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Addition of the Multidimensional Prognostic Index to the Estimated Glomerular Filtration Rate Improves Prediction of Long-Term All-Cause Mortality in Older Patients with Chronic Kidney Disease

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Abstract

Current prognostic scores of chronic kidney disease (CKD) are not accurate in older patients. The aim of this study was to evaluate the prognostic accuracy of the Multidimensional Prognostic Index (MPI) in comparison with and in addition to the estimated glomerular filtration rate (eGFR) to predict long-term all-cause mortality in hospitalized older patients with CKD. In a prospective cohort study with a mean follow-up of 2 years, we calculated eGFR according to the Modification of Diet in Renal Disease study and collected information on functional, cognitive, nutritional, co-morbidities, drug use, and co-habitation status to calculate the MPI on 1,198 patients aged ≥65 years with a diagnosis of CKD from an hospital-based sample. The all-cause mortality incidence rate for 100 person-years was 18.3 (men 22.7 vs. women 15.3, $p < 0.0001$). Adding the MPI to the eGFR model significantly improved all-cause mortality prediction accuracy: The C-index increased from 0.579 to 0.648 ($p < 0.0001$), with correct reclassification of 25.9% of patients (Net Reclassification Improvement [NRI], 0.259, $p < 0.0001$; Integrated Discrimination Improvement [IDI], 3.8%, $p < 0.0001$). The correct reclassification was higher in patients who did not die (259/741 patients, reclassification rate = 34.9%) than in patients who died (62/457 patients, reclassification rate = 13.6%). Conversely, adding the eGFR to the MPI model seems to improve prediction accuracy less consistently. In fact, the C-index increased, but not significantly (from 0.639 to 0.648, $p = 0.444$), with correct reclassification of 5.8% of patients (NRI, 0.058, $p = 0.012$; IDI, 0.009, $p = 0.001$), suggesting a small, although significant improvement. Adding MPI information to the eGFR markedly improved the prediction of 2-year all-cause mortality in older patients with CKD. A multidimensional evaluation for all-cause mortality risk prediction should be considered in older patients with CKD.

Introduction

The prevalence of chronic kidney disease (CKD) increases with age, reaching 31%–48% in patients older than 70 years.[1,2] Recent studies have reported that CKD is a leading medical cause of hospitalization among older people,[3] and that a decrease in the estimated glomerular filtration rate (eGFR) is associated with an increased risk of all-cause and cardiovascular mortality.[4,5] Several methods to assess renal function have been described in older patients,[5,6] including the Modification of Diet in Renal Disease (MDRD),[7] the Cockroft–Gault equations[8] or the more recent Chronic Kidney Disease Epidemiology Collaboration formulas (CKD-EPI).[9] Although the eGFR is widely used in

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clinical practice, its prognostic role in older patients has been questioned because there is no evidence that it is causally linked to adverse outcomes, including mortality in this selected population.[10,11]

Recent lines of research have suggested that the prognosis of older patients with chronic medical conditions is strongly affected by a multiplicity of functional, cognitive, and nutritional factors that are not directly related to their primary disease,[12] indicating that the prognostic model for mortality for these patients should be multidimensional in nature rather than disease specific.[13,14] Interestingly, such a comprehensive prognostic approach has never been tested in older patients with CKD. Recently, a Multidimensional Prognostic Index (MPI) for 1-year all-cause mortality, based on a Comprehensive Geriatric Assessment (CGA) with information on clinical, functional, cognitive, nutritional, social status, and drug use, was developed and validated in two different cohorts of hospitalized older patients.[15] Further studies demonstrated that the MPI score was an accurate predictor of all-cause mortality in older patients with several acute and chronic diseases,[16–19] including CKD.[20] At present it is unknown, however, whether the MPI may improve the predictive accuracy of the eGFR in clinical practice. The aim of this study was to evaluate the prognostic accuracy of the MPI in comparison with and in addition to the eGFR to predict long-term all-cause mortality in hospitalized older patients with CKD.

