Frequency of Renal Dysfunction and Frailty in Patients ≥80 Years of Age With Acute Coronary Syndromes

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Although a significant association between renal function and outcomes in patients with acute coronary syndromes (ACS) has been consistently described, little information exists about the magnitude of this association in patients at older ages. No study assessed the prognostic role of renal function according to frailty in patients with ACS. The *LONGEVO-SCA* registry included unselected ACS patients aged ≥80 years. Frailty was asessed by the FRAIL scale, and baseline creatinine clearance was calculated by the Cockroff-Gault formula. We evaluated the impact of renal function on mortality or readmission at 6-months according to frailty status by the Cox regression method. A total of 473 patients were assessed, with a mean age of 84.2 years. The distribution of patients across estimated glomerular filtration rate (eGFR) subgroups was as follows: (1) <30 ml/min: n = 76 (16.1%); (2) 30 to 44 ml/min: n = 147 (31.1%); (3) 45 to 60 ml/min: n = 136 (28.8%); and (4) >60 ml/min: n = 114 (24.1%). Patients with lower eGFR values were older, had a higher proportion of comorbidities and other geriatric syndromes (p = 0.001) and underwent less often an invasive management during admission (p < 0.001). The incidence of mortality or readmission at 6 months progressively increased across renal function subgroups (p = 0.001). After adjusting for potential confounders, this association became nonsignificant (p = 0.802). The association between eGFR and outcomes was only significant in patients without frailty (p = 0.001). In conclusion, most patients aged ≥80 years with NSTEACS had renal function impairment at admission. The association between renal function and outcomes was different according to frailty status. **(Am J Cardiol 2019;123:729−735)**

The progressive aging of the population is leading to an increase in the number of older patients admitted for acute coronary syndrome (ACS).[1] These patients are underrepresented in clinical trials.[2] Although a significant association between renal function and outcomes in patients with ACS has been consistently described,[3−7] little information exists about the magnitude of this association in patients at older ages.[8,9] On the other hand, frailty is a common condition in these patients, and is strongly associated with a more conservative management and poorer outcomes in patients with ACS.[10−14] Patients with renal dysfunction (RD) have also a higher prevalence of frailty.[15] Risk stratification in frail patients with comorbidities is challenging, due to the complex interactions between frailty, comorbidity,[16] and the most recommended tools for risk stratification in this setting.[17] To our knowledge no study has previously assessed the prognostic role of renal function according to frailty status in older patients with ACS. The aim of this substudy was to analyze the impact of renal function on outcomes according to frailty status in a series of nonselected older patients with ACS from routine clinical practice.

Methods

The LONGEVO-SCA registry[18] (*Impacto de la fragiLidad y Otros síNdromes GEriátricos en el manejo y pronóstico Vital del ancianO con Síndrome Coronario Agudo sin elevación de segmento ST*) is a prospective, observational study conducted in 44 Spanish hospitals in order to assess the characteristics of a cohort of unselected older patients with NSTEACS. In this study a comprehensive geriatric assessment was performed during admission, assessing clinical outcomes at 6 months. The design has previously been described in detail.[18] The study included 532 consecutive patients aged ≥80 years admitted for NSTEACS, defined as the presence of chest pain and at least one of the following: (1) ECG changes suggestive of myocardial ischemia, and/or (2) elevated markers of myocardial damage. Signed informed consent by the patient or representative was required. Patient refusal to

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participate in the registry and the impossibility to obtain the geriatric tests were considered exclusion criteria. Although distinguishing this situation in routine clinical practice may be sometimes difficult, patients with severe comorbidities were only excluded if symptoms of myocardial ischemia were clearly triggered only by other conditions such as acute anemia, severe decompensated respiratory insufficiency, active infectious diseases, or severe coexisting valvular disease (type 2 myocardial infarction). For the purpose of this subanalysis only patients with available data regarding estimated glomerular filtration rates (eGFR) were included (n = 473, 88.9%). Decisions on antithrombotic treatment and performance of coronary angiography were left to the discretion of each medical team according to current recommendations. If coronary angiography was performed, vascular access, antithrombotic drugs, and the choice of stents or other devices were left to the operator's decision.

