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Cystatin C blood level as a risk factor for death after heart surgery

Didier Ledoux[1]*, Mehran Monchi[2], Jean-Paul Chapelle[3], and Pierre Damas[1]

[1]*Intensive Care Unit, Liège University Hospital, Sart Tilman Bat B35, B-4000 Liège, Belgium;* [2]*Intensive Care Unit, Institut Jacques Cartier, Massy, France; and* [3]*Department of Clinical Chemistry, Liège University Hospital, Sart Tilman Bat B35, B-4000 Liège, Belgium*

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KEYWORDS
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Risk stratification

Aims Pre-operative renal dysfunction is a known risk factor for mortality and morbidity after heart surgery. Despite limited accuracy, serum creatinine is widely used to estimate glomerular filtration rate (GFR). Cystatin C is more accurate for assessing GFR. The aim of the present study was to assess associations between GFR estimated from serum cystatin C levels before heart surgery and hospital mortality, hospital morbidity, and 1 year mortality.
Methods and results In a prospective single-centre observational study, clinical risk factors for morbidity and mortality were recorded and serum creatinine and cystatin C levels were measured in patients admitted for heart surgery. Hospital mortality and morbidity and 1 year mortality were recorded. Over an 8 month period, 499 patients were screened, among whom 376 (74.5%) were included in the study. Hospital mortality was 5.6% (21 patients) and 1 year mortality was 10.2%. Hospital morbidity, defined by a length of stay above the 75th percentile, was 22.1% (83 patients). In the multivariable analysis, GFR estimated from serum cystatin C, but not GFR estimated from serum creatinine, was an independent risk factor for hospital morbidity/mortality (odds ratio per 10 mL/min of GFR decrease, 1.20 (1.07–1.34), $P = 0.001$) and for 1 year mortality (hazards ratio per 10 mL/min of GFR decrease, 1.26 (1.09–1.46), $P = 0.002$).
Conclusion Pre-operative GFR estimation from serum cystatin C may provide a better risk assessment than pre-operative GFR estimation from serum creatinine in patients scheduled for heart surgery.

Introduction

The identification of pre-operative risk factors for adverse outcomes after heart surgery is important to determine which resources and interventions will ensure an optimal outcome. Another benefit is risk adjustment in studies of quality of care.

Renal dysfunction increases the risk of peri-operative morbidity and mortality in patients undergoing heart surgery.[1–8] The rate of chronic renal impairment is increasing in the general population, and mild renal impairment often escapes recognition.[9] In numerous studies including patients with cardiovascular disease or diabetes, glomerular filtration rate (GFR) was an independent risk factor for overall mortality and new cardiovascular events.[9] In clinical practice, GFR is estimated from the serum creatinine level. However, serum creatinine is of limited value for the early detection of renal impairment, because creatinine is not only filtered by the glomeruli, but also secreted by the tubules.[10] Moreover, serum creatinine may not adequately assess acute changes in GFR.[11] Serum creatinine is influenced not only by renal function, but also by lean body mass (i.e. muscle mass), sex, age, and ethnicity.[12]

Serum cystatin C is a newly identified marker of renal function. Cystatin C is a low-molecular-weight protein (13 359 Da) that is produced by all nucleated cells at a constant rate, released into the bloodstream, freely filtered by the renal glomeruli, and catabolized in the proximal tubules.[13] Serum cystatin C concentration is independent of age, sex, and muscle mass. Several studies have shown that serum cystatin C is a better indicator of GFR and a more reliable marker of mild renal dysfunction, compared with serum creatinine.[14–16] In an observational study, Shlipak *et al.*[17] found that serum cystatin C was an independent risk factor for heart failure in elderly adults and a better risk marker than serum creatinine.

In the present study, we hypothesized that pre-operative GFR estimated from serum cystatin C would be a better predictor of post-operative mortality and morbidity than GFR estimated from serum creatinine in patients undergoing heart surgery.

Methods

Patient recruitment

Over the period from March 2003 to January 2004, we conducted a prospective observational study in a single university hospital.

* Corresponding author. Tel: +32 4366 7494; fax: +32 4366 8898.
E-mail address: dledoux@chu.ulg.ac.be

The study complied with the Declaration of Helsinki and was approved by the institutional Ethics Committee. Informed consent was obtained from all patients or from their guardians prior to inclusion. Consecutive patients admitted for heart surgery were included prospectively in the study.

