



**HAL**  
open science

# One-year mortality of patients with ST-Elevation myocardial infarction: Prognostic impact of creatinine-based equations to estimate glomerular filtration rate

Yoann Bataille, Olivier Costerousse, Olivier F. Bertrand, Olivier Moranne, Hans Pottel, Pierre Delanaye

## ► To cite this version:

Yoann Bataille, Olivier Costerousse, Olivier F. Bertrand, Olivier Moranne, Hans Pottel, et al.. One-year mortality of patients with ST-Elevation myocardial infarction: Prognostic impact of creatinine-based equations to estimate glomerular filtration rate. PLoS ONE, 2018, 13 (7), pp.e0199773. 10.1371/journal.pone.0199773 . hal-02360321

**HAL Id: hal-02360321**

**<https://hal.science/hal-02360321>**

Submitted on 25 Feb 2020

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

RESEARCH ARTICLE

# One-year mortality of patients with ST-Elevation myocardial infarction: Prognostic impact of creatinine-based equations to estimate glomerular filtration rate

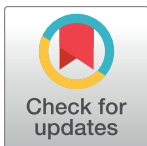
Yoann Bataille<sup>1,2</sup>, Olivier Costerousse<sup>1</sup>, Olivier F. Bertrand<sup>1</sup>, Olivier Moranne<sup>3</sup>, Hans Pottel<sup>4</sup>✉‡, Pierre Delanaye<sup>5</sup>✉‡\*

**1** Quebec Heart-Lung Institute, Quebec, Canada, **2** Department of Cardiology, Centre Hospitalier Régional la Citadelle, Liège, Belgium, **3** Department of Nephrology-Dialysis-Apheresis, CHU de Nîmes, Medical School, University Montpellier-Nîmes, Nîmes, France, **4** Department of Public Health and Primary Care, Kulak, University of Leuven, Kortrijk, Belgium, **5** Department of Nephrology, Dialysis, Transplantation, University of Liège (CHU ULg), Liège, Belgium

✉ These authors contributed equally to this work.

‡ These authors contributed equally to this work.

\* [pierre\\_delanaye@yahoo.fr](mailto:pierre_delanaye@yahoo.fr)



**OPEN ACCESS**

**Citation:** Bataille Y, Costerousse O, Bertrand OF, Moranne O, Pottel H, Delanaye P (2018) One-year mortality of patients with ST-Elevation myocardial infarction: Prognostic impact of creatinine-based equations to estimate glomerular filtration rate. PLoS ONE 13(7): e0199773. <https://doi.org/10.1371/journal.pone.0199773>

**Editor:** Emmanuel A. Burdmann, University of Sao Paulo Medical School, BRAZIL

**Received:** January 16, 2018

**Accepted:** June 13, 2018

**Published:** July 6, 2018

**Copyright:** © 2018 Bataille et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Data Availability Statement:** All relevant data are within the paper and its Supporting Information files.

**Funding:** The authors received no specific funding for this work.

**Competing interests:** The authors have declared that no competing interests exist.

## Abstract

### Background

Renal dysfunction is associated with worse outcomes after primary percutaneous coronary intervention (PCI). However, whether glomerular filtration rate (GFR) estimated with various equations can equally predict outcomes after ST-Elevation Myocardial Infarction (STEMI) is still debated.

### Methods

We compared the clinical impact of 3 different creatinine-based equations (Cockcroft and Gault (CG), CKD-epidemiology (CKD-EPI) and Full Age Spectrum (FAS)) to predict 1-year mortality in STEMI patients.

### Results

Among 1755 consecutive STEMI patients who had undergone primary PCI included between 2006 and 2011, median estimated GFR was 79 (61;96) with the CG, 81 (65;95) with CKD-EPI and 75 (60;91) mL/min/1.73 m<sup>2</sup> with FAS equation. Reduced GFR values were independently associated with 1-year mortality risk with the 3 equations. Receiver operating curves (ROC) of CG and FAS equations were significantly superior to the CKD-EPI equation,  $p = 0.03$  and  $p = 0.01$ , respectively. Better prediction with FAS and CG equations was confirmed by net reclassification index.

### Conclusions

Our results suggest that in STEMI patients who have undergone primary PCI, 1-year mortality is better predicted by CG or FAS equations compared to CKD-EPI.

## Introduction

Chronic Kidney Disease (CKD) is associated with higher early and late mortality risk in many cardiovascular diseases [1–4]. This over-risk has been specifically studied in patients with ST-Elevation Myocardial Infarction (STEMI) both on the short- and long term [5–21]. We have previously demonstrated the impact of CKD in STEMI patients after primary percutaneous coronary intervention (PCI)[22,23]. CKD diagnosis is, however, not so simple and debate still occurs in the literature to know how GFR must be evaluated [24,25]. In daily clinical practice, glomerular filtration rate (GFR) is still the best way to assess renal function. GFR can be measured with high precision by the so-called reference method (inulin, iothalamate or iothalamate), but these methods remain relatively cumbersome and are not frequently used in epidemiological studies [26]. Conversely, serum creatinine is easily measured and GFR can be estimated by different equations. The first equation to be used extensively has been the Cockcroft-Gault (CG) equation, proposed in 1976 [27]. Since then, other equations have been developed and more recent data suggest that these equations are more performant to estimate GFR [28–30]. However, the better accuracy of one-given equation to estimate GFR does not necessarily mean that this equation is also better to predict events or mortality. The main objective of this study was to compare the performance of 3 different creatinine-based equations: the CG [27], the CKD-epidemiology (CKD-EPI)[29] and the Full Age Spectrum (FAS) [30]) to predict 1-year mortality in STEMI patients after primary PCI. Because age is a variable in all estimating GFR equations, the second objective of this study was to compare the effect on age on the prediction considering equations but also serum creatinine only.

## Material and methods

The cohort of STEMI patients has been described elsewhere [22,23]. Briefly, the study population included all consecutive 2144 STEMI patients who were referred to our center for primary PCI within 12 hours after symptom onset between 01/2006 and 01/2011. Patients with previous coronary artery bypass graft ( $n = 73$ ) as well as STEMI patients without significant coronary lesion ( $n = 51$ ) were excluded from the study. Among the remaining 2020 patients, baseline serum creatinine was available in 1755 patients.

All patients signed an informed consent to be part of a STEMI registry. The registry has been approved by the institution research board of the Quebec Heart-Lung Institute. The inclusion criteria were: chest pain lasting  $> 30$  min, ST-segment elevation  $\geq 1$ mm in  $\geq 2$  adjacent ECG leads, new left bundle branch block or true posterior MI. All STEMI patients were pre-treated with aspirin, clopidogrel and heparin. Cardiac catheterization was performed via radial approach using 6Fr-guiding catheters in the majority of patients. Adjunctive pharmacotherapy such as bivalirudin or glycoprotein IIb/IIIa inhibitors (GPI) was left at the operators' discretion. If the coronary anatomy was suitable for PCI, the procedure was performed with standard techniques.