Materials and Methods

Study population

The present study was conducted according to the Declaration of Helsinki, the guidelines for Good Clinical Practice, and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (available at www.strobe-statement.org/) and was approved by the local Ethic Committee for human experimentation. All consecutive patients aged 65 years and older admitted with a diagnosis of CKD from January, 2005, to December, 2007, to the Geriatrics Unit of the Casa Sollievo della Sofferenza Hospital, IRCCS, San Giovanni Rotondo, Italy, were screened for inclusion in the study. Inclusion criteria were: (1) Age ≥ 65 years; (2) ability to provide an informed consent or availability of a proxy for informed consent; (3) a diagnosis of CKD defined as an eGFR ≤ 60 mL/min per 1.73 m^2; and (4) complete CGA during hospitalization. At baseline, a structured interview, clinical evaluation, and extensive review of records from the patients' general practitioners were performed. Moreover, serum sample were taken for the analysis of creatinine, blood urea nitrogen (BUN), and hemoglobin. All patients were followed for a median period of 2 years (patients who had not died were followed for at least 1 year). Vital status was assessed by directly contacting the participants or consulting the Registry Offices of the cities in which the patients were residents at the time of hospital admission. Dates of death were identified from death certificates.

Estimated Glomerular Filtration Rate

The eGFR was calculated according to the MDRD four-component equation incorporating age, gender, race, and serum creatinine level[7]; eGFR was expressed as mL/min per 1.73 m^2, and an eGFR <60 mL/min per 1.73 m^2 was used to define presence of decreased renal function. The CKD stages were defined according to the MDRD[7] as follows: eGFR from <60 to 30 mL/min per 1.73 m^2 = CKD stage 3; eGFR from <30 to 15 mL/min per 1.73 m^2 = CKD stage 4; and eGFR from <15 mL/min per 1.73 m^2 = CKD stage 5. Anemia was defined as hemoglobin level <12 g/dL.

The Multidimensional Prognostic Index

A standard CGA, which included information on eight domains, was carried out using assessment instruments widely employed in geriatric practice (Table 1). Functional status was evaluated by Activities of Daily Living (ADL)[21] and by Instrumental Activities of Daily Living (IADL) scales.[22] Cognitive status was screened by the Short Portable Mental Status Questionnaire (SPMSQ).[23] Nutritional status was explored with the Mini Nutritional Assessment (MNA).[24] The Exton–Smith Scale (ESS) was used to evaluate the risk of developing pressure sores.[25] Co-morbidity was

Table 1. The Comprehensive Geriatric Assessment-Based Domains of the Multidimensional Prognostic Index

Multidimensional Prognostic Index (MPI)	
Domain	*Score*
ADL (score)	
6–5	0
4–3	0.5
2–0	1
IADL (score)	
8–6	0
5–4	0.5
3–0	1
SPMSQ (score)	
0–3	0
4–7	0.5
8–10	1
CIRS (score)	
0	0
1–2	0.5
≥ 3	1
MNA (score)	
≥ 24	0
17–23.5	0.5
<17	1
ESS (score)	
16–20	0
10–15	0.5
5–9	1
Number of medications	
0–3	0
4–6	0.5
≥ 7	1
Co-habitation status	
Living with family	0
Institutionalized	0.5
Living alone	1

ADL, Activities of Daily Living; IADL, Instrumental ADL; SPMSQ, Short Portable Mental Status Questionnaire; CIRS, Cumulative Illness Rating Scale ; MNA, Mini Nutritional Assessment; ESS, Exton–Smith Scale.

examined using the Cumulative Illness Rating Scale (CIRS),[26] and the number of drugs taken by patients at admission was recorded. Co-habitation status included alone, in family, or in institute. The MPI was calculated by the inclusion of information from the above-reported eight domains of the CGA. For each domain, a tripartite hierarchy was used, *i.e.*, 0 = no problems, 0.5 = minor problems, and 1 = major problems, based on conventional cutoff points derived from the literature for the ADL,[21] IADL,[22] SPMSQ,[23] MNA,[24] and ESS[25] or observing the frequency of distribution of patients in the previous validation study for co-morbidities and number of medication. The sum of the calculated scores from the eight domains was divided by 8 to obtain a final MPI score from 0 to 1. For analytical purposes, absolute values of MPI were not considered, and to determine the best MPI cutoff points, MPI values were expressed as three grades of risk: MPI-1 low risk (MPI value ≤ 0.33), MPI-2 moderate risk (MPI value between 0.34 and 0.66), and MPI-3 severe risk of mortality (MPI value > 0.66) as previously reported.[15] The approximate time required for collecting data for the CGA was 20 min, plus 3–5 min for data input (www.operapadrepio.it/it/content/view/1091/976/). Details on mathematical methods used to identify the best MPI cutoff points and validation of the algorithm have been reported elsewhere.[15]