Clinical assessments and follow-up

At baseline, we collected demographic characteristics, established risk factors for heart surgery complications,[18] and details on the surgical procedure. With this information, we calculated the EuroSCORE[19] for all patients. EuroSCORE stands for European System for Cardiac Operative Risk Evaluation. This scoring system involves 17 variables distributed in three groups of risk factors: patient-related factors, cardiac-related factors, and operation-related factors. In the score, weights attributed to each variable were obtained from the logistic regression beta coefficients. At the end of the hospital stay, we recorded new cardiac events, length of ICU stay, length of hospital stay, and vital status. Finally, 1 year after surgery, we contacted each patient's general practitioner to obtain information on vital status and hospital admissions. Our primary endpoint was 1 year mortality. Secondary endpoints were hospital mortality and hospital morbidity defined as a length of hospital stay greater than the 75th percentile, determined in the study population. The choice of this length of stay threshold was made arbitrarily but was justified by the fact that it maximized the probability that these patients truly presented comorbidity and that they were those who inflated significantly care cost.

Laboratory methods

In each patient, a 5 mL blood sample was drawn pre-operatively for determination of serum creatinine using the kinetic compensated Jaffé assay (CREA kit, Roche Diagnostics, Basel, Switzerland) and of serum cystatin C using a particle-enhanced nephelometric immunoassay (N latex Cystatin C kit, Dade Behring, Marburg, Germany). Serum creatinine levels were communicated to the physicians in charge of the patients, but serum Cystatin C levels were not.

Creatinine based estimates of GFR were calculated using the simplified version of the Modification of the Diet in Renal Disease (MDRD) formula:[20] GFR (mL/min/1.73 m^2) = 186.3 × serum creatinine concentration (mg/dL)$^{-1.154}$ × age$^{-0.203}$ × 1.212 (if black) × 0.742 (if female).

Cystatin C based estimates of GFR were calculated using the following formula:[21] GFR (mL/min/1.73 m^2) = 84.69 × Plasma Cystatin C (mg/L)$^{-1.68}$ × 0.948 (if female). A GFR equal or above 90 mL/min/1.73 m^2 was considered as normal.[22]

Statistical analysis

Continuous variables are reported as the median and interquartile range. In addition to the studied markers of the renal function, the following established risk factors were assessed in the univariate analysis: age, female gender, chronic pulmonary disease, extracardiac arteriopathy, previous cardiac surgery, active endocarditis, critical pre-operative state, unstable angina, left ventricular dysfunction, recent myocardial infarction, pulmonary hypertension, emergent, surgery procedure other than isolated coronary surgery and the EuroSCORE. To assess the relationship between cardiac risk factors and renal function markers, we divided our study population into quartiles of pre-operative GFR estimated from serum cystatin C concentrations. We compared the characteristics of patients across these quartiles using the likelihood ratio χ^2 test and Kruskal–Wallis test as appropriate.

We performed univariate logistic regression and Cox proportional hazard models to assess associations linking established risk factors for cardiac surgery complications and renal function markers to hospital mortality, hospital morbidity, and 1 year mortality. We then used multivariable analysis (logistic regression and Cox proportional hazard models) in order to assess associations between GFR estimated from cystatin C or from creatinine with the outcome when other risk factors are controlled. In this multivariable analysis, we decided to use only the EuroSCORE as a control risk factor. Doing so, we intended to avoid overfitting or underfitting, which would have resulted if all the risk factors were included in the model because of the small amount of outcome events (1 year survival and hospital outcome). The choice of EuroSCORE as a risk adjustment variable was reasonable since it is a well-validated tool for risk assessment after heart surgery but also because it takes into account all the risk factors mentioned earlier. We build two models, one including the EuroSCORE and the GFR estimated from cystatin C, the other including the EurosCORE and the GFR estimated from creatinine. We assessed the fit of these two models by using the Akaike's information criterion (AIC).

Finally, in order to select the variables having the strongest association with the measured outcomes, we performed a backward stepwise logistic regression and a backward stepwise Cox proportional hazard regression including the following variables: EuroSCORE, GFR estimated with cystatin C, and GFR estimated with creatinine. Variables with a significant partial regression coefficient of $P < 0.10$ were added to the model, and those with $P < 0.10$ in the stepwise procedure were retained.

Collinearity was checked with a matrix of correlations, using the Spearman rank correlation coefficient between independent variables. We chose an $r \geq 0.4$ as the criterion for collinearity. A significant correlation ($r = 0.73$, $P < 0.001$) was found between GFR estimated from cystatin C and GFR estimated from creatinine.