Data were prospectively collected by local investigators during the admission, using standardized case report forms. Demographics, baseline clinical features, electrocardiographic data and echocardiographic, laboratory and angiographic parameters were collected. *GRACE*[19] and *CRUSADE*[20] risk scores were calculated for each patient. In-hospital clinical outcomes were also registered, such as the need of invasive procedures and in-hospital complications. Major bleeding was defined by the CRUSADE definition.[20] An invasive strategy was defined as the performance of coronary angiography during the admission. eGFR were calculated at admission by the Cockroff-Gault[21] formula. Additionally, the recently developed BIScrea formula[22] was used to validate the results regarding the association between eGFR and outcomes according to frailty status.

A baseline geriatric assessment was done during admission by trained physicians through interviews with the patient and/or family/caregivers and referring to the patient's status before admission. Investigators were encouraged to include all patients during the first 72 hours. Previous frailty was assessed by the FRAIL scale.[23] This is a simple, interview based tool which evaluates 5 items (fatigue, resistance, ambulation, concomitant diseases, and weight loss). Prefrailty is defined as the presence of one or two criteria and frailty as the presence of 3 or more criteria. The rest of geriatric assessment included disability (Barthel Index,[24] Lawton Brody index[25]), cognitive status (Pfieffer test[26]), comorbidity (Charlson index[27]), and nutritional risk (Mini Nutritional Assessment-Short Form [MNA-SF][28]).

The primary endpoint of this study was the composite of all-cause death or readmission at 6 months of follow-up. Clinical follow-up was carried out, by medical visit, review of medical history or telephone contact with the patient, family, or referring physician at 6 months.

All patients or their representatives signed an informed consent before being included in this registry. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Confidential information of the patients was protected according to national normative. Management of patients was performed according to current recommendations. This manuscript has been revised for its publication by the Clinical Research Ethics Committee of Bellvitge Hospital (IRB00005523).

For the statistical analysis, continuous variables are described either by the mean and standard deviation, or by the median and interquartile range when appropriate. Categorical variables are expressed as number and percentage. Baseline characteristics, clinical management and in-hospital clinical course were compared across groups according to eGFR status (as measured by the Cockroff-Gault formula). Patients were divided into 4 groups: (1) eGFR <30 ml/min (n = 76); (2) 30 to 44 ml/min (n = 147); (3) 45-60 ml/min (n = 136); and (4)> 60 ml/min (n = 114). The association between categorical variables was analyzed with the Chi-square test, with the correction of continuity when indicated. The analysis of quantitative variables according to creatinin clearance status was performed by ANOVA test. The association between eGFR and the primary endpoint at 6-months was assessed by a Cox regression model, considering the primary endpoint (mortality or readmission at 6 months) as dependent variable. Reference category for eGFR groups was >60 ml/min. Variables included in the multivariate analysis were those with an association ($p < 0.1$) both with the exposition (eGFR groups) and the effect (the composite of death or readmission at 6 months), and not considered to be an intermediate variable between them. Additionally, the association between eGFR and the incidence of the primary endpoint was assessed separately in two groups according to frailty status (nonfrail, n = 349 and frail, n = 117). Survival analysis was performed using Kaplan Meier curves. Statistical significance of differences was assessed by log rank test. The PASW Statistics 18 (Chicago, IL) and STATA 14.1 were used for the analyses.

Results

The mean age of the 473 patients included was 84.2 years (SD 4). Most patients (296 of 473, 62.6%) were male. The prevalence of cardiovascular risk factors and comorbidities such as previous myocardial infarction, stroke, or peripheral artery disease was high. Most patients had high-risk criteria at admission, with a high proportion of signs of heart failure, positive troponin, and high values of *GRACE* and *CRUSADE* scores. Most patients (399 of 473, 84.4%) underwent an invasive strategy during the admission, with a not negligible proportion of multivessel disease.