Statistical analysis

Patients' baseline characteristics were reported as mean ± standard deviation (SD) or frequencies and percentages for continuous and categorical variables, respectively. Baseline comparisons between men and women were made using the chi-squared test for categorical variables and the Mann–Whitney U-test for continuous variables. Baseline differences according to MPI grades were assessed with the Jonckheere–Terpstra trend test or Mantel–Haenszel chi-squared test for continuous and categorical variables, respectively. Incidence rates for 100 person-years were reported with respect to both gender and MPI grades, and p values were assessed with Poisson regression models. The discriminatory power of both the eGFR and the MPI scores for all-cause mortality risk was assessed by estimating survival C-indices, along with their 95% confidence interval (95% CI). Comparison between C-indices was carried out following the Pencina and D'Agostino approach.[27] Univariate proportional hazard regression models were employed to predict all-cause mortality risk with eGFR and MPI as predictors.

Models' calibration, *i.e.*, the agreement between observed outcomes and predictions, was assessed for each nested model separately using the survival-based Hosmer–Lemeshow (HL) goodness-of-fit test,[28] a chi-squared test based on grouping observations into quintiles of predicted risk and testing associations with observed outcomes.

The improvement in model performance was evaluated by the inclusion of MPI into the model. The predicted probabilities derived by the models without MPI were then classified into three risk categories, according to tertiles cutoffs used to build reclassification tables for patients with event (death) and without event. Improvement in all-cause mortality risk prediction by adding the MPI to the eGFR was assessed estimating the Net Reclassification Improvement (NRI) and the Integrated Discrimination Improvement (IDI).[29] The NRI focused on reclassification tables built separately for patients with and without events and quantifies the correct movement in predefined categories (upward for events and downward for nonevents). The IDI can be seen as an average over the range of all possible risk cutoffs of the improvements on sensitivity minus the worsening on specificity. Indeed, IDI does not require predefined risk categories. Increase in the C-indices was also assessed using proportional hazard regression analyses adding the MPI to eGFR and tested according to Pencina and colleagues.[29] A p value < 0.05 was considered for statistical significance. All analyses were performed using SAS Release 9.1 (SAS Institute, Cary, NC) and R.

Results

Characteristics of the study population

During the enrollment period, 1,242 consecutive patients were admitted to the Geriatric Unit with a diagnosis of CKD and were eligible for the study. Nine patients were excluded because they were younger than 65 years, 14 patients were excluded because the CGA was not completed, and 21 patients were excluded because they did not consent to participate in the study. The final study population included 1,198 patients, 534 men (44.5%) and 664 women (55.5%). The mean age was 80.5 ± 6.8 years (range, 65–100 years). The mean follow-up time was 2.1 ± 1.3 years. The overall all-cause mortality incidence rate for 100 person-years was 18.3, with a significantly higher rate in men than women (men 22.7 vs. women 15.3, $p < 0.0001$). Table 2 shows the baseline clinical and functional characteristics of patients according to gender. Table 3 reports the characteristics of patients divided according to their MPI grade.