Tests for linearity were performed for all continuous variables (age, LVEF, EuroSCORE, creatinine, cystatin C, and the estimated GFR). These variables were tested in two ways. First, a quadratic term (x^2) was included in addition to the linear term (x) in the logistic and Cox regression models. A significant coefficient for x^2 indicates a lack of linearity. Secondly, continuous variables were considered as categorical variables by dividing them into quartiles. Then we fitted univariate logistic regression model for the prediction of hospital mortality and morbidity and a univariate Cox model for 1 year survival analysis and plotted the average value of each quartile vs. the coefficient of the quartile. The plot was then examined with respect to the shape of the resulting curve. We found the relationship not linear only for serum creatinine.

The assumption of proportional hazards was checked by observing a constant vertical difference between plots of log-integrated hazard against t for the different quartiles of each variable. This graphical assessment was further confirmed using the Kolmogorov-type supremum tests for proportional hazards assumption. We found that proportional hazard assumption was respected for all the variables.

Statistical tests were performed using SAS software (version 9.1.3 Service Pack 4, SAS Institute Inc., Cary, NC, USA). *P*-values lower than 0.05 were considered statistically significant.

Results

Baseline characteristics

Over the 8 month period, 499 patients admitted to our heart surgery department were screened for study eligibility. Among them, 376 (75.4%) patients gave their informed consent before surgery and were included in the study. Of the 123 patients who were not included in the study, the reasons for non-inclusion in the protocol were: 53/499 (11%) patients' refusals; 32/499 (6%) unavailability of a physician to obtain the informed consent; 26/499 (5%) patients in whom the study blood samples were not drown pre-operatively; and 12/499 (2%) patients who were too sick to give consent. Patients' median age was 71 years (range 20–86) and 254 (67.6%) patients were men. The following surgical procedures were

Table 1 Baseline characteristics of the study patients ($n = 376$) by estimated GFR quartiles[a]

Patient characteristics	All patients	GFR estimated from serum cystatin C concentration				*P*-value
		Quartile 1 $<$ 48 mL/min/1.73 m^2 ($n = 93$)	Quartile 2 48–65 mL/min/1.73 m^2 ($n = 90$)	Quartile 3 66–81 mL/min/1.73 m^2 ($n = 98$)	Quartile 4 $\geq$ 82 mL/min/1.73 m^2 ($n = 95$)	
Age, years	71 (63–76)	75 (70–78)	74 (69–78)	68 (60–72)	64 (57–71)	$<$0.001
Female, *n* (%)	122 (32.4)	39 (40.6)	35 (38.9)	21 (21.6)	27 (29.0)	0.015
Body mass index, kg/m^2	26.1 (23.5–28.7)	26.3 (22.7–28.3)	25.7 (23.7–28.7)	26.4 (23.5–29.3)	25.4 (23.5–28.7)	0.765
EuroSCORE	5 (3–8)	6 (7–9)	6 (4.8–8.0)	5 (3.0–7.0)	3 (2.0–5.0)	$<$0.001
Pre-operative LVEF, %	63 (50–74)	58 (46–70)	62 (47–73)	69 (54.3–76.3)	65 (56.0–75.5)	0.003
COPD, *n* (%)	106 (28.2)	37 (38.5)	20 (22.2)	27 (27.8)	22 (23.7)	0.060
Diabetes, *n* (%)	81 (21.5)	29 (30.2)	20 (22.2)	15 (15.5)	17 (18.3)	0.077
Hypertension, *n* (%)	267 (71)	76 (79.2)	63 (70.0)	69 (71.1)	59 (63.4)	0.120
Pulmonary hypertension, *n* (%)	83 (22.1)	24 (25.0)	27 (30.0)	22 (22.7)	10 (10.8)	0.009
NYHA class IV[b]	31 (8.4)	16 (16.8)	4 (4.5)	6 (6.4)	5 (5.4)	0.013
Recent myocardial infarction, *n* (%)	51 (13.6)	14 (14.6)	11 (12.2)	16 (16.5)	10 (10.8)	0.667
Previous heart surgery, *n* (%)	24 (6.4)	12 (12.5)	2 (2.2)	5 (5.2)	5 (5.4)	0.035
Extracardiac arteriopathy, *n* (%)	94 (25)	35 (36.5)	20 (22.2)	26 (26.8)	13 (14.0)	0.004
Emergency surgery, *n* (%)	19 (5.1)	7 (7.3)	5 (5.6)	5 (5.2)	2 (2.2)	0.392
Complex surgery[c], *n* (%)	134 (35.6)	45 (46.9)	35 (38.9)	29 (29.9)	25 (26.9)	0.017
IABP[d], *n* (%)	14 (3.7)	9 (9.4)	2 (2.0)	3 (3.4)	0 (0)	0.004
Serum cystatin C, mg/L	66 (49–81)	1.69 (1.53–1.99)	1.27 (1.21–1.33)	1.08 (1.06–1.1)	0.95 (0.83–0.98)	$<$0.001
Serum creatinine, mg/L	10.3 (8.7–12.1)	13.0 (11.1–16.4)	10.4 (9.0–12.0)	10.1 (8.7–11.2)	8.7 (7.7–9.9)	$<$0.001
Estimated GFR, cystatin C (mL/min)	66 (49–81)	35 (26–41)	55 (51–61)	73 (70–77)	91 (85–110)	$<$0.001
Estimated GFR, creatinine (mL/min)	71 (58–84)	50 (39–61)	66 (57–77)	77 (68–88)	87 (79–100)	$<$0.001
ICU stay, days		3 (2.3–5.0)	3 (2.0–4.0)	2 (2.0–4.0)	2 (2.0–3.0)	$<$0.001
Hospital stay, days		12 (10–16.8)	11 (10.0–14.3)	11 (10.0–14.0)	10 (10–12.0)	0.001
Death in the ICU, *n* (%)		9 (9.4)	1 (1.1)	2 (2.1)	0 (0)	0.001
Death in hospital, *n* (%)	21 (5.6)	13 (13.5)	4 (4.4)	3 (3.1)	1 (1.1)	0.002
1 year re-admission, *n* (%)	42 (11.3)	16 (34.8)	13 (15.3)	10 (10.8)	7 (7.7)	0.098
1 year mortality, *n* (%)	38 (10.1)	19 (19.8)	11 (12.2)	6 (6.2)	2 (2.2)	$<$0.001

