Original Research

Urine NGAL as a Biomarker of Kidney Damage After On- and Off-Pump Coronary Artery Bypass Graft Surgery: A Prospective Pilot Study

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Key words:
Neutrophil gelatinase-associated lipocalin, off-pump, on-pump, coronary artery bypass grafting, acute kidney injury.

Introduction: Acute kidney injury (AKI) is a relatively frequent complication after coronary artery bypass graft surgery (CABG). We compared the off- and on-pump CABG procedures with respect to changes in renal function as reflected by levels of urine neutrophil gelatinase-associated lipocalin (UrNGAL).

Methods: In a prospective design, we studied patients who underwent CABG, off- or on-pump, with respect to changes in glomerular filtration rate (GFR) and UrNGAL pre- and postoperatively. UrNGAL was measured using a chemiluminescent microparticle immunoassay. We recorded patients' demographics, past medical history, cardiac function and laboratory findings. Patients were grouped according to the CABG type.

Results: Of 72 patients, 31 underwent off-pump and 41 on-pump CABG. The mean age was 65.7 ± 8.1 years and 81.9% were males. Groups were similar with respect to the prevalence of hypertension, diabetes, dyslipidaemia, body mass index, and smoking at entry. No patient experienced acute renal failure and there were no deaths. At both time points, the UrNGAL levels were similar in the two groups. Patients in the on-pump group showed a significant improvement in renal function 48 hours postoperatively compared to baseline ($p<0.001$). UrNGAL levels decreased significantly 3 hours after surgery in the on-pump group ($p=0.001$), while they tended to decrease in the off-pump group ($p=0.057$). The overall change in UrNGAL did not differ significantly between groups.

Conclusions: According to the UrNGAL measurements, neither of the two CABG techniques was superior in terms of their effect on postoperative renal function. Renal function significantly improved in the on-pump group while UrNGAL levels decreased after surgery in the same group.

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Coronary heart disease is a major cause of death and disability in developed countries. It is responsible for about one third of all deaths among individuals over 35 years old, although a decrease in mortality rates has been observed over the past four decades.[1-2] Consequently, cardiopulmonary bypass (CPB) surgery is the most frequent major surgical procedure performed each year on hospitalized adults.[3] As a result, a large number of coronary artery bypass graft (CABG) surgeries take place worldwide, with renal failure being a quite frequent and certainly severe complication.[4-6]

To be more specific, acute kidney injury (AKI) following cardiac surgery is the second most common cause of AKI in critically-ill patients.[7] CABG without cardiopulmonary bypass (off-pump CABG sur-

gery) has been proposed as an alternative to CABG with cardiopulmonary bypass (on-pump CABG surgery) as a means of attenuating renal injury. Until recently, the severity of renal damage has mainly been evaluated in terms of changes in serum creatinine levels, with conflicting results regarding the superiority of either method.[8-11] Thus, renal markers or systemic indicators have been studied to facilitate the early detection or prediction of acute injury. The latter has led to the investigation of the use of neutrophil gelatinase-associated lipocalin (NGAL), which has been identified as one of the most up-regulated genes in the kidney soon after ischaemic injury.[12-14]

NGAL protein expression has been shown to increase radically in human kidney tubules in cases with AKI of different aetiologies.[15-16] Interestingly, urinary NGAL (UrNGAL) has been recognised as an early predictive biomarker for AKI in several clinical scenarios,[17] which specifically correlate with the duration and the severity of renal injury after CABG surgery.[18]

The aim of this study was to identify the differences between the off- and on-pump CABG operative techniques with respect to potential alterations in renal function, as reflected by changes in the UrNGAL levels.

Methods

Study population

All patients who were referred to our hospital with cardiac symptoms between January 2011 and May 2012, were considered for inclusion in this study. The study was designed to include patients who required CABG, according to the international guidelines,[19] in the absence of any exclusion criteria.