A significant proportion of patients had some degree of cognitive impairment, nutritional risk, and frailty criteria (Table 1).

Mean eGFR was 48.3 ml/min. Most patients (359 of 473, 75.9%) presented some degree of renal failure. The distribution of patients across eGFR subgroups was as follows: (1) <30 ml/min: n = 76 (16.1%); (2) 30 to 44 ml/min: n = 147 (31.1%); (3) 45 to 60 ml/min: n = 136 (28.8%); and (4)> 60 ml/min: n = 114 (24.1%). Patients with lower eGFR were older and had a higher proportion of hypertension, peripheral artery disease, previous myocardial infarction, chronic heart failure, and history of bleeding. These patients had also higher risk criteria at admission, with a significantly higher proportion of signs of heart failure at admission, elevated troponin, lower hemoglobin values,

Table 1
Clinical characteristics of the overall cohort (n = 473)

Age (years) (mean, SD)	84.2 (4)
Men	296 (62.6%)
Body mass index (kg/m^2) (mean, SD)	26.7 (4)
Hypertension	409 (86.5%)
Dyslipidemia	302 (63.8%)
Diabetes mellitus	186 (39.3%)
Active smoker	19 (4%)
Previous stroke	78 (16.5%)
Previous myocardial infarction	167 (35.3%)
PAD	63 (13.3%)
Previous heart failure	86 (18.2%)
Previous bleeding	27 (5.7%)
Previous neoplasm	82 (17.3%)
Dementia	21 (4.4%)
Depression	58 (12.3%)
Number of chronic treatments (mean, SD)	7.8 (4)
Baseline creatinine clearance (ml/min) (mean, SD)	48.3 (19)
Baseline hemoglobin (g/dL) (mean, SD)	12.7 (2)
Killip class >=2	135 (28.5%)
Postive troponin	399 (84.4%)
GRACE score (mean, SD)	165 (29)
CRUSADE score (mean, SD)	41 (13)
Invasive strategy	399 (84.4%)
Multivessel disease	210 (5.6%)
Left ventricle ejection fraction (%)	53 (12)
Disability (activities of daily living)	
None	308 (65.1%)
Mild	119 (25.2%)
Moderate	27 (5.7%)
Severe	7 (1.5%)
Complete dependency	8 (1.7%)
Lawton Brody index (mean, SD)	5.6 (2)
Comorbidity (Charlson index) (mean, SD)	2.4 (2)
Cognitive impairment (Pfeiffer test)	
-None	328 (69.3%)
-Mild or moderate	131 (27.7%)
-Severe	9 (1.9%)
Nutritional risk* (MNA-SF)	239 (50.5%)
Frailty (*FRAIL* scale)	
Non-frail	162 (34.2%)
Pre-frail	187 (39.5%)
Frail	117 (24.7%)

MNA-SF = mini nutritional assessment short form; PAD = peripheral arterial disease.

* Nutritional risk was defined a MNA-SF test score below 11.

poorer left ventricular systolic function, and higher values of *GRACE* and *CRUSADE* score. Patients with poorer renal function showed also a higher prevalence of disability, cognitive impairment, nutritional risk and frailty, and a higher degree of comorbidity (Table 2). The proportion of patients undergoing an invasive management during the admission progressively declined across eGFR subgroups (>60 ml/min: 103of 114 (90.4%); 45 to 60 ml/min: 115of 136 (84.6%); 30 to 44 ml/min: 111 of 147 (75.5%), and <30 ml/min: 45 of 76 (59.2%)). In contrast, no significant differences were observed regarding treatment at discharge, except for a higher proportion of diuretic prescription in patients with lower eGFR (Annex Table 1).