IABP was used in case of failure to wean patient from cardiopulmonary bypass. LVEF, left ventricular ejection fraction; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; ICU, intensive care unit.

[a]Data are presented as median and interquartile range for continuous variables and count plus percentage for categorical variables.

[b]NYHA, New York Heart Association classification system for heart dysfunction.

[c]Major cardiac surgery other than or in addition to coronary artery bypass grafting.

[d]Intra-aortic balloon counter-pulsation during the post-operative period.

performed: coronary artery bypass graft (CABG) 235/376 (62.5%); valve surgery 81/376 (21.5%); combined CABG and valve surgery 38/376 (10.1%); ascending aorta surgery 15/376 (4%); atrial septal defect closure 5/376 (1.3%); and left atrial myxoma surgery 2/376 (0.5%). Median follow-up was 368 days; four patients (1.1%) were lost to follow-up. Of the 376 patients, 21 (5.6%) died during the hospital stay, 83 (22.1%) had a prolonged hospital stay (longer than 75th percentile), and 38 (10.2%) died within the first year. The median and interquartile range of serum creatinine were 10.3 (8.7–12.1) mg/L; and the median and interquartile range of serum cystatin C were 1.16 (1.0–1.41) mg/L. Serum creatinine was above the upper limit of normal (10.2 mg/L in women and 12.1 mg/L in men) in 113 (30.1%) patients and serum cystatin C was above the upper limit of normal (0.95 mg/L) in 322 (85.6%) patients. When serum creatinine was used, 302/376 (80%) patients had an estimated GFR below normal, whereas 323/376 (86%) patients had abnormal GFR when serum cystatin C was used to estimate GFR. In 282 patients, GFR was below 90 mL/min/1.73 m^2 whether it was estimated with creatinine or with cystatin C (*Table 1*).

Cardiovascular risk factors and outcomes associated with cystatin C

Patients in the lower quartile of GFR based on cystatin C were older, more likely to be female, and more likely to have risk factors for post-operative morbidity and mortality as shown by higher EuroSCORE values.[19] These patients were also more likely to experience a prolonged ICU stay, a prolonged hospital stay, and death within the first year after surgery (*Table 1*).