Comparison between MPI grades and CKD stages

All-cause mortality incidences for 100 person-years were progressively higher with increasing the MPI grade (MPI 1 = 11.3, MPI 2 = 22.4, MPI 3 = 39.7, p for trend < 0.0001), as well as with increasing the CKD stage (CKD stage 3 = 15.5, CKD stage 4 = 30.6, CKD stage 5 = 46.5, p for trend < 0.0001). Univariate proportional hazards regression models showed that both MPI grades and CKD stages were significantly associated with an increased all-cause mortality. Hazard ratios (HR) along with both their 95% CI were estimated for MPI grades and CKD stages, respectively: MPI 1, HR = 1 reference category; MPI 2, HR = 1.96, 1.59–2.41; MPI 3, HR = 3.35, 2.55–4.40 (p for trend < 0.0001) and CKD stage 3, HR = 1 reference category; CKD stage 4, HR = 1.92, 1.55–2.39; CKD stage 5, HR = 2.69, 1.80–4.02 (p for trend < 0.0001). Both models were well calibrated according to HL test ($\chi^2 = 3.703$, $p = 0.883$ and $\chi^2 = 9.588$, $p = 0.295$ for MPI and eGFR, respectively). MPI risk score had a significant higher discriminatory power than eGFR, *i.e.*, survival C-indices were MPI = 0.649, 95% CI = 0.621–0.677 vs. eGFR = 0.579, 95% CI = 0.551–0.607 ($p < 0.0001$).

Predictive model of eGFR implemented with MPI

As shown in Table 4, adding MPI to the eGFR model significantly improved all-cause mortality prediction accuracy. The C-index derived by the model with eGFR without

Table 2. Baseline Characteristics of Older Hospitalized Patients with Chronic Kidney Disease According to Gender

	All (n = *1,198*)	*Men* (n = *534*)	*Women* (n = *664*)	p *value*
Patients (%)[a]	100	44.5	55.5	—
Follow-up, mean (SD), years	2.1 (1.3)	1.9 (1.3)	2.2 (1.3)	< 0.001
Age, mean (SD), years[b]	80.5 (6.8)	80.2 (7.0)	80.8 (6.6)	0.332
Weight, mean (SD), kg[b]	64.2 (13.5)	67.9 (12.2)	61.2 (13.8)	< 0.001
MPI, mean (SD) score[b]	0.38 (0.2)	0.35 (0.2)	0.4 (0.2)	< 0.001
eGFR, mean (SD)[b]	41.7 (13.0)	42.4 (12.9)	41.0 (13.1)	0.057
ADL, mean (SD) score[b]	4.4 (2.1)	4.5 (2.2)	4.3 (2.1)	0.008
IADL, mean (SD) score[b]	3.9 (2.9)	3.8 (2.7)	4.1 (3.1)	0.394
SPMSQ, mean (SD) score[b]	2.2 (2.3)	1.9 (2.3)	2.4 (2.4)	< 0.001
Exton–Smith, mean (SD) score[b]	16.2 (3.0)	16.4 (3.0)	15.9 (3.0)	0.001
CIRS-CI, mean (SD) score[b]	3.0 (1.7)	3.0 (1.7)	2.9 (1.6)	0.153
MNA, mean (SD) score[b]	21.1 (5.4)	21.7 (5.5)	20.6 (5.2)	< 0.001
Drugs number, mean (SD)[b]	4.6 (2.8)	4.7 (3.0)	4.6 (2.7)	0.970
Co-morbidity				
Hypertension (*n*, %)[a]	781 (65.2)	310 (58.1)	471 (70.9)	< 0.001
Ischemic heart disease (*n*, %)[a]	127 (10.6)	75 (14.0)	52 (7.8)	< 0.001
Heart Failure (*n*, %)[a]	148 (12.4)	63 (11.8)	85 (12.8)	0.600
Diabetes mellitus (*n*, %)[a]	264 (22.0)	96 (18.0)	168 (25.3)	0.002
Anemia (*n*, %)[a]	441 (36.8)	187 (35.0)	254 (38.3)	0.249
Medications				
NSAIDs (*n*, %)[a]	84 (7.0)	31 (5.8)	53 (8.0)	0.142
Oral blood glucose lowering drugs (*n*, %)[a]	153 (12.8)	49 (9.2)	104 (15.7)	0.001
Low dose aspirin (*n*, %)[a]	366 (30.6)	155 (29)	211 (31.8)	0.238
ACE inhibitors (*n*, %)[a]	438 (36.6)	188 (35.2)	250 (37.7)	0.294
Angiotensin II antagonists (*n*, %)[a]	233 (19.4)	81 (15.2)	152 (22.9)	0.001
Calcium channel blockers (*n*, %)[a]	214 (17.9)	82 (15.4)	132 (19.9)	0.032
Diuretics (*n*, %)[a]	420 (35.1)	171 (32.0)	249 (37.5)	0.048
Mortality (events/PY, % IR)	456/2496 (18.3)	229/1009 (22.7)	227/1487 (15.3)	< 0.001