The exclusion criteria included pre-existing renal disease, peripheral vascular disease, active bacterial infections and inflammatory or neoplastic lesions of the trachea, lungs and gastrointestinal tract, according to the experience of similar studies on the subject.[20] Pre-existing renal insufficiency was considered to be present if the patient already carried this diagnosis, or was defined by the presence of a reduced estimated glomerular filtration rate (eGFR<50 mL/min/1.73m^2),[21] corresponding to the mean serum creatinine level (>2.5 mg/dL) within the month before consideration for inclusion in the study, as well as by the related ultrasound findings. Estimated GFR was computed using the Cockcroft–Gault formula.[22]

The decision whether or not to use CPB was made according to the patient's Euroscore[23] and the surgeon's decision and preference. All participants were evaluated in a prospective protocol, including daily clinical examination and laboratory measurements, starting one day prior to the procedure and continuing for 48 hours after the operation.

We recorded patients' demographics in addition to comorbidities such as hypertension, diabetes, dyslipidaemia, and the smoking status at admission. In addition, for all participants we recorded the body mass index (BMI) and the existence or not of a family history of coronary artery disease. Pre-existing hypertension was defined as the long-term (>6 months) use of antihypertensive drugs, or systolic blood pressure values over 140 mmHg arising from three consecutive measurements. Dyslipidaemia was recorded if the patient was on therapy with any statin or fibrate, or both, at the time of entry. Finally, smokers were considered to be the patients who were either active smokers up to the admission day or had stopped less than 5 years before. Patients with a BMI >30 kg/m^2 were considered to be obese. Written informed consent was obtained from all participants and the locally appointed ethics committee of Hippokration hospital approved the research protocol (Registration Number: EΣ 10/29-6-2009).

Preparation protocol for CABG

The fluid volume administered to each patient was individualised and was estimated according to the central venous pressure (CVP) and the pulmonary capillary wedge pressure (PCWP), which were measured by a Swan-Ganz catheter placed immediately preoperatively, during anaesthesia induction in the anaesthesia room. The goal was to maintain CVP levels between 8 and 12 cm H_2O and PCWP between 10–14 mmHg, in order to achieve the optimal blood volume status. Ringer's lactate was the solution most commonly used. Based on systemic blood pressure measurements, inotropes (dobutamine) and vasoconstrictors (norepinephrine) were given to all patients, in order to achieve mean blood pressure levels between 70-90 mmHg. Dobutamine was available in 250 mL Dextrose Water 5% (D/W 5%) and was infused in a concentration of 1 mg/mL. The usual dose was between 3 to 15 μg/kg/min with the aim of increasing cardiac output. Four mg of norepinephrine were added in 250 mL Dextrose 5% to achieve a drug concentration of 16 μg/mL. The initial dose rate was 1 μg/min (15 microdrops/min), titrated upward to the

desired effect. Additionally, antibiotics, respiratory system drugs (bronchodilators, corticosteroids), diuretics, analgesics, as well as gastro-protective agents were administered as needed. More specifically, our clinical protocol included drugs such as ipratropium and budesonide for bronchodilation, furosemide as a diuretic, and paracetamol and meperidine as analgesics. Beyond furosemide, which was used on demand and with caution because of potential renal function impairment, the rest of the regimens are known not to significantly affect renal function. Non-steroidal anti-inflammatory drugs were not administered. As far as antibiotics are concerned, piperacillin/tazobactam meropenem and teicoplanin were the drugs of choice for prophylaxis in our setting.

Surgical techniques

All the procedures were performed through a standard median sternotomy. Within a standard cardiopulmonary bypass system, an arterial cannula was inserted in the distal ascending aorta and a two-stage venous cannula was inserted through the right atrium. This system consists of a membrane-coated oxygenator with a cardiotomy reservoir, a standard roller pump, a heater-cooler device and an arterial filter. During aortic cross-clamping, myocardial protection was achieved by hyperkalaemic cold-blood intermittent anterograde or retrograde cardioplegia delivered every 15 min. Suturing the left internal mammary artery as first-choice arterial conduit on the left anterior descending coronary artery and using segments of saphenous vein and the right internal mammary artery in other vessels were the methods of myocardial revascularisation. In the off-pump coronary artery bypass technique, coronary stabilisation was achieved with the Medtronic Octopus III stabilising devices, and cardiac displacement and presentation were performed with deep pericardial traction sutures.