The incidence of complications during admission was similar across eGFR subgroups, except for a higher incidence of refractory ischemia and higher requirements for blood transfusion (Table 3). Patients with poorer renal function had also a higher in-hospital mortality and longer hospital stay. Both the incidence of readmission and mortality at 6 months progressively increased along with the degree of RD (Table 3). The incidence of the combined of mortality or readmission at 6 months progressively increased across eGFR subgroups. After adjusting for potential confounders, the association between renal function and the incidence of mortality or readmission at 6 months became nonsignificant (Annex Table 2).

The association between eGFR subgroups and the incidence of mortality or readmission at 6 months was different according to frailty status. A significantly higher incidence of outcomes across eGFR subgroups was observed in patients without frailty. In contrast, this association was clearly not significant in frail patients (Table 4). Figure 1 shows the cumulative incidence of mortality or readmission according to renal function subgroups: (1) in the whole cohort, (2) in robust patients, and (3) in patients with established frailty criteria.

The distribution of patients across eGFR subgroups as measured by the BIScrea formula was as follows: (1) <30 ml/min: n = 50 (10.6%); (2) 30 to 44 ml/min: n = 155 (32.8%); (3) 45 to 60 ml/min: n = 175 (37.0%); and (4)>60 ml/min: n = 93 (19.7%).

The distribution of patients by renal function stages according to the 2 formulas is shown in Annex Table 3. There were significant differences at classifying patients into different stages of renal function. BIScrea classified significantly fewer patients as having normal/mild renal and severe RD as compared with Cockroff-Gault formula. In contrast, BIScrea classified significantly more patients as having moderate RD. Weighted Cohen's kappa coefficient revealed moderate concordance between both formulas (weighted kappa 0.581, 95% confidence interval [CI] 0.552 to 0.610). The association between eGFR subgroups by the BIScrea formula and the incidence of mortality or readmission at 6 months was also different according to frailty status. Again a significantly higher incidence of outcomes across eGFR subgroups was observed in patients without frailty. In contrast, this association was clearly not significant in frail patients (Table 4). Figure 2 shows the cumulative incidence of mortality or readmission according to renal function subgroups (as measured by the BIScrea formula): (1) in the whole cohort, (2) in robust patients, and (3) in frail patients.

Discussion

The main findings of this study are: (1) 3 quarters of older patients with NSTEACS from this series (75.9%) had RD at admission; (2) patients with RD were significantly older, with more comorbidities and geriatric syndromes, and underwent more often a conservative management; (3) a significant association between eGFR and mortality or readmission at 6 months was observed, but this association became nonsignificant after adjusting for potential confounders; and (4) the association between eGFR and outcomes was different according to frailty status, being only significant in patients without frailty criteria.

Table 2
Clinical characteristics according to creatinine clearance status (Cockroff-Gault)