[a]Categorical variables.
[b]Continuous variables.
MPI, Multidimensional Prognostic Index; eGFR, estimated glomerular filtration rate; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living; SPMSQ, Short-Portable Mental Status Questionnaire; ESS, Exton–Smith Scale; CIRS-CI, Cumulative Illness Rating Scale–Comorbidity Index; MNA, Mini Nutritional Assessment; NSAID, nonsteroidal antiinflammatory drug; ACE, angiotensin-converting enzyme; PY, person-year; IR, incidence rate.

and with MPI score increased from 0.579 to 0.648 ($p < 0.0001$). The model including both MPI and eGFR resulted well calibrated ($\chi 2 = 6.813$, $p = 0.557$). The estimated NRI was 0.259 and was highly significant ($p < 0.0001$), suggesting that by adding MPI to the model with the eGFR alone 25.9% of patients were reclassified correctly. The addition of MPI into the model was particularly powerful for the correct reclassification into a lower risk category of patients who did not die during the follow-up (259 of the 741 patients who did not die, 34.9%), whereas among patients who died ($n = 457$), 62 (13.6%) were correctly reclassified into a higher all-cause mortality risk-category. Such results were confirmed by the estimated IDI of 0.038 ($p < 0.0001$).

Predictive model of MPI implemented with eGFR

Conversely, adding the eGFR to the MPI model seems to improve prediction accuracy less consistently. Indeed, the C-index derived by the model with MPI score without the estimated eGFR was not statistically significant different from the model with both MPI and eGFR (from 0.639 to 0.648, $p = 0.444$). Nevertheless, the estimated NRI was 0.058 ($p = 0.012$), suggesting that adding the eGFR to the model with the MPI score alone, about 5.8% of patients were correctly reclassified. The estimated IDI of 0.009 ($p = 0.001$) suggested a small, although significant improvement.

Discussion

The present study demonstrated that the MPI may provide useful information for predicting 2-year all-cause mortality in older patients hospitalized with CKD. Indeed, integrating the MPI information in the prediction model of the eGFR resulted in a significant improvement in the performances of eGFR. These findings confirm the notion that has already emerged in the recent literature that inclusion of information collected by a multidimensional approach should be used to evaluate prognosis and need for medical surveillance in older patients.[13–15]

This finding was corroborated by robust statistical methods for prognostic assessment that included the evaluation of improvement in risk classification by computing the NRI and the IDI. The NRI focuses on reclassification tables constructed separately for participants with and without events (in this study "death") and quantifies the correct movement in risk categories—upward for events and downward for nonevents. The NRI should be interpreted with caution, because it is dependent on the arbitrary choice of categories; the

Table 3. Baseline Characteristics of Older Hospitalized Patients with Chronic Kidney Disease Subdivided According to the Multidimensional Prognostic Index Grade