The baseline serum creatinine was measured directly on hospital admission in the emergency department or in the catheterization laboratory. Serum creatinine was determined using Jaffe method (Modular P, Roche Diagnostics) and standardized to isotope dilution mass spectrometry [31]. Ability of serum creatinine concentration to predict mortality was tested, and compared to serum creatinine indexed to Q (SCr/Q)[32]. SCr/Q is a variable of the FAS equation and Q is defined as the median SCr value for age-/sex-specific healthy populations [30]. SCr/Q in adults make the concentration independent of gender (as the Q value is not influenced by age in adults, the Q value is 0.7 mg/dL for women, and 0.9 mg/dL for men)[33]. The creatinine-based GFR equations considered are shown in Table 1 [27,29,30]. Both the FAS and CKD-EPI equation give results indexed for body surface area (BSA), therefore the CG had been indexed according to the Gehan equation [34]. Because it is possible that some patients

have acute renal dysfunction after STEMI (especially if they were hemodynamically unstable), we used the term “renal dysfunction” instead of “CKD”. Renal dysfunction status was defined by eGFR and 3 stages were considered according to the “Kidney Disease: Improving Global Outcomes”: over 60 mL/min/1.73m<sup>2</sup> (no renal dysfunction, the reference), between 45 and 60 mL/min/1.73m<sup>2</sup> and below 45 mL/min/1.73m<sup>2</sup> [35].

Clinical follow-up information was obtained from the referring physicians or by phone contact with patients. Finally, information on vital status at one year of those who were lost for follow-up was collected from the Quebec death registry “Directeur de l’Etat Civil” service counter. The primary outcome was 1-year all-cause mortality and follow-up was completed in 100% of patients.

### Statistical analysis

Data are expressed as mean ± standard deviation (SD) when distribution was normal and as median with interquartile range (IQR) when not. Normality was assessed by the Shapiro-Wilk test. Agreement between equation to classify patients according to CKD stage (above 60 mL/min/1.73m<sup>2</sup>, between 45 and 60 mL/min/1.73m<sup>2</sup> and below 45 mL/min/1.73m<sup>2</sup>) was tested by Kappa statistics [36].

Cox proportional hazard regressions models were used to study the risk of 1-year mortality associated with renal dysfunction based on the different eGFR equations, where eGFR was used as a categorical or a continuous variable, in non-adjusted models and adjusted for age and gender [37].

Receiver operating curves (ROC curves) (with subgroups based on death) were evaluated from logistic regression models with eGFR, and with eGFR adjusted for age and gender, by comparing the area under the curve [38]. Univariate survival curves (Kaplan-Meier) were calculated for subgroups defined by the fixed eGFR-threshold of 60 mL/min/1.73m<sup>2</sup> (renal dysfunction versus no renal dysfunction) for the various eGFR-equations [39]. Lastly, net reclassification index (NRI) was also calculated according to the method described by Pencina *et al.*[40,41]. We assumed that a shift to a higher category was an improvement in the non-event group, and a shift to a lower category was an improvement in the event group.

## Results

### Characteristics of the cohort

Baseline clinical and angiographic characteristics of the cohort are summarized in Table 2. In summary, 23.4% of patients were women. Median age was 60 (53;70) years, with 2.3%

Table 1. Creatinine-based equations.

Cockcroft-Gault (mL/min/1.73m <sup>2</sup> )		$[(140 - \text{age}) / (72 \times \text{SCr})] \times \text{weight} \times (0.85 \text{ if woman}) \times 1.73 / \text{BSA}$
CKD-EPI (mL/min/1.73m <sup>2</sup> )	Women	$144 \times (\text{SCr}/0.7)^{-0.329} \times 0.993^{\text{age}}$
	SCr ≤ 0.7 mg/dL	
	Women	$144 \times (\text{SCr}/0.7)^{-1.209} \times 0.993^{\text{age}}$
	SCr > 0.7 mg/dL	
	Men	$141 \times (\text{SCr}/0.9)^{-0.411} \times 0.993^{\text{age}}$
	SCr ≤ 0.9 mg/dL	
FAS (mL/min/1.73m <sup>2</sup> )	Men	$141 \times (\text{SCr}/0.9)^{-1.209} \times 0.993^{\text{age}}$
	SCr > 0.9 mg/dL	
	for 2 ≤ age ≤ 40 years	$107.3 / (\text{SCr}/\text{Q})$
	for age > 40 years	$107.3 / (\text{SCr}/\text{Q}) \times 0.988^{(\text{age}-40)}$

BSA: body surface area, SCr: Serum Creatinine (mg/dL), Q is the median SCr value for age-/sex-specific healthy populations. CKD-EPI: Chronic Kidney Disease-epidemiology; FAS: Full Age Spectrum

<https://doi.org/10.1371/journal.pone.0199773.t001>

**Table 2. Baseline clinical, biological, and angiographic characteristics.**

Clinical Variables	Patients (n = 1755)
Age, years	62 ± 12
Female, n (%)	411 (23)
BMI (median, IQR)	(26.4, 23.9–29.4)
BSA (median, IQR)	(1.9, 1.7–2.0)
Diabetes mellitus, n (%)	214 (12)
Hypertension, n (%)	757 (43)
Current smoking, n (%)	746 (42)
Hyperlipidemia, n (%)	721 (41)
Prior MI, n (%)	213 (12)
Shock, n (%)	132 (7)
SCr creatinine (median, IQR)	0.96 (0.81;1.12)
eGFR by CG (median, IQR)	79 (61;96)
eGFR by CKD-EPI (median, IQR)	81 (65;95)
eGFR by FAS (median, IQR)	75 (60;91)
Single vessel disease, n (%)	1219 (69)
IRA LM, n (%)	11 (0.6)
IRA LAD, n (%)	703 (40)
IRA RCA, n (%)	793 (45)
IRA CX, n (%)	248 (14)
TIMI flow 0 pre-PCI, n (%) (n = 1752)	1024 (58)
Door to balloon time (n = 1703) (minutes, median, IQR)	40 (29, 69)
TIMI flow 0/1 post-PCI, n (%) (n = 1744)	48 (3)
MBG 0/1, n (%) (n = 1646)	160 (9)
LVEF (%) (n = 1544)	51 ± 13
LVEF <40%, n (%) (n = 1544)	363 (23)
Peak CK-MB (µg/l, median, IQR) (n = 1651)	149 (65, 281)

SCr: serum creatinine concentration; eGFR: estimated glomerular filtration rate; CKD-EPI: CKD-epidemiology; FAS: Full Age Spectrum; BMI: body mass index; BSA: body surface area; MI: myocardial infarction; Shock: end organ hypoperfusion and hemodynamically as systemic systolic pressure < 90 mmHg or systemic systolic pressure ≥ 90 mmHg while using inotropic drugs; SVD: single vessel disease; IRA: infarct-related artery; LM: left main; LAD: left anterior descending artery; RCA: right coronary artery; CX, left circumflex; TIMI: Thrombolysis In Myocardial Infarction; MBG: myocardial blush grade; LVEF: left ventricular ejection fraction; CK-MB: Serum myocardial band of creatine kinase.

<https://doi.org/10.1371/journal.pone.0199773.t002>

(n = 41) being younger than 40 years and 37.5% (n = 659) older than 65 years. Median body mass index and body surface area was 26.4 (23.9;29.4) kg/m<sup>2</sup> and 1.89 (1.75;2.02) m<sup>2</sup>, respectively.

