to optimize their care.

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Ethical approval

Approved by the Ethics Committee from "Dr. C. I. Parhon" Hospital.

Conflict of interest

The authors declare no conflict of interest.

References

1. Hill NR, Fatoba ST, Oke JL, et al. Global prevalence of chronic kidney disease – a systematic review and meta-analysis. PLoS One 2016; 11: e0158765.
2. Report:, U.R.D.S.A.D. https://www.scribd.com/document/45074 8540/USRDS-2019-ES-final
3. Zandecki L, Janion M, Sadowski M, et al. Associations of changes in patient characteristics and management with decrease in mortality rates of men and women with ST-elevation myocardial infarction – a propensity score-matched analysis. Arch Med Sci 2020; 16: 772-80.
4. Li Y, Meng X, Zhou C, Zhou X. Pregnancy-associated plasma protein A as a predictor of all-cause mortality and cardiovascular events in patients with chronic kidney disease: a meta-analysis of prospective studies. Arch Med Sci 2020; 16: 8-15.
5. Wilhelm-Leen ER, Hall YN, Tamura MK, Chertow GM. Frailty and chronic kidney disease: the Third National Health and Nutrition Evaluation Survey. Am J Med 2009; 122: 664-71.e2.
6. Nixon AC, Bampouras TM, Pendleton N, Woywodt A, Mitra S, Dhaygude A. Frailty and chronic kidney disease: current evidence and continuing uncertainties. Clin Kidney J 2018; 11: 236-45.
7. Lee SJ, Son H, Shin SK. Influence of frailty on health-related quality of life in pre-dialysis patients with chronic kidney disease in Korea: a cross-sectional study. Health Qual Life Outcomes 2015; 13: 70.
8. Piątek Ł, Wilczek K, Kurzawski J, et al. Gender-related disparities in the treatment and outcomes in patients with non-ST-segment elevation myocardial infarction: results from the Polish Registry of Acute Coronary Syndromes (PL-ACS) in the years 2012-2014. Arch Med Sci 2020; 16: 781-8.
9. O'Hare AM, Choi AI, Bertenthal, et al. Age affects outcomes in chronic kidney disease. J Am Soc Nephrol 2007; 18: 2758-65.
10. Farrington K, Covic A, Nistor I, et al. Clinical Practice Guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR<45 mL/min/1.73 m2): a summary document from the European Renal Best Practice Group. Nephrol Dial Transplant 2017; 32: 9-16.
11. Tangri N, Stevens LA, Griffith J, et al. A predictive model for progression of chronic kidney disease to kidney failure. JAMA 2011; 305: 1553-9.
12. Bansal N, Katz R, De Boer IH, et al. Development and validation of a model to predict 5-year risk of death without ESRD among older adults with CKD. Clin J Am Soc Nephrol 2015; 10: 363-71.
13. Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. Am J Kidney Dis 2010; 55: 622-7.
14. Harris TB, Visser M, Everhart J, et al. Waist circumference and sagittal diameter reflect total body fat better than visceral fat in older men and women. The Health, Aging and Body Composition Study. Ann N Y Acad Sci 2000; 904: 462-73.
15. Tangri N, Grams ME, Levey A, et al. Multinational assessment of accuracy of equations for predicting risk of kidney failure: a meta-analysis. JAMA 2016; 315: 164-74.
16. Ramer SJ, McCall NN, Robinson-Cohen C, et al. Health outcome priorities of older adults with advanced CKD and concordance with their nephrology providers' perceptions. J Am Soc Nephrol 2018; 29: 2870-8.
17. Hallan SI, Rifkin DE, Potok OA, et al. Implementing the European Renal Best Practice Guidelines suggests that prediction equations work well to differentiate risk of end-stage renal disease vs. death in older patients with low estimated glomerular filtration rate. Kidney Int 2019; 96: 728-37.
18. Xiong J, Zhang M, Guo X, et al. Acute kidney injury in critically ill cirrhotic patients with spontaneous bacterial peritonitis: a comparison of KDIGO and ICA criteria. Arch Med Sci 2020; 16: 569-76.
19. Prakash S, O'Hare AM. Interaction of aging and chronic kidney disease. Semin Nephrol 2009; 29: 497-503.
20. Ren Q, Shi Q, Ma, et al. Quality of life, symptoms, and sleep quality of elderly with end-stage renal disease receiving conservative management: a systematic review. Health Qual Life Outcomes 2019; 17: 78.
21. Ladin K, Pandya R, Kannam A, et al. Discussing conservative management with older patients with CKD: an interview study of nephrologists. Am J Kidney Dis 2018; 71: 627-35.
22. Aguayo GA, Donneau AF, Vaillant MT, et al. Agreement between 35 published frailty scores in the general population. Am J Epidemiol 2017; 186: 420-34.