Characteristics	All (n = 1,198)	Multidimensional Prognostic Index			p value[a]
		MPI 1 Low risk (n = 543)	MPI 2 Moderate risk (n = 525)	MPI 3 Severe risk (n = 130)	
Patients (%)[b]	100	45.3	43.8	10.9	—
Follow-up, mean (SD), years	2.1 (1.3)	2.3 (1.2)	2.0 (1.3)	1.6 (1.4)	< 0.001
Age, , mean (SD), years[c]	80.5 (6.8)	79.1 (6.4)	81.3 (6.8)	82.9 (7.1)	< 0.001
Weight, mean (SD), kg[c]	64.2 (13.5)	65.4 (12.2)	64.0 (14.0)	59.6 (15.4)	< 0.001
eGFR, mean (SD) score[c]	41.7 (13.0)	44.6 (11.6)	39.7 (13.5)	37.3 (13.7)	< 0.001
ADL, mean (SD) score[c]	4.4 (2.1)	5.8 (0.5)	3.8 (2.1)	1.0 (1.4)	< 0.001
IADL, mean (SD) score[c]	3.9 (2.9)	6.2 (2.2)	2.5 (2.1)	0.5 (0.9)	< 0.001
SPMSQ, mean (SD) score[c]	2.2 (2.3)	1.2 (1.2)	2.6 (2.1)	5.7 (3.5)	< 0.001
ESS, mean (SD) score[c]	16.2 (3.0)	18.2 (1.6)	15.1 (2.4)	11.4 (2.8)	< 0.001
CIRS-CI, mean (SD) score[c]	3.0 (1.7)	2.3 (1.3)	3.3 (1.5)	4.4 (2.1)	< 0.001
MNA, mean (SD) score[c]	21.1 (5.4)	24.0 (3.7)	19.8 (4.4)	14.0 (5.9)	< 0.001
Drugs number, mean (SD)[c]	4.6 (2.8)	3.7 (2.5)	5.3 (2.9)	5.7 (2.9)	< 0.001
Co-morbidity					
Hypertension (*n*, %)[b]	781 (65.2)	363 (66.9)	336 (64.0)	82 (63.1)	0.284
Ischemic heart disease (*n*, %)[b]	127 (10.6)	51 (9.4)	59 (11.2)	17 (13.1)	0.168
Heart failure (*n*, %)[b]	148 (12.4)	42 (7.7)	83 (15.8)	23 (17.7)	< 0.001
Diabetes mellitus (*n*, %)[b]	264 (22.0)	85 (15.7)	138 (26.3)	41 (31.5)	< 0.001
Anemia (*n*, %)[b]	441 (36.8)	153 (28.2)	222 (42.3)	66 (50.8)	< 0.001
Medications					
NSAIDs (*n*, %)[b]	84 (7.0)	41 (7.6)	37 (7.0)	6 (4.6)	0.304
Oral blood glucose-lowering drugs (*n*, %)[b]	153 (12.8)	53 (9.8)	77 (14.7)	23 (17.7)	0.003
Low-dose aspirin (*n*, %)[b]	366 (30.6)	139 (25.6)	185 (35.2)	42 (32.3)	0.003
ACE inhibitors (*n*, %)[b]	438 (36.6)	206 (37.9)	187 (35.6)	45 (34.6)	0.652
Angiotensin II antagonists (*n*, %)[b]	233 (19.4)	105 (19.3)	97 (18.5)	31 (23.8)	0.382
Calcium channel blockers (*n*, %)[b]	214 (17.9)	94 (17.3)	96 (18.3)	24 (18.5)	0.901
Diuretics (*n*, %)[b]	420 (35.1)	136 (25.0)	229 (43.6)	55 (42.3)	< 0.001
Mortality (events/PY, % IR)	456/2,496 (18.3)	141/1,249 (11.3)	233/1,040 (22.4)	82/207 (39.7)	< 0.001

[a]*p* values calculated using Jonckheere–Terpstra trend test for continuous variables and Mantel–Haenszel chi-squared test for categorical variables.

[b]Categorical variables.

[c]Continuous variables.

eGFR, Estimated glomerular filtration rate; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living; SPMSQ, Short-Portable Mental Status Questionnaire; ESS, Exton–Smith Scale; CIRS-CI, Cumulative Illness Rating Scale–Comorbidity Index; MNA, Mini Nutritional Assessment; NSAID, nonsteroidal antiinflammatory drug; ACE, angiotensin-converting enzyme; PY, person-year; IR, incidence rate.

information from IDI does not suffer from arbitrary choice of categories, and therefore it can be interpreted as an equivalent of increase in average sensitivity without changes in specificity. In this study, the IDI-based analysis confirmed unequivocally that the improvement in all-cause mortality risk prediction by adding MPI to eGFR was highly significant.