Median serum creatinine concentration was 0.96 (0.81;1.12) mg/dL. Median estimated GFR was 79 (61;96), 81 (65;95) and 75 (60;91) mL/min/1.73 m<sup>2</sup> with the CG, CKD-EPI and FAS equations, respectively. Clinical follow-up was complete for 100% of patients at 1 year

(median follow-up: 569 (389;951) days). Cardiologic characteristics of the patients were described in Table 2. The overall 1-year mortality was 8.21%, with the majority of deaths occurring prematurely after STEMI (median 5 (1;29.5) days).

### Renal dysfunction prevalence and mortality according to estimating equations

Prevalence of eGFR below 45 mL/min/1.73m<sup>2</sup> was 9.3%, 6.8% and 8.8% according to the CG, CKD-EPI and FAS equations, respectively. Concordance was good between CG and CKD-EPI ( $\kappa = 0.75$ , 95% CI: 0.69–0.81) and very good between CG and FAS ( $\kappa = 0.87$ , 95% CI: 0.83–0.91) and between FAS and CKD-EPI ( $\kappa = 0.82$ , 95% CI: 0.77–0.88). The prevalence of eGFR between 45 and 60 mL/min/1.73 m<sup>2</sup> was 13.8%, 12% and 16.4%. Concordance was moderate between CG and CKD-EPI ( $\kappa = 0.45$ , 95% CI: 0.39–0.52), good between CG and FAS ( $\kappa = 0.67$ , 95% CI: 0.62–0.71) and moderate between FAS and CKD-EPI ( $\kappa = 0.58$ , 95% CI: 0.52–0.63).

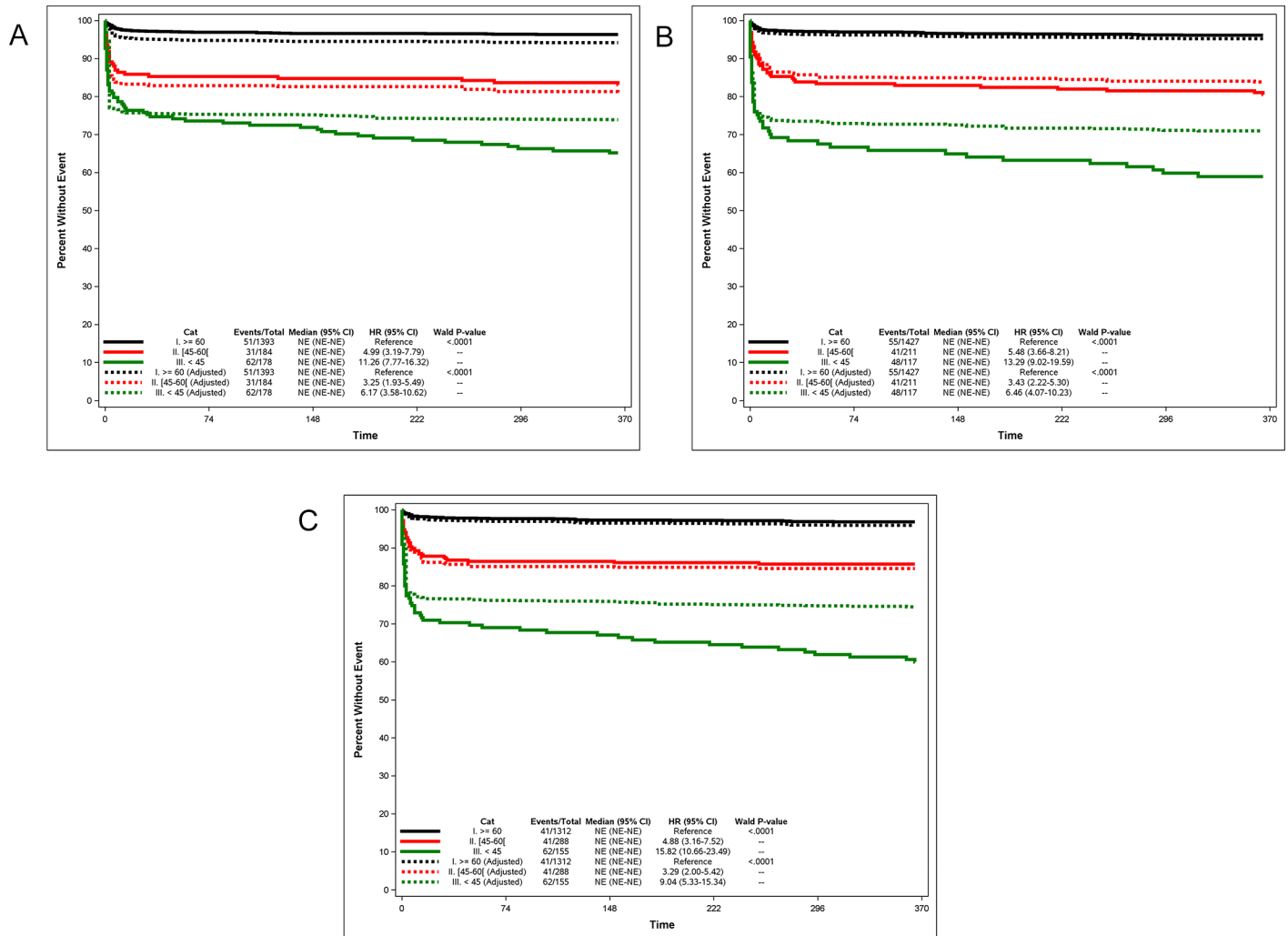
### Serum creatinine, equations and mortality at one-year

**Cox proportional hazard models.** We considered 3 groups according to the eGFR: eGFR $\geq$  60 mL/min/1.73m<sup>2</sup> (no renal dysfunction, the reference, Group 1), eGFR between 45 and 60 mL/min/1.73m<sup>2</sup> (Group 2) and eGFR<45 mL/min/1.73m<sup>2</sup> (Group 3). We used the CG, CKD-EPI and FAS equation to estimate GFR. In the unadjusted analysis, renal dysfunction was highly associated with the mortality risk in group 2: hazard rate (HR): 4.99 95% CI: 3.19–7.79, HR: 5.48 95% CI: 3.66–8.21 and 4HR: .88 95% CI: 3.16–7.52 for the CG, CKD-EPI and FAS equation, respectively. The same observation was made in group 3: HR: 11.26 95% CI: 7.77–16.32, HR: 13.29 95% CI: 9.02–19.59 and HR: 15.82 95% CI: 10.66–23.49 for the CG, CKD-EPI and FAS equations, respectively. Survival curves (and HRs) were significantly different (Logrank test,  $p < 0.0001$ ) between group 1 and groups 2 and 3, but also between group 2 and 3. However, HRs observed were not significantly different between the eGFR equations. After adjustment for age and gender, renal dysfunction remained associated with 1-year mortality: in group 2: HR: 3.25 95% CI: 1.93–5.49 for CG, HR: 3.43 95% CI: 2.22–5.30 for CKD-EPI and HR: 3.29 95% CI: 2.00–5.42 for the FAS equation; in group 3: HR: 6.17 95% CI: 3.58–10.62 for CG, HR: 6.46 95% CI: 4.07–10.23 for CKD-EPI and HR: 9.04 95% CI: 5.33–15.34 for the FAS equation. Survival curves (and HRs) were significantly different (Logrank test,  $p < 0.0001$ ) between group 1 and groups 2 and 3, but also between group 2 and 3 (Fig 1).