Creatinine clearance (ml/min) Variable	<30 (n = 76)	30-45 (n = 147)	45-60 (n = 136)	>60 (n = 114)	p value for trend
Age (years) (mean, SD)	85.5 (4)	85.2 (4)	83.9 (3)	81.8 (5)	0.001
Men	42 (55.3%)	87 (59.2%)	90 (66.2%)	77 (67.5%)	0.043
Body mass index (kg/m^2) (mean, SD)	24.9 (4)	25.9 (4)	27.2 (3)	28.5 (3)	0.001
Body surface area (m^2) (mean, SD)	1.69 (0.2)	1.74 (0.2)	1.80 (0.2)	1.87 (0.1)	0.001
Hypertension	73 (96.1%)	129 (87.8%)	116 (85.3%)	91 (79.8%)	0.002
Diabetes	26 (34.2%)	66 (44.9%)	51 (37.5%)	43 (37.7%)	0.836
Dyslipidemia	51 (67.1%)	97 (66%)	81 (59.6%)	73 (64%)	0.460
Active smoker	5 (6.6%)	4 (2.7%)	2 (1.5%)	8 (7%)	0.820
Previous stroke	11 (14.5%)	28 (19%)	27 (19.8%)	12 (10.5%)	0.309
PAD	16 (21.1%)	20 (13.7%)	9 (14%)	8 (7%)	0.010
Previous myocardial infarction	35 (46.1%)	57 (38.8%)	39 (28.7%)	36 (31.6%)	0.016
Previous heart failure	25 (32.9%)	36 (24.5%)	15 (11%)	10 (8.8%)	0.001
Previous bleeding	7 (9.2%)	13 (8.8%)	4 (2.9%)	3 (2.6%)	0.009
Previous neoplasm	10 (13.2%)	25 (17%)	28 (20.6%)	19 (16.7%)	0.470
Dementia	5 (6.6%)	9 (6.1%)	5 (3.7%)	2 (1.8%)	0.055
Depression	4 (5.3%)	20 (13.6%)	20 (14.7%)	14 (12.3%)	0.233
Number of treatments (mean, SD)	9 (4)	8.2 (4)	7.0 (3)	7.3 (4)	0.001
SBP (mm Hg) (mean, SD)	138 (28)	140 (27)	143 (26)	140 (27)	0.394
Heart rate (bpm) (mean, SD)	78 (20)	77 (20)	76 (19)	74 (15)	0.395
Killip class >=II	39 (51.3%)	45 (30.6%)	27 (19.9%)	24 (21.1%)	0.001
Positive troponin levels	71 (93.4%)	123 (83.7%)	114 (83.8%)	91 (79.8%)	0.026
Baseline hemoglobin (g/dL) (mean, SD)	11.8 (2)	12.4 (2)	13.0 (2)	13.3 (2)	0.001
Baseline creatinine (mg/dL)	2.12 (0.9)	1.29 (0.3)	1.02 (0.2)	0.8 (0.2)	0.001
Glucose level (mg/DL)(mean, SD)	153 (61)	158 (80)	144 (59)	140 (54)	0.003
LVEF (%) (mean, SD)	49 (13)	55 (12)	53 (12)	56 (11)	0.001
GRACE score (mean, SD)	182 (31)	166 (29)	160 (24)	154 (28)	0.001
CRUSADE score (mean, SD)	54 (9)	44 (9)	42 (9)	28 (10)	0.001
Multivessel disease	22 (52.4%)	70 (64.5%)	65 (57%)	53 (54.1%)	0.455
Disability (Barthel index)					0.001
None	45 (59.2%)	88 (59.9%)	90 (67.2%)	85 (75.9%)	
Mild	16 (21.1%)	45 (30.6%)	35 (26.1%)	23 (20.5%)	
Moderate	6 (7.9%)	10 (6.8%)	7 (5.2%)	4 (3.6%)	
Severe	5 (6.6%)	2 (1.4%)	0	0	
Complete dependency	4 (5.3%)	2 (1.4%)	2 (1.5%)	0	
Lawton Brody Index (mean, SD)	4.7 (2.6)	5.2 (2.7)	5.7 (2.3)	6.3 (1.9)	0.001
Charlson index (mean, SD)	3.1 (2.2)	2.6 (1.9)	2.2 (1.7)	1.9 (1.7)	0.001
Cognitive impairment (Pfeiffer test)					0.003
-None	42 (56.8%)	104 (71.2%)	93 (68.4%)	89 (79.5%)	
-Mild or moderate	29 (39.2%)	39 (26.7%)	41 (30.1%)	22 (19.6%)	
-Severe	3 (4.1%)	3 (2.1%)	2 (1.5%)	1 (0.9%)	
Nutritional risk* (MNA-SF)	54 (72)	75 (51.7)	64 (47.4)	46 (41.8)	0.001
Frailty (FRAIL scale)					0.005
Non-frail	22 (29.3%)	43 (29.5%)	49 (36.8%)	48 (42.9%)	
Pre-frail	26 (34.7%)	64 (43.8%)	57 (42.9%)	40 (35.7%)	
Frail	27 (36%)	39 (26.7%)	27 (20.3%)	24 (21.4%)	

MNA-SF = mini nutritional assessment short form = PAD: peripheral arterial disease.
* Nutritional risk was defined a MNA-SF test score below 11.