UrNGAL quantification

All the laboratory investigations were performed at the Hippokration Hospital of Athens in the Department of Biochemistry. Urine samples were analyzed using the ARCHITECT i 2000 SR analyser (Abbott Diagnostics Division) by the ARCHITECT UrNGAL kit, which utilises a two-step immunoassay for the quantitative detection of UrNGAL in humans using chemiluminescent microparticle immunoassay technology. Serum creatinine levels were measured in centrifuged plasma samples at the same laboratory.

Sample handling

Spot urine samples were obtained preoperatively and three hours after the CABG surgical procedure. The samples were immediately centrifuged at ≥400 RCF (Relative Centrifugal Force) for 5 minutes and the supernatants were stored in aliquots at a room temperature of 22-30˚C.

Statistical methods

Continuous variables are presented as mean ± standard deviation. Qualitative variables are presented as absolute and relative frequencies. For the comparison of proportions, the chi-square and Fisher's exact tests were used. Student's t-test was used to compare study variables between the group of patients with off-pump CABG surgery and the group undergoing CABG with CPB. Differences between the two study groups in the changes of serum creatinine, eGFR and UrNGAL levels during the follow-up period were evaluated using repeated measures analysis of variance (ANOVA). A repeated measures ANOVA power analysis was conducted. The effect size for this calculation used the ratio of the standard deviation of the effects for a particular factor or interaction and the standard deviation of within-subject effects. The power analysis was conducted for a single, two-group between-subjects factor, and a single within-subjects factor assessed over three time points. For this design, 72 participants achieved a power of 0.95 for the between-subjects main effect at an effect size of 0.35; a power of 0.95 for the within-subjects main effect at an effect size of 0.20; and a power of 0.95 for the interaction effect at an effect size of 0.19.

UrNGAL was log-transformed for the analysis of variance, because of its skewed distribution. Random effects regression analyses were used to longitudinally assess changes in creatinine and clearance levels, after adjusting for Euroscore, New York Heart Association (NYHA) class, hypertension and diabetes. Regression coefficients (β) with their standard errors (SE) were computed from the results of the random effects regression analysis. All p-values reported are two-tailed. Statistical significance was set at 0.05 and analyses were conducted using SPSS statistical software (version 19.0).

Results

Study population

A total of 88 patients were considered for inclusion in the this study, but 16 of them were excluded for the following reasons: 10 patients already carried a diagnosis of chronic kidney disease, typically with serum creatinine values greater than 3 mg/dL; 3 patients suffered from peripheral arterial disease; 2 patients had a recent hospitalisation with documented lung inflammation; and 1 patient had recently undergone operation for colon malignancy. The final study population consisted of 72 patients. This number of patients seems to be comparable to that of many other studies on the subject, which enrolled similar or even fewer number of patients.[20,24-25] Of these patients, 31 (43.06%) underwent the off-pump procedure and 41 (56.94%) the on-pump procedure. The demographics and clinical characteristics of the two study groups are shown in Table 1. The mean age was 66.8 ± 7.8 years in the off-pump group, and 64.9 ± 8.4 years in the on-pump group. There were 26 (84%) males in the off-pump group and 34 (82%) in the on-pump group. The two groups were similar with respect to the prevalence of hypertension, diabetes, smoking, family history of coronary artery disease, obesity, and concomitant diseases at the time of enrolment in the study. The mean serum creatinine was 1.18 ± 0.56 mg/dL for the off-pump group and 0.9 ± 0.17 mg/dL for the on-pump group (p=0.003; Table 2). Respectively, eGFR was 78.7 ± 31.2 mL/min/1.73m^2 and 94.4 ± 26.5 mL/min/1.73m^2 (p=0.024). A greater proportion of patients with dyslipidaemia was found in the off-pump group. The ejection fraction was similar between groups (p=0.454). The frequency of previous myocardial infarction, previous percutaneous intervention and NYHA class was comparable in the two groups, while a greater mean Euroscore was found in the off-pump group compared to the on-pump group (p=0.029). Likewise, the proportion of diseased vessels was similar in the two CAGB surgery groups.

Evaluation of renal function

All changes in serum creatinine and eGFR during

Table 1. Demographics and clinical characteristics in total and by study group.