However, HRs observed were not significantly different between the eGFR equations. Considering eGFR as a continuous variable, decreased GFR values was also associated with the mortality risk with all 3 equations. By univariate analysis, renal dysfunction (per 10 mL/min/1.73 m<sup>2</sup> decrease) was related to 1-year mortality by HR 1.62 95% CI: 1.50–1.74 for CG, HR: 1.62 95% CI: 1.51–1.74 for CKD-EPI and HR: 1.68 95% CI: 1.55–1.81 for FAS equation.

After adjustment renal dysfunction (per 10 mL/min/1.73 m<sup>2</sup> decrease) remained an independent predictor of 1-year mortality with HR 1.52 95% CI: 1.37–1.68 for CG, HR: 1.46 95% CI: 1.34–1.59 for CKD-EPI and HR: 1.68 95% CI: 1.36–1.68 for FAS equation.

**ROC curves.** Using the eGFR equations as the only variable in the logistic regression models, the AUCs observed to predict one-year mortality were 0.81 (95% CI: 0.77 to 0.85) for CG, 0.79 (95% CI: 0.75 to 0.84) for CKD-EPI, and 0.805 (95% CI: 0.77 to 0.85) for FAS equation. Pairwise comparison of ROC curves did not show any difference between AUC of CG and FAS equations but AUC of CKD-EPI equation was significantly lower than CG ( $p = 0.03$ ) and FAS ( $p = 0.01$ ) (Fig 2). Serum creatinine concentration and SCr/Q also predicted mortality at one-year: 0.72 (95% CI: 0.67 to 0.77) and 0.76 (95% CI: 0.71 to 0.81). AUC observed with SCr/Q was better than AUC of serum creatinine alone ( $p = 0.0001$ ). However, AUCs of all



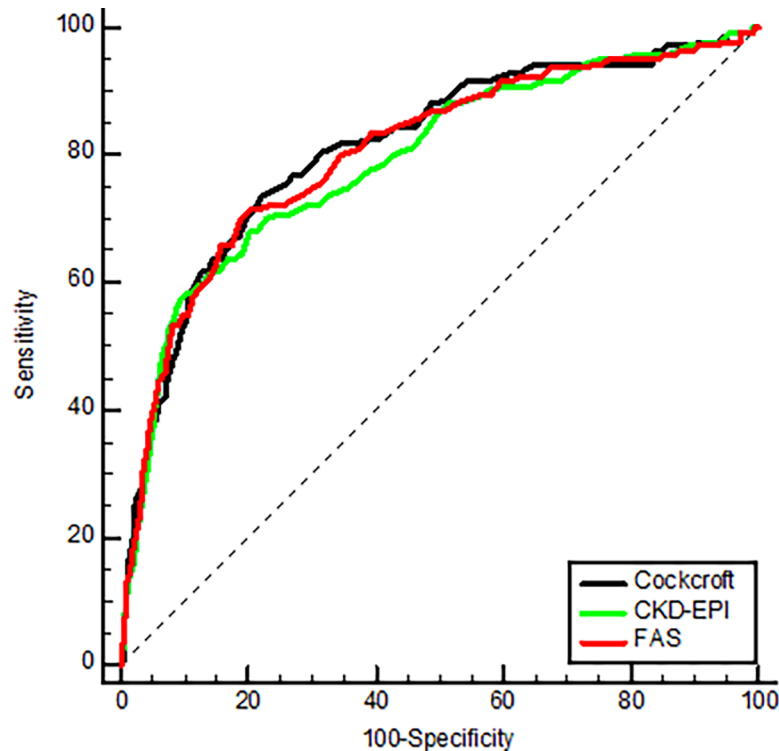
**Fig 1. Kaplan-Meier survival curves over one-year in patients with STEMI according to CKD stages and with different equations to estimate GFR. (1A: Cockcroft-Gault, 1B: CKD-EPI and 1C: FAS equation). All survival curves ( $\geq 60$  mL/min/1.73m<sup>2</sup>, (45-60 mL/min/1.73m<sup>2</sup> and <45 mL/min/1.73m<sup>2</sup>) were significantly different from each other, but no significant difference between estimating GFR equations.**

<https://doi.org/10.1371/journal.pone.0199773.g001>

three equations were significantly higher than AUC of both serum creatinine and SCr/Q ( $p < 0.0001$ ).

Adding age to the model, the AUC observed to predict one-year mortality was 0.813 (95% CI: 0.773 to 0.853), 0.812 (95% CI: 0.774 to 0.851), and 0.809 (95% CI: 0.769 to 0.849) for CG, CKD-EPI and FAS equations respectively. The models smooth off the differences between AUC, resulting in no significant pairwise differences between “age+eGFR” models. The models including age only improved the AUC of the CKD-EPI equation in comparison to the unadjusted model (from 0.794 to 0.812,  $p = 0.0243$ ). Adding gender next to “age” and “eGFR” in the model did not further improve the AUCs.

Applying age and gender adjustment to serum creatinine and age adjustment SCr/Q impacted the results. AUC of the model including serum creatinine, age and gender was 0.79 (95% CI: 0.75 to 0.83) while AUC for the model with age and SCr/Q was 0.80 (95% CI: 0.76 to 0.84). The 2 models showed the same performance to predict 1-year mortality but the adjusted model for serum creatinine was significantly better than unadjusted ( $p = 0.04$ ). Moreover,



**Fig 2. Pairwise comparison of ROC curves to predict one-year mortality with different estimating equations (unadjusted data).** No difference between AUC of Cockcroft-Gault and FAS equations but AUC of CKD-EPI equation was significantly lower than Cockcroft-Gault ( $p = 0.03$ ) and FAS ( $p = 0.01$ ).

<https://doi.org/10.1371/journal.pone.0199773.g002>

AUCs observed with adjusted models for serum creatinine and SCr/Q were not different from AUCs from adjusted models with the three equations.

**Net reclassification index (NRI).** NRI analyses are given in [Table 3](#) (CG versus CKD-EPI), [Table 4](#) (CG versus CKD-EPI) and [Table 5](#) (FAS versus CKD-EPI). Analyses showed a worse NRI for CKD-EPI compared to CG (-7.9%, 95% CI: -15.6–0.1%,  $p = 0.0477$ ), a non-significant NRI for FAS compared to CG (3.5%, 95% CI: -2.2–9.2%, NS) and a better NRI for FAS compared to CKD-EPI (11.7%, 95% CI: 4.5–18.8%,  $p = 0.0014$ ).