Chronic kidney disease (CKD) is a common condition in patients with ACS, especially in patients at older ages. Several authors have described an association between CKD and clinical outcomes. However, most of these studies assessed younger patients with a relatively low prevalence of comorbidities.[3–7] The information about the impact of RD on outcomes in ACS patients at older ages is scarce. Fischer et al[8] described a retrospective cohort (n = 7413) of patients hospitalized with ACS, assessing clinical outcomes at 1 year according to renal function. Mean age was 66.3 years, and the prevalence of CKD was 46.1%. A progressive increase in mean age and frequency of most comorbid conditions were observed among individuals with lower eGFR strata. In addition, performance of revascularization was significantly less frequent in those with lower eGFR. RD was associated with higher risk of death and readmission due to myocardial infarction. The authors described an independent association between eGFR and mortality or readmission for myocardial infarction. Likewise, Liu et al[9] assessed the impact of RD on long-term outcomes in a prospective series of 184 consecutive patients with ACS. Mean age of 73.7 years, and most patients (156

Table 3
Clinical course according to creatinine clearance status (Cockroff-Gault)

Creatinine clearance (ml/min) Variable	<30 (n = 76)	30-45 (n = 147)	45-60 (n = 136)	>60 (n = 114)	p value for trend
Refractory ischemia	7 (9.2%)	7 (4.8%)	11 (8.1%)	0	0.024
Reinfarction	4 (5.3%)	6 (4.1%)	7 (5.1%)	2 (1.8%)	0.295
Ventricular fibrillation	0	2 (1.4)	0	0	0.216
Atrioventricular block	2 (2.6%)	1 (0.7%)	2 (1.5%)	1 (0.9%)	0.506
CRUSADE major bleeding	8 (10.5%)	11 (7.5%)	11 (8.1%)	7 (6.1%)	0.354
Need for transfusion	9 (11.8%)	8 (5.4%)	7 (5.1%)	4 (3.5%)	0.035
Infections	8 (10.5%)	6 (4.1%)	10 (7.4%)	7 (6.1%)	0.601
Delirium	3 (4%)	11 (7.6%)	13 (9.6%)	4 (3.5%)	0.382
In-hospital mortality	4 (5.3%)	4 (2.7%)	4 (2.9%)	0	0.037
Hospital stay (median, p25-75)	8 (5-14)	7 (5-11)	6 (4-10)	6 (3-9)	0.008
Readmission at 6 months	31 (40.8%)	43 (29.3%)	28 (20.6%)	25 (21.9%)	0.002
6-month mortality	14 (19.2%)	21 (14.8%)	8 (6.4%)	7 (6.4%)	0.001

of 184, 84.8%) had eGFR <60 ml/min. Patients with severe RD were older and had higher rates of comorbid conditions and higher Killip class. More severe RD was also associated with a lower hemoglobin level and lower left ventricular ejection fraction. Severe RD was an independent risk factor for clinical outcomes (p = 0.034), and was associated with poor prognosis.