The clinical usefulness of this finding may be relevant if we consider that the prognostic value of formulas commonly used to estimate renal function in older patients was limited.[10] Conversely, adding the eGFR to the MPI model seems to improve prediction accuracy less consistently, suggesting a small, although significant, improvement. Among various validated systems to calculate eGFR, we selected the MDRD equation that has wide diffusion and seems to correctly identify older patients at different mortality risk. Indeed, in this study, eGFR appeared significantly accurate in predicting long-term all-cause mortality in agreement with several other studies.[4,5,30] The overall all-cause mortality incidence rate for 100 person-years in this population was 18.3, quite similar to rates reported in other studies of older patients with CKD.[4,30] As expected, all-cause mortality rates were higher in men than women, whereas the multidimensional impairment, as evaluated by the MPI, was significantly higher in women than men. These findings are in agreement with recent data in older people, reporting that the sex difference in life expectancy was not entirely linked to sex difference in disability,[12] because men with the same chronological age and biological impairments had a higher risk of death compared with women.[15]

In the present study, patients with higher MPI grade showed lower eGFR values and higher prevalence of a series of concomitant diseases, such as heart failure, diabetes, and anemia. However, the fact that the MPI significantly improved the prognostic value of eGFR, an organ system–oriented tool, suggests that loss of functional capabilities, diminishing cognitive skills, malnutrition, and immobilization could be a final common pathway of a global involutional condition for the frail elderly with chronic systemic illnesses, as recently reported in older patients.[12] Indeed, the MPI is calculated from information conventionally collected for the assessment of older patients, particularly in those admitted to hospital, including functional disability, cognitive

Table 4. Discrimination Improvement and Reclassification Tables of Older Hospitalized Patients with Chronic Kidney Disease Who Died (Events) and Who Were Alive (Non-Events) after 2 Years by Adding Multidimensional Prognostic Index to Estimated Glomerular Filtration Rate to Evaluate the Improvement on Mortality Risk Prediction

	Estimate	*SE*	p *value*
NRI eGFR vs. eGFR + MPI	0.259	0.033	< 0.001
IDI eGFR vs. eGFR + MPI	0.038	0.005	< 0.001

Events (n = *457*)

		With MPI		
Without MPI		< 24.7%	24.7%– 35.8%	> 35.8%
	< 24.7%	251	33	7
	24.7%–35.8%	28	36	22
	> 35.8%	4	14	62

Non-Events (n = *741*)

		With MPI		
Without MPI		< 24.7%	24.7%– 35.8%	> 35.8%
	< 24.7%	73	23	8
	24.7%–35.8%	142	106	62
	> 35.8%	21	96	210

NRI, corresponding estimated Net Reclassification Improvement. NRI focused on reclassification tables and quantifies the correct movement in categories (upward for events and downward for non-events).

IDI, corresponding estimated Integrated Discrimination Improvement. Models' discrimination is the ability to distinguish subjects who will develop an event from those who will not. IDI focused on differences between sensitivity and "one minus specificity" for all possible cutoffs for models with and without MPI and does not require predefined risk categories.

eGDR, Estimated glomerular filtration rate.

impairment, malnutrition, co-morbidity, and polypharmacy. The roles of malnutrition, concomitant diseases, and/or functional status have been reported recently as strong prognostic indicators in elderly patients who needed dialysis for end-stage renal disease.[31,32] No patients with end-stage kidney disease receiving dialysis for renal replacement therapy were included in our study, hence we cannot rule out the prognostic accuracy of MPI in older patients with this condition.

This study has some limitations. First, because the study population included older patients hospitalized in a geriatric unit, it is plausible that our findings may not be applicable to other settings. In addition, patients were recruited within a single hospital. This was a rather well-identified and selected population, which limits the possibility of selection bias. Larger prospective multicenter studies are still needed to confirm our findings and explore the variability of performance across different settings. Third, recent studies carried out in non-older populations reported that the risk of mortality associated with a given level of eGFR is increased in patients with proteinuria assessed by urine dipstick or albumin-to-creatinine ratio.[5,33] We did not collect any data on proteinuria in this population, so we could not explore the additive role of this condition on survival, over and above the presence of renal impairment as measured by the eGFR. Finally, collection of information to calculate the MPI requires adjunctive time to the standard clinical visit, which may make this less feasible in certain clinical settings. In conclusion, the inclusion of multidimensional information of older patients, as expressed by the MPI, markedly improved the predictive accuracy for long-term all-cause mortality of eGFR. Further studies are needed to evaluate the potential usefulness of this prognostic tool in clinical practice.

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Author Disclosure Statement

All authors report no conflict of interest.

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