Factors associated with 1 year mortality

Full follow-up data were obtained for all patients. In the univariate analysis, in addition to estimated GFR, eight variables were significantly associated with 1 year mortality: age; EuroSCORE; COPD; recent myocardial infarction; extracardiac arteriopathy; critical pre-operative state; unstable angina; and emergency surgery. According to the AIC, the multivariable model including EuroSCORE and GFR estimated from Cystatin C (AIC = 414.973) fitted better than the model including EuroSCORE and GFR estimated from creatinine (AIC = 417.204). Moreover, Euroscore and GFR estimated from cystatin C were the two variables selected by the backward stepwise logistic regression. When other risk factors were adjusted, GFR estimated from cystatin C was found to be a better marker for 1 year mortality than GFR estimated from creatinine [odds ratio per 10 mL/min of GFR decrease, 1.20 (1.07–1.34), $P = 0.001$] (*Table 2*).

Factors associated with hospital morbidity or mortality

In the univariate analysis, hospital mortality and morbidity were significantly associated with GFR, as well as with seven of the 15 assessed risk factors (age, EuroSCORE, COPD, diabetes mellitus, recent myocardial infarction, previous cardiac surgery, extracardiac arteriopathy, emergency surgery, and complex surgery). *Table 3* lists the other risk factors. The multivariable model including EuroSCORE and GFR estimated from cystatin C (AIC = 368.591) fitted better than the model including the EuroSCORE and the GFR estimated from creatinine (AIC = 371.992). The Cox regression model with backward stepwise variable selection kept EuroSCORE and GFR estimated from cystatin C in the

Table 2 Univariate and multivariable Cox regression analysis for 1-year mortality rate

Patient characteristics	Univariate analysis		Multivariable analysis	
	Hazard ratio (95% CI)	*P*-value	Hazard ratio (95% CI)	*P*-value
Age, years	1.06 (1.02–1.10)	0.005		
Female	0.85 (0.42–1.72)	0.653		
EuroSCORE	1.23 (1.14–1.33)	<0.001	1.19 (1.09–1.29)	<0.001
COPD	2.18 (1.15–4.14)	0.017		
Extracardiac arteriopathy	2.02 (1.05–3.87)	0.034		
Previous heart surgery	1.39 (0.43–4.53)	0.581		
Active endocarditis	1.02 (0.14–7.42)	0.986		
Critical pre-operative state	4.98 (2.416–10.261)	<0.001		
Unstable angina	2.51 (1.26–4.97)	0.008		
Pre-operative LVEF, %	0.99 (0.97–1.01)	0.175		
Recent myocardial infarction	2.78 (1.38–5.60)	0.004		
Pulmonary hypertension	1.32 (0.64–2.72)	0.449		
NYHA class IV[a]	1.37 (0.484–3.85)	0.557		
Emergency surgery	4.82 (2.12–10.96)	<0.001		
Complex surgery[b]	0.87 (0.44–1.73)	0.697		
Diabetes	1.54 (0.77–3.11)	0.225		
Creatinine (mg/dL)	1.44 (1.11–1.86)	0.006		
Cystatin C (mg/L)	1.67 (1.27–2.18)	<0.001		
GFR estimated from cystatin C, mL/min/1.73 m^2	0.97 (0.96–0.98)	<0.001	0.97 (0.96–0.99)	0.002
GFR estimated from creatinine, mL/min/1.73 m^2	0.97 (0.95–0.98)	<0.001		

LVEF, left ventricular ejection fraction; COPD, chronic obstructive pulmonary disease; 95% CI, 95% confidence interval.
[a]NYHA, New York Heart Association classification system for heart dysfunction.
[b]Complex surgery: major cardiac surgery other than or in addition to coronary artery bypass grafting.

Table 3 Univariate and multivariable logistic regression analysis to identify factors associated with hospital morbidity and mortality

Patient characteristics	Univariate analysis		Multivariable analysis	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Age, years	1.03 (1.01–1.06)	0.013		
Female	0.77 (0.46–1.29)	0.316		
EuroSCORE	1.23 (1.15–1.33)	<0.001	1.18 (1.10–1.28)	<0.001
COPD	1.69 (1.03–2.78)	0.040		
Extracardiac arteriopathy	2.45 (1.48–4.07)	0.001		
Previous heart surgery	4.02 (1.73–9.32)	0.001		
Active endocarditis	3.16 (0.89–11.17)	0.074		
Critical pre-operative state	5.94 (2.69–13.108)	<0.001		
Unstable angina	1.52 (0.829–2.77)	0.177		
Pre-operative LVEF, %	0.99 (0.98–1.01)	0.447		
Recent myocardial infarction	1.82 (0.97–3.41)	0.063		
Pulmonary hypertension	1.13 (0.65–1.97)	0.672		
NYHA class IV[a]	1.81 (0.83–3.94)	0.135		
Emergency surgery	4.61 (1.80–11.85)	0.001		
Complex surgery[b]	1.14 (0.70–1.85)	0.599		
Diabetes	1.87 (1.10–3.19)	0.022		
Creatinine (mg/dL)	2.84 (1.48–5.48)	0.002		
Cystatin C (mg/L)	3.07 (1.74–5.41)	<0.001		
GFR estimated from cystatin C, mL/min/1.73 m^2	0.97 (0.96–0.98)	<0.001	0.98 (0.97–0.99)	0.001
GFR estimated from creatinine, mL/min/1.73 m^2	0.97 (0.96–0.99)	<0.001		