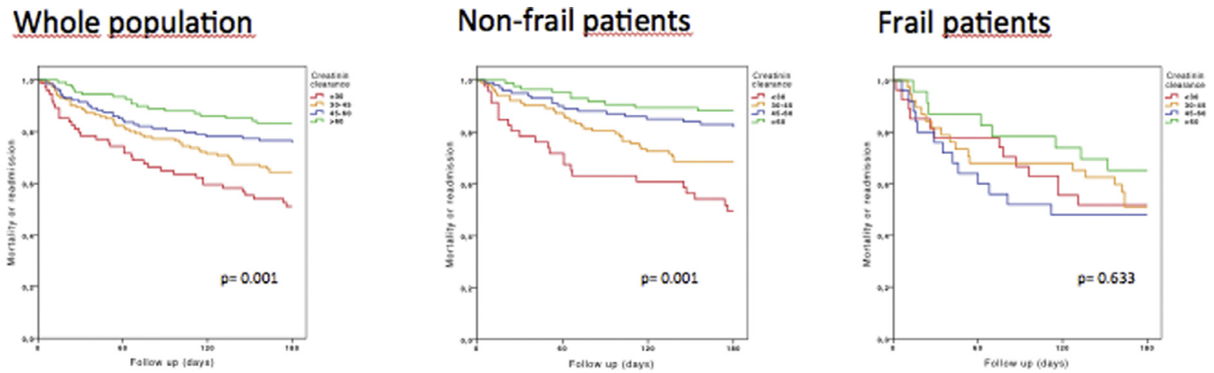
Consistently with previous data, data from our oldest patients cohort revealed a significant association between poorer renal function, older ages, and higher prevalence of the most important comorbidities. In addition, patients with lower eGFR underwent a more conservative management. However, after adjusting for all potential confounders the association between RD and clinical outcomes became clearly nonsignificant, suggesting that the poorer prognosis in patients with RD was mostly due their higher clinical risk profile rather than the presence of RD per se. In our opinion, these different results as compared with previous studies might be related to the different characteristics of populations regarding age (mean age from this series was >10 years older than those described in previous registries[8,9]), clinical presentation and prevalence of comorbidities, as well as the quality of data regarding potential confounders. Older patients have usually a higher prevalence of comorbidities and frailty, and risk stratification in this setting is very difficult. In this sense, information about ageing-related variables might contribute to explore the different magnitude of the association between RD and outcomes in these populations. In addition, the strong association between RD and a conservative approach observed in these patients might also have contributed to their poorer outcomes.

Interestingly, data from this study showed for the first time a differential prognostic impact of renal function on outcomes according to frailty status. Although a significant association was observed in robust patients, this association seemed mostly due to preexisting comorbidities in patients with frailty criteria. Frailty is commonly associated with a higher degree of comorbidity, a lower likelihood for an invasive management[10,12] and a higher proportion of disability and other geriatric syndromes.[16] Importantly, frailty has been consistently associated to higher mortality in older patients with ACS. Risk assessment in this clinical setting is challenging, since most risk stratification tools in patients with ACS come from younger series with a lower overall risk.[19,20] In our opinion, the lack of association between renal function and outcomes in frail patients might be due to their poorer prognosis and the complex interactions between frailty, comorbidities and the more often conservative management observed in these patients.

On the other hand, the assessment of renal function in patients at older ages is also challenging, since there is an ongoing debate on whether the reduction in eGFR that occurs with aging should be considered as a "disease" or an "age-related decline".[29] It has been suggested the need for an age adapted equations in the last few years. The BIScrea equation[23] was recently developed in community-living elders aged ≥70 years. A better correlation with directly measured GFR has been suggested, as well as an improved risk prediction in patients with ACS at older ages.[30] To our

Table 4
Association between eGFR categories and mortality or readmission at 6 months according to frailty status

Variable	Hazard ratio (95% CI)	p value
Cockroff-Gault formula		
Non-frail patients		
>60 ml/min	Ref	0.001
45-60	0.98 (0.50-1.92)	
30-45	1.99 (1.10-3.56)	
<30	3.97 (2.13-7.37)	
Frail patients		
>60 ml/min	Ref	0.633
45-60	1.66 (0.76-3.62)	
30-45	1.28 (0.61-2.68)	
<30	1.19 (0.53-2.65)	
BIScrea formula		
Non-frail patients		
>60 ml/min	Ref	0.001
45-60	0.95 (0.50-1.79)	
30-45	1.88 (1.04-3.41)	
<30	3.90 (1.98-7.69)	
Frail patients		
>60 ml/min	Ref	0.995
45-60	1.11 (0.48-2.57)	
30-45	1.12 (0.48-2.62)	
<30	1.09 (0.41-2.93)	