## Discussion

In the current analysis, we showed that the CG and FAS equations were better predictors of mortality than the recommended CKD-EPI formula, with better NRI and AUC. As expected, the proportion of women admitted for STEMI is concordant with the current literature, as cardiovascular disease develops 7 to 10 years later in women than in men. It is assumed that exposure to endogenous estrogens during the fertile period of life delays the manifestation of atherosclerotic disease in women [42]. We also showed that age is, as expected, an important variable for mortality prediction. Indeed, in ROC curve analyses, the difference in AUC between equations disappeared when age was considered in the model. Still more illustrative, the better prediction using creatinine-based equations (all including the age variable) over serum creatinine alone (or scaled creatinine) totally disappears when age is included in the model. Also, in Cox regression analyses, we showed that age strongly impacts mortality risk in the lower GFR group ( $<45$  mL/min/1.73m<sup>2</sup>), which is not unexpected given the physiological decline of GFR with aging [43,44]. Accordingly, a GFR below 45 mL/min/1.73m<sup>2</sup> means a



**Table 3. Reclassification of renal function stages by the CG equation with respect to CKD-EPI equation, and effect of reclassification on mortality risk prediction.**

Non-event						Event					
CG						CG					
	> = 60	45–60	<45	Total		> = 60	45–60	<45	Total		
CKD-EPI	> = 60	1263	103	6	1372	CKD-EPI	> = 60	42	12	1	55
	45–60	40	96	34	170		45–60	4	23	14	41
	<45	0	6	63	69		<45	0	3	45	48
Total	1303	205	103	1611	Total	46	38	60	144		
Reclassified by CKDEPI						Reclassified by CKDEPI					
	correct	8,88%					correct	4,86%			
	Incorrect	2,86%					Incorrect	18,75%			
	NRIne	6,02%					NRIne	-13,89%			
				NRI	-7,9%						
				SE	4,0%						
				95%CI	[-1.6%,0.0%]						
				p	0,0477						

CG: Cockcroft-Gault; CKD-EPI: Chronic Kidney Disease-epidemiology

<https://doi.org/10.1371/journal.pone.0199773.t003>

much larger relative decline in young patients than in the elderly for who a GFR between 45 and 60 mL/min/1.73m<sup>2</sup> could even been considered as normal [45,46].

There are several ways to estimate GFR as different creatinine-based equations have been developed and these equations have potentially different impacts on the mortality risk [1,5,6,8,10,11,13,14,20,21]. Our data showed that the predictive argument, i.e. the potential better ability of a given equation to predict mortality or other outcomes, to favor for one equation over another, may be spurious. As an example, the promoters of the CKD-EPI equation, an equation published in 2009 by Levey et al, frequently argue that CKD-EPI equation is a better risk prediction factor than Modified Diet in Renal Disease (MDRD) study equation [1,5,8,14], which was published by the same group in 1999 and became first equation to be

**Table 4. Reclassification of renal function stages by the FAS equation with respect to CG equation, and effect of reclassification on mortality risk prediction.**

Non-event						Event					
CG						CG					
	> = 60	45–60	<45	Total		> = 60	45–60	<45	Total		
FAS	> = 60	1235	36	0	1271	FAS	> = 60	39	2	0	41
	45–60	68	159	20	247		45–60	7	31	3	41
	<45	0	10	83	93		<45	0	5	57	62
Total	1303	205	103	1611	Total	46	38	60	144		
Reclassified by FAS						Reclassified by FAS					
	correct	3,48%					correct	8,33%			
	Incorrect	4,84%					Incorrect	3,47%			
	NRIne	-1,37%					NRIne	4,86%			
				NRI	3,5%						
				SE	2,9%						
				95%CI	[-0.2%,0.9%]						
				p	0,2321						

CG: Cockcroft-Gault; FAS: Full Age Spectrum

<https://doi.org/10.1371/journal.pone.0199773.t004>

**Table 5. Reclassification of renal function stages by the FAS equation with respect to CKD-EPI equation, and effect of reclassification on mortality risk prediction.**

Non-event					Event						
CKD-EPI					CKD-EPI						
	> = 60	45–60	<45	Total		> = 60	45–60	<45	Total		
FAS	> = 60	1260	<b>11</b>	<b>0</b>	1271	FAS	> = 60	41	<b>0</b>	<b>0</b>	41
	45–60	<b>112</b>	134	<b>1</b>	247		45–60	<b>14</b>	25	<b>2</b>	41
	<45	<b>0</b>	<b>25</b>	68	93		<45	<b>0</b>	<b>16</b>	46	62
	Total	1372	170	69	1611		Total	55	41	48	144
Reclassified by FAS					Reclassified by FAS						
	correct		0,74%				correct		20,83%		
	Incorrect		8,50%				Incorrect		1,39%		
	NRIne		-7,76%				NRIne		19,44%		
				NRI	<b>11,7%</b>						
				SE	<b>3,7%</b>						
				95%CI	<b>[0.5%,1.9%]</b>						
				p	<b>0,00140</b>						

Chronic Kidney Disease-epidemiology; FAS: Full Age Spectrum

<https://doi.org/10.1371/journal.pone.0199773.t005>

more popular than the CG equation [47]. However, these authors have not tested other equations, such as the old CG equation in comparison with the MDRD or CKD-EPI equations. When compared to these two equations, the CG equation has been shown to be better predictive of mortality in patients with STEMI or ischemic heart disease [10–12,20,21], but also in other cardiologic populations [48–54]. On the contrary, Orvin et al showed a slightly better performance of the MDRD than CG to predict mortality at one-year after acute coronary syndrome [13]. However, the difference was not significant between the CG and CKD-EPI equations. Similar predictive values of CG and CKD-EPI were also shown in two other cohorts of patients with heart failure [55,56].

As suggested by some authors and supported by our own data, the ability of one equation to better predict mortality could be due to the mathematical exponent applied to age in the equation [11]. Having said that, one can though discuss the balance of each equation in their ability to predict the risk on one side and estimate GFR (in comparison to true measured GFR) on the other side. If CG is doing well in predicting the risk, data from the literature have clearly shown that its performance is less good than other recent equations to estimate GFR, especially with a lack of precision [28,57]. The CKD-EPI equation does not seem a superior equation to predict the risk in our cohorts, and in others [10–12,20,21]. Eventually, the FAS equation could be considered as the best balance between GFR estimation, equivalent to CKD-EPI in adults and even better in the elderly, and risk mortality, equivalent to CG [25,30,58].

There are limitations to our work. In all creatinine-based equations, the most important variable is serum creatinine and this biomarker is dependent on non-GFR determinants, the most important being muscle mass [59]. Measured GFR by a reference method was not available in this cohort [60]. Moreover, cystatin C, another GFR biomarker, was not available while this biomarker was shown to better predict mortality and morbidity [2,5,7,9,14]. However, the added value of cystatin C as a predictor could be explained by non-GFR determinants, such as inflammation [61]. Also, in our cohort, data on the evolution of renal function in the days after STEMI and PCI are unfortunately not available. Another limitation is the fact that eGFR assessment was based on a single serum creatinine measurement at the time of hospital admission. This measurement could have been affected by hemodynamic instability in some

patients. In other words, it is possible that part of decreased GFR results are due to acute kidney dysfunction, and not CKD. We do not have complete data on hemodynamic stability at admission, except that 7.5% of patients were considered in cardiogenic shock. As expected, the percentage of patients in cardiogenic shock was higher in those with low eGFR (25.2% in the patients with eGFR by FAS below 45 mL/min/1.73m<sup>2</sup>; 13.9% in the patients with eGFR by FAS between 45 and 60 mL/min/1.73m<sup>2</sup>; 4% in the patients with eGFR by FAS above 60 mL/min/1.73m<sup>2</sup>). Again, this limitation is shared by all studies on the topic. Also in clinical practice, “true” baseline serum creatinine is not known at admission. The last limitation was that patients included here were all Caucasians and our results might not be directly applicable to other ethnicities. Finally, the goal of our analysis was to study the impact of the choice of eGFR equation on the prognosis of STEMI patients, not on the effect of renal dysfunction *per se*, as this point has been previously published [23]. However, we have added some adjusted results in supplements (S1 File).