LVEF, left ventricular ejection fraction; COPD, chronic obstructive pulmonary disease; 95% CI, 95% confidence interval.
[a]NYHA, New York Heart Association classification system for heart dysfunction.
[b]Complex surgery: major cardiac surgery other than or in addition to coronary artery bypass grafting.

model [hazards ratio per 10 mL/min of GFR decrease, 1.26 (1.09–1.46), $P = 0.002$].

After adjustment for other risk factors, GFR estimated from cystatin C appeared to be a better marker for hospital morbidity or mortality.

Discussion

In this prospective cohort study in 376 patients, we found that pre-operative GFR estimated from serum cystatin C was strongly associated with 1 year mortality and with hospital mortality and morbidity. GFR estimated from serum cystatin C was better than GFR estimated using MDRD equation based on serum creatinine for predicting adverse outcomes. Several reasons may explain our findings, as serum cystatin C is more sensitive than serum creatinine for detecting renal dysfunction. Serum creatinine tends to overestimate GFR in patients with renal dysfunction. The relationship between serum creatinine and GFR is not linear, and serum creatinine starts to rise only when GFR falls below 50% of normal.[23] Therefore, serum creatinine often misses mild-to-moderate renal function impairment. Several mechanisms may contribute to worsen outcomes after heart surgery in patients with renal dysfunction. Renal dysfunction is associated with other risk factors such as older age, left ventricle dysfunction, and extracardiac arteriopathy (included in EuroSCORE). Renal dysfunction is also associated with a wide range of metabolic derangements, including hyperhomocysteinaemia,[24] elevated asymmetrical dimethylarginine,[25] elevated lipoprotein (a),[26] chronic inflammation, and increased oxidative stress.[27] These derangements, which have been identified even in patients with moderate renal dysfunction, are associated with adverse outcomes in patients with kidney disease[28–31] and may have mediated the higher risk seen in patients with cystatin C elevation in our study.

GFR estimated from serum cystatin C adds information to the EuroSCORE in terms of hospital mortality and morbidity. This may be ascribable to the use of serum creatinine in the EuroSCORE to estimate renal function. GFR estimated from serum cystatin C was the only variable in our study that added information to the EuroSCORE regarding 1 year mortality. Although the EuroSCORE is not designed to predict long-term outcomes, our findings constitute further evidence that serum creatinine is not an optimal marker of renal function and risk associated with heart surgery.

Serum creatinine assay is less expensive (0.4 US Dollars) than cystatin C assay (5 US Dollars). Whether the greater accuracy of cystatin C in estimating renal function is associated with clinical benefits needs to be determined. Our results suggest that the increased cost related to a single pre-operative cystatin C measurement may be acceptable in the setting of patient evaluation before heart surgery. Shlipak *et al.*[17] also found that cystatin C was a better marker for the risk of death and cardiovascular events than serum creatinine in elderly individuals. In patients with acute coronary syndrome, cystatin C performs better than creatinine in discriminating between survivors and non-survivors.[32] Thus, cystatin C assay may have a favourable cost/benefit ratio.

Our study has some limitations. Informed consent could not be obtained for 123 patients (including 12 who were too sick to give consent) of 499 admitted patients. Our study was performed in a single centre, and its results may not apply to other centres. A large multicentre study is needed to further evaluate associations linking pre-operative cystatin C

to mortality after cardiac surgery. Another limitation is that we did not study the cause of death in our patients and therefore did not obtain data on the mechanisms linking renal function impairment and outcomes.

Conclusion

Although the present study has to be considered as preliminary, cystatin C appears to be a promising marker for impaired renal function that provides more information than the established estimates of GFR, thereby improving the identification of high-risk patients before heart surgery.

Conflict of interest: none declared.

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