Patients at risk

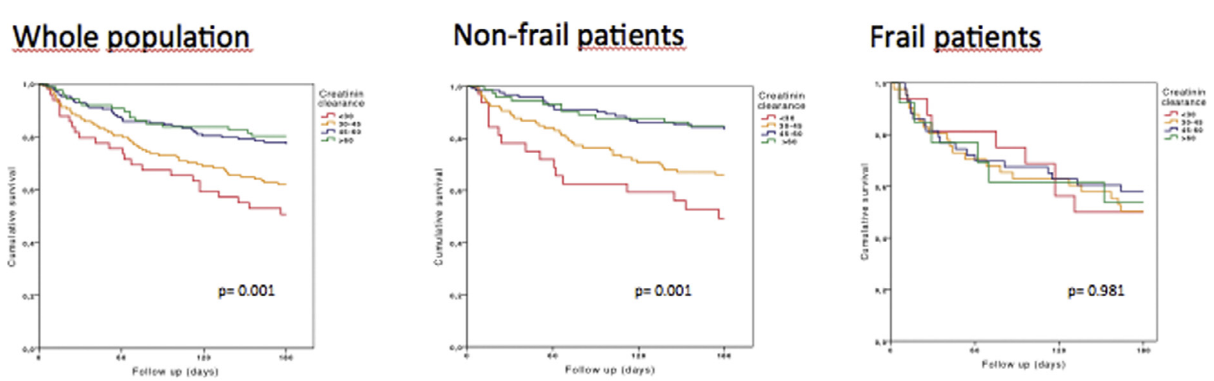
<30	74	55	44	34	46	33	28	21	27	21	15	12
30-45	141	115	100	81	102	89	74	64	38	25	25	16
45-60	128	108	99	88	100	90	84	75	25	15	12	11
>60	108	101	92	74	85	81	75	61	23	20	17	13

Figure 1. Cumulative incidence of mortality or readmission according to creatinine clearance subgroups (Cockroff-Gault formula) in *(A)* the whole cohort; *(B)* nonfrail patients, and *(C)* frail patients.

judgment, the confirmation of the differential impact of renal function on outcomes according to frailty status also by using the BIScrea formula improves the strength of our results. We believe that this is an important finding, since frailty can be easily assessed,[23] providing important information about risk stratification and the potential benefit of different therapeutic strategies in patients with ACS. However, these results should be cautiously interpreted and require further validation in larger series.

This study has several limitations. The sample size of subgroups was moderate and the number of events was relatively small, so this should be considered a hypothesis generating study to be further confirmed in larger series. Including only patients with available eGFR data may lead to some degree of selection bias. Due to its observational nature we cannot rule out the presence of selection bias and unmeasured confounding. In addition, only admission creatinine level was used for classifying patients, without information regarding renal function at discharge. Finally, a 6-month follow-up may have not been sufficient to fully detect the impact of renal function on outcomes. However, we believe that despite these limitations our study retrieves novel and interesting data regarding the potential prognostic role of renal function in nonselected older patients with ACS, especially according to frailty status. Improving risk prediction and clinical management of these poorly studied age subgroup may lead to important social and economic consequences.

In conclusion, 3 quarters of these nonselected older patients with NSTEACS had RD at admission. Patients



Patients at risk

<30	49	23	19	14	32	23	19	14	16	13	9	7
30-45	106	89	75	67	106	89	75	67	41	28	25	17
45-60	128	108	99	88	122	113	104	89	43	30	27	21
>60	122	113	104	89	73	68	63	51	13	10	8	7

Figure 2. Cumulative incidence of mortality or readmission according to creatinine clearance subgroups (BIScrea formula) in *(A)* the whole cohort; *(B)* nonfrail patients, and *(C)* frail patients.

with RD were older, with a higher prevalence of comorbidities, higher risk criteria at admission and higher prevalence of geriatric syndromes. A significant association between eGFR and mortality or readmission at 6 months was observed, but this association seemed mostly due to potential confounders. The association between renal function and outcomes was different according to frailty status.

Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.amjcard.2018.11.048.

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