In conclusion, we showed that renal dysfunction is associated with one-year mortality in our cohort of patients with STEMI. Beyond serum creatinine and whatever creatinine-based equation, age is an important variable that could explain the superiority of one equation over another in its ability to predict the risk. Our results suggest that in STEMI patients who have undergone primary PCI, 1-year mortality is better associated by CG or FAS equations compared to CKD-EPI.

## Supporting information

**S1 File. FAS equation and association with mortality in a multivariate model.**  
(DOCX)

## Author Contributions

**Conceptualization:** Pierre Delanaye.

**Data curation:** Olivier Costerousse, Pierre Delanaye.

**Formal analysis:** Olivier Moranne, Hans Pottel, Pierre Delanaye.

**Investigation:** Yoann Bataille, Hans Pottel.

**Methodology:** Yoann Bataille, Olivier Costerousse, Hans Pottel, Pierre Delanaye.

**Resources:** Yoann Bataille.

**Supervision:** Olivier Costerousse, Olivier F. Bertrand, Hans Pottel, Pierre Delanaye.

**Writing – review & editing:** Yoann Bataille, Olivier Costerousse, Olivier F. Bertrand, Olivier Moranne, Hans Pottel, Pierre Delanaye.

## References

1. Matsushita K, Mahmoodi BK, Woodward M, Emberson JR, Jafar TH, Jee SH, et al. Comparison of risk prediction using the CKD-EPI equation and the MDRD study equation for estimated glomerular filtration rate. *JAMA*. 2012; 307: 1941–1951. <https://doi.org/10.1001/jama.2012.3954> PMID: 22570462
2. Shlipak MG, Sarnak MJ, Katz R, Fried LF, Seliger SL, Newman AB, et al. Cystatin C and the risk of death and cardiovascular events among elderly persons. *N Engl J Med*. 2005; 352: 2049–2060. <https://doi.org/10.1056/NEJMoa043161> PMID: 15901858
3. Matsushita K, Ballew SH, Coresh J, Arima H, Ärnlöv J, Cirillo M, et al. Measures of chronic kidney disease and risk of incident peripheral artery disease: a collaborative meta-analysis of individual participant data. *Lancet Diabetes Endocrinol*. 2017; 5: 718–728. [https://doi.org/10.1016/S2213-8587\(17\)30183-3](https://doi.org/10.1016/S2213-8587(17)30183-3) PMID: 28716631

4. Anavekar NS, McMurray JJV, Velazquez EJ, Solomon SD, Kober L, Rouleau J-L, et al. Relation between Renal Dysfunction and Cardiovascular Outcomes after Myocardial Infarction. *N Engl J Med*. 2004; 351: 1285–1295. <https://doi.org/10.1056/NEJMoa041365> PMID: 15385655
5. Almeida I, Caetano F, Barra S, Madeira M, Mota P, Leitão-Marques A. Estimating glomerular filtration rate in acute coronary syndromes: Different equations, different mortality risk prediction. *Eur Heart J Acute Cardiovasc Care*. 2016; 5: 223–230. <https://doi.org/10.1177/2048872615576219> PMID: 25740222
6. Rioboo Lestón L, Abu-Assi E, Raposeiras-Roubin S, Cobas-Paz R, Caneiro-Queija B, Rodríguez-Rodríguez JM, et al. Prognostic usefulness of an age-adapted equation for renal function assessment in older patients with acute coronary syndrome. *Eur Heart J Acute Cardiovasc Care*. 2017; 204887261773004. <https://doi.org/10.1177/2048872617730040> PMID: 28920703
7. Abu-Assi E, Raposeiras-Roubin S, Riveiro-Cruz A, Rodríguez-Girondo M, González-Cambeiro C, Alvarez-Alvarez B, et al. Creatinine-or cystatin C-based equations to estimate glomerular filtration rate in acute myocardial infarction: A disparity in estimating renal function and in mortality risk prediction. *Int J Cardiol*. 2013; 168: 4300–4301. <https://doi.org/10.1016/j.ijcard.2013.04.194> PMID: 23714598
8. Osadnik T, Wasilewski J, Lekston A, Strzelczyk J, Kurek A, Gutowski AR, et al. Comparison of modification of diet in renal disease and chronic kidney disease epidemiology collaboration formulas in predicting long-term outcomes in patients undergoing stent implantation due to stable coronary artery disease. *Clin Res Cardiol*. 2014; 103: 569–576. <https://doi.org/10.1007/s00392-014-0687-1> PMID: 24609482
9. Åkerblom A, Wallentin L, Larsson A, Siegbahn A, Becker RC, Budaj A, et al. Cystatin C- and creatinine-based estimates of renal function and their value for risk prediction in patients with acute coronary syndrome: Results from the PLATelet inhibition and patient outcomes (PLATO) study. *Clin Chem*. 2013; 59: 1369–1375. <https://doi.org/10.1373/clinchem.2012.200709> PMID: 23698074
10. Coceani M, Carpeggiani C, L'Abbate A. Comparative prognostic value of glomerular filtration rate estimating formulas in ischaemic heart disease. *Eur J Cardiovasc Prev Rehabil*. 2008; 15: 423–427. <https://doi.org/10.1097/HJR.0b013e3282fa40da> PMID: 18677166
11. Sederholm Lawesson S, Alfredsson J, Szummer K, Fredrikson M, Swahn E. Prevalence and prognostic impact of chronic kidney disease in STEMI from a gender perspective: data from the SWEDEHEART register, a large Swedish prospective cohort. *BMJ Open*. 2015; 5: e008188. <https://doi.org/10.1136/bmjopen-2015-008188> PMID: 26105033
12. Tomaszuk-Kazberuk A, Kozuch M, Malyszko J, Bachorzewska-Gajewska H, Dobrzycki S, Musial WJ. Which method of GFR estimation has the best prognostic value in patients treated with primary PCI: Cockcroft-Gault formula, MDRD, or CKD-EPI equation?—A 6-year follow-up. *Ren Fail*. 2011; 33: 983–9. <https://doi.org/10.3109/0886022X.2011.618922> PMID: 22013931
13. Orvin K, Eisen A, Goldenberg I, Farkash A, Shlomo N, Gevriellov-Yusim N, et al. The proxy of renal function that most accurately predicts short- and long-term outcome after acute coronary syndrome. *Am Heart J*. 2015; 169: 702–712.e3. <https://doi.org/10.1016/j.ahj.2015.01.012> PMID: 25965718
14. Flores-Blanco PJ, López-Cuenca Á, Januzzi JL, Marín F, Sánchez-Martínez M, Quintana-Giner M, et al. Comparison of Risk Prediction With the CKD-EPI and MDRD Equations in Non-ST-Segment Elevation Acute Coronary Syndrome. *Clin Cardiol*. 2016; 39: 507–15. <https://doi.org/10.1002/clc.22556> PMID: 27249221
15. Campbell NG, Varagunam M, Sawhney V, Ahuja KR, Salahuddin N, De Palma R, et al. Mild chronic kidney disease is an independent predictor of long-term mortality after emergency angiography and primary percutaneous intervention in patients with ST-elevation myocardial infarction. *Heart*. 2012; 98: 42–7. <https://doi.org/10.1136/heartjnl-2011-300024> PMID: 21880649
16. Sabroe JE, Thayssen P, Antonsen L, Hougaard M, Hansen KN, Jensen LO. Impact of renal insufficiency on mortality in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention. *BMC Cardiovasc Disord*. 2014; 14: 15. <https://doi.org/10.1186/1471-2261-14-15> PMID: 24506974
17. Lin T-H, Lai W-T, Kuo C-T, Hwang J-J, Chiang F-T, Chang S-C, et al. Additive effect of in-hospital TIMI bleeding and chronic kidney disease on 1-year cardiovascular events in patients with acute coronary syndrome: Data from Taiwan Acute Coronary Syndrome Full Spectrum Registry. *Heart Vessels*. 2015; 30: 441–50. <https://doi.org/10.1007/s00380-014-0504-9> PMID: 24802367
18. Gibson CM, Pinto DS, Murphy SA, Morrow DA, Hobbach HP, Wiviott SD, et al. Association of creatinine and creatinine clearance on presentation in acute myocardial infarction with subsequent mortality. *J Am Coll Cardiol*. 2003; 42: 1535–43. PMID: 14607434
19. Best PJM, Lennon R, Ting HH, Bell MR, Rihal CS, Holmes DR, et al. The impact of renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary interventions. *J Am Coll Cardiol*. 2002; 39: 1113–9. PMID: 11923033

20. Abu-Assi E, Lear P, Cabanas-Grandío P, Rodríguez-Gironde M, Raposeiras-Roubin S, Pereira-López E, et al. A comparison of the CKD-EPI, MDRD-4, and Cockcroft–Gault equations to assess renal function in predicting all-cause mortality in acute coronary syndrome patients. *Int J Cardiol.* 2013; 167: 2325–2326. <https://doi.org/10.1016/j.ijcard.2012.11.014> PMID: 23218581
21. Szummer K, Lundman P, Jacobson SH, Lindbäck J, Stenstrand U, Wallentin L, et al. Cockcroft-Gault is better than the Modification of Diet in Renal Disease study formula at predicting outcome after a myocardial infarction: Data from the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated. *Am Heart J.* 2010; 159: 979–986. <https://doi.org/10.1016/j.ahj.2010.03.028> PMID: 20569709
22. Bataille Y, Déry J-P, Larose E, Déry U, Costerousse O, Rodés-Cabau J, et al. Prevalence, predictors and clinical impact of unique and multiple chronic total occlusion in non-infarct-related artery in patients presenting with ST-elevation myocardial infarction. *Heart.* 2012; 98: 1732–7. <https://doi.org/10.1136/heartjnl-2012-302376> PMID: 23014480
23. Bataille Y, Plourde G, Machaalany J, Abdelaal E, Déry J-P, Larose E, et al. Interaction of chronic total occlusion and chronic kidney disease in patients undergoing primary percutaneous coronary intervention for acute ST-elevation myocardial infarction. *Am J Cardiol.* 2013; 112: 194–9. <https://doi.org/10.1016/j.amjcard.2013.03.010> PMID: 23601580
24. Delanaye P, Mariat C. The applicability of eGFR equations to different populations. *Nat Rev Nephrol.* 2013; 9: 513–522. <https://doi.org/10.1038/nrneph.2013.143> PMID: 23856996
25. Björk J, Grubb A, Gudnason V, Indridason OS, Levey AS, Palsson R, et al. Comparison of glomerular filtration rate estimating equations derived from creatinine and cystatin C: validation in the Age, Gene/Environment Susceptibility-Reykjavik elderly cohort. *Nephrol Dial Transplant.* 2017; <https://doi.org/10.1093/ndt/gfx272> PMID: 29040701
26. Delanaye P, Ebert N, Melsom T, Gaspari F, Mariat C, Cavalier E, et al. Iohexol plasma clearance for measuring glomerular filtration rate in clinical practice and research: a review. Part 1: How to measure glomerular filtration rate with iohexol? *Clin Kidney J.* 2016; 9: 682–99. <https://doi.org/10.1093/ckj/sfw070> PMID: 27679715
27. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron.* 1976; 16: 31–41. <https://doi.org/10.1159/000180580> PMID: 1244564
28. Froissart M, Rossert J, Jacquot C, Paillard M, Houillier P. Predictive performance of the modification of diet in renal disease and Cockcroft-Gault equations for estimating renal function. *J Am Soc Nephrol.* 2005; 16: 763–773. <https://doi.org/10.1681/ASN.2004070549> PMID: 15659562
29. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF III, Feldman HI, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009; 150: 604–612. PMID: 19414839
30. Pottel H, Hoste L, Dubourg L, Ebert N, Schaeffner ES, Eriksen BO, et al. A new estimating glomerular filtration rate equation for the full age spectrum. *Nephrol Dial Transplant.* 2016; 31: 798–806. <https://doi.org/10.1093/ndt/gfv454> PMID: 26932693
31. Piéroni L, Delanaye P, Boutten A, Bargnoux A-S, Rozet E, Delatour V, et al. A multicentric evaluation of IDMS-traceable creatinine enzymatic assays. *Clin Chim Acta.* 2011; 412: 2070–2075. <https://doi.org/10.1016/j.cca.2011.07.012> PMID: 21803031
32. Pottel H, Dubourg L, Schaeffner E, Eriksen BO, Melsom T, Lamb EJ, et al. The diagnostic value of rescaled renal biomarkers serum creatinine and serum cystatin C and their relation with measured glomerular filtration rate. *Clin Chim Acta.* 2017; 471: 164–170. <https://doi.org/10.1016/j.cca.2017.06.005> PMID: 28601669
33. Pottel H, Vrydags N, Mahieu B, Vandewynckele E, Croes K, Martens F. Establishing age/sex related serum creatinine reference intervals from hospital laboratory data based on different statistical methods. *Clin Chim Acta.* 2008; 396: 49–55. <https://doi.org/10.1016/j.cca.2008.06.017> PMID: 18621041
34. Gehan EA, George SL. Estimation of human body surface area from height and weight. *Cancer Chemother Rep.* 1970; 54: 225–235. PMID: 5527019
35. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl.* 2013; 3: 1–150.
36. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics.* 1977; 33: 159–174. PMID: 843571
37. Christensen E. Multivariate survival analysis using Cox’s regression model. *Hepatology.* 7: 1346–58. PMID: 3679094
38. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology.* 1982; 143: 29–36. <https://doi.org/10.1148/radiology.143.1.7063747> PMID: 7063747

39. Kaplan EL, Meier P. Nonparametric Estimation from Incomplete Observations. *J Am Stat Assoc.* 1958; 53: 457–481.
40. Mühlenbruch K, Kuxhaus O, Pencina MJ, Boeing H, Liero H, Schulze MB. A confidence ellipse for the Net Reclassification Improvement. *Eur J Epidemiol.* 2015; 30: 299–304. <https://doi.org/10.1007/s10654-015-0001-1> PMID: 25724473
41. Pencina MJ, D'Agostino RB, Steyerberg EW. Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. *Stat Med.* 2011; 30: 11–21. <https://doi.org/10.1002/sim.4085> PMID: 21204120
42. Berger JS, Elliott L, Gallup D, Roe M, Granger CB, Armstrong PW, et al. Sex Differences in Mortality Following Acute Coronary Syndromes. *JAMA.* 2009; 302: 874. <https://doi.org/10.1001/jama.2009.1227> PMID: 19706861
43. Delanaye P, Schaeffner E, Ebert N, Cavalier E, Mariat C, Krzesinski J-MM, et al. Normal reference values for glomerular filtration rate: what do we really know? *Nephrol Dial Transplant.* 2012; 27: 2664–2672. <https://doi.org/10.1093/ndt/gfs265> PMID: 22802582
44. Pottel H, Delanaye P, Weekers L, Selistre L, Goffin K, Gheysens O, et al. Age-dependent reference intervals for estimated and measured glomerular filtration rate. *Clin Kidney J.* 2017; 10: 545–551. <https://doi.org/10.1093/ckj/sfx026> PMID: 28852494
45. Glasscock R, Delanaye P, El Nahas M. An Age-Calibrated Classification of Chronic Kidney Disease. *JAMA.* 2015; 314: 559–560. <https://doi.org/10.1001/jama.2015.6731> PMID: 26023760
46. Delanaye P, Glasscock RJ, Pottel H, Rule AD. An Age-Calibrated Definition of Chronic Kidney Disease: Rationale and Benefits. *Clin Biochem Rev.* 2016; 37: 17–26. PMID: 27057075
47. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med.* 1999; 130: 461–70. PMID: 10075613
48. Szummer K, Evans M, Carrero JJ, Alehagen U, Dahlström U, Benson L, et al. Comparison of the Chronic Kidney Disease Epidemiology Collaboration, the Modification of Diet in Renal Disease study and the Cockcroft-Gault equation in patients with heart failure. *Open Heart.* 2017; 4: e000568. <https://doi.org/10.1136/openhrt-2016-000568> PMID: 28761677
49. Ferreira JP, Girerd N, Pellicori P, Duarte K, Girerd S, Pfeffer MA, et al. Renal function estimation and Cockcroft–Gault formulas for predicting cardiovascular mortality in population-based, cardiovascular risk, heart failure and post-myocardial infarction cohorts: The Heart “OMics” in AGEing (HOMAGE) and the high-risk myocardia. *BMC Medicine.* 2016; 14: 181. <https://doi.org/10.1186/s12916-016-0731-2> PMID: 27829460
50. Weidmann ZM, Breidthardt T, Twerenbold R, Zusli C, Nowak A, von Eckardstein A, et al. Prediction of mortality using quantification of renal function in acute heart failure. *Int J Cardiol.* 2015; 201: 650–657. <https://doi.org/10.1016/j.ijcard.2015.08.097> PMID: 26355241
51. Mandelli S, Riva E, Tettamanti M, Detoma P, Giacomini A, Lucca U. Mortality Prediction in the Oldest Old with Five Different Equations to Estimate Glomerular Filtration Rate: The Health and Anemia Population-based Study. *Plos One.* 2015; 10: e0136039. <https://doi.org/10.1371/journal.pone.0136039> PMID: 26317988
52. Barra S, Providência R, Faustino C, Paiva L, Fernandes A, Leitão Marques A. Performance of the Cockcroft-Gault, MDRD and CKD-EPI Formulae in Non-Valvular Atrial Fibrillation: Which one Should be Used for Risk Stratification? *J Atri Fibrillation.* 2013; 6: 896.
53. Kontos MC, Jamal SM, Ornato JP, Tatum JL, Jesse RL, Anderson FP. Comparison of the modification of diet in renal disease and the Cockcroft-Gault equations for predicting mortality in patients admitted for exclusion of myocardial ischemia. *Am J Cardiol.* 2008; 102: 140–5. <https://doi.org/10.1016/j.amjcard.2008.03.023> PMID: 18602510
54. Zamora E, Lupón J, Vila J, Urrutia A, de Antonio M, Sanz H, et al. Estimated glomerular filtration rate and prognosis in heart failure: value of the Modification of Diet in Renal Disease Study-4, chronic kidney disease epidemiology collaboration, and cockcroft-gault formulas. *J Am Coll Cardiol.* 2012; 59: 1709–15. <https://doi.org/10.1016/j.jacc.2011.11.066> PMID: 22554602
55. Smilde TDJ, van Veldhuisen DJ, Navis G, Voors A a., Hillege HL. Drawbacks and prognostic value of formulas estimating renal function in patients with chronic heart failure and systolic dysfunction. *Circulation.* 2006; 114: 1572–1580. <https://doi.org/10.1161/CIRCULATIONAHA.105.610642> PMID: 17015793
56. Plischke M, Neuhold S, Kohl M, Heinze G, Sunder-Plassmann G, Pacher R, et al. Renal function in heart failure: a disparity between estimating function and predicting mortality risk. *Eur J Heart Fail.* 2013; 15: 763–770.
57. Levey AS, Coresh J, Greene T, Stevens L a., Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med.* 2006; 145: 247–254. PMID: 16908915

58. Björk J, Bäck SE, Ebert N, Evans M, Grubb A, Hansson M, et al. GFR estimation based on standardized creatinine and cystatin C: a European multicenter analysis in older adults. *Clin Chem Lab Med*. 2018; 23: 422–435
59. Delanaye P, Cavalier E, Pottel H. Serum Creatinine: Not So Simple! *Nephron*. 2017; 136: 302–308. <https://doi.org/10.1159/000469669> PMID: 28441651
60. Delanaye P, Melsom T, Ebert N, Bäck S-E, Mariat C, Cavalier E, et al. Iohexol plasma clearance for measuring glomerular filtration rate in clinical practice and research: a review. Part 2: Why to measure glomerular filtration rate with iohexol? *Clin Kidney J*. 2016; 9: 700–4. <https://doi.org/10.1093/ckj/sfw071> PMID: 27679716
61. Schei J, Stefansson VTN, Mathisen UD, Eriksen BO, Solbu MD, Jenssen TG, et al. Residual Associations of Inflammatory Markers with eGFR after Accounting for Measured GFR in a Community-Based Cohort without CKD. *Clin J Am Soc Nephrol*. 2016; 11: 280–286. <https://doi.org/10.2215/CJN.07360715> PMID: 26668020