	Total	CAGB surgery		p
		Off-pump	On-pump	
Age (years), mean ± SD	65.7 ± 8.1	66.8 ± 7.8	64.9 ± 8.4	0.328*
Sex:				0.712
Women	13 (18.1)	5 (16.1)	8 (19.5)	
Men	59 (81.9)	26 (83.9)	33 (80.5)	
Hypertension	45 (65.2)	20 (66.7)	25 (64.1)	0.825
Dyslipidaemia	39 (56.5)	21 (70)	18 (46.2)	0.048
Diabetes mellitus	28 (40.6)	13 (43.3)	15 (38.5)	0.683
Smoking	34 (49.3)	16 (53.3)	18 (46.2)	0.554
Family history	21 (30.9)	12 (40)	9 (23.7)	0.148
BMI (kg/m^2)	28 ± 4.1	27.2 ± 4.9	28.5 ± 3.4	0.205*
Obese	23 (32.4)	8 (26.7)	15 (36.6)	0.378
Concomitant diseases	49 (74.2)	22 (78.6)	27 (71.1)	0.490
EF (%)	50 ± 10.9	48.9 ± 10.3	51 ± 11.5	0.454*
History of MI	35 (49.3)	13 (43.3)	22 (53.7)	0.390
LMA	15 (21.4)	3 (10.3)	12 (29.3)	0.057
LAD	67 (94.4)	28 (93.3)	39 (95.1)	1.000†
LCX	43 (60.6)	19 (63.3)	24 (58.5)	0.683
RCA	50 (70.4)	21 (70)	29 (70.7)	0.947
PDA	22 (31)	11 (36.7)	11 (26.8)	0.376
History of PTCA	2 (3.3)	1 (5)	1 (2.4)	1.000†
Euroscore	4.9 ± 2.4	5.6 ± 2.1	4.3 ± 2.5	0.029*
NYHA:				0.818†
I	2 (2.8)	1 (3.2)	1 (2.4)	
II	37 (51.4)	17 (54.8)	20 (48.8)	
III	33 (45.8)	13 (41.9)	20 (48.8)	

Data are given as n (%) or mean ± SD. *Student's t-test. †Fisher's exact test. Other p-values are by χ^2 test. EF – ejection fraction; MI – myocardial infarction; LMA – left main artery; LAD – left anterior descending artery; LCx – left circumflex artery; RCA – right coronary artery; PDA – posterior descending artery; PTCA – percutaneous transluminal coronary angioplasty.

Table 2. Changes in serum creatinine and estimated glomerular filtration rate (eGFR) during the follow-up period for the two study groups.

		Serum creatinine (mg/dL)			eGFR (mL/min/1.73m^2)		
		Off-pump CABG	On-pump CABG	p*	Off-pump CABG	On-pump CABG	p*
Preoperative		1.18 ± 0.56	0.9 ± 0.17	0.003	78.7 ± 31.2	94.4 ± 26.5	0.024
24 hours postoperative		1.18 ± 0.57	1.17 ± 0.43	0.900	79.7 ± 30.7	79.3 ± 32.5	0.963
48 hours postoperative		1.19 ± 0.63	1.06 ± 0.55	0.380	82.8 ± 35.9	89.0 ± 34	0.459
% Change from preoperative to 48 h		0.7	18.5		5.2	-5.8	
p†	Preoperative vs. 24 h postoperative	1.000	<0.001		0.987	<0.001	
	24 h vs. 48 h postoperative	0.999	0.063		0.547	<0.001	
	Preoperative vs. 48 h postoperative	0.999	0.027		0.555	0.200	
p‡		<0.001			0.039		

Data values are mean ± SD. *p-value for group effect. †p-value for time effect. ‡Effects reported include differences between the two groups in the degree of change in each particular variable (repeated measurements ANOVA). CABG – coronary artery bypass graft surgery.

the follow-up period for the on-pump and the off-pump CABG surgery group are shown in Table 2. Preoperatively, the on-pump group had a lower mean serum creatinine level and greater clearance levels compared to the off-pump group. At 24 hours and 48 hours postoperatively, serum creatinine and eGFR levels did not differ between the two groups (creatinine p=0.900 and p=0.380, GFR p=0.963 and p=0.459, respectively). Both serum creatinine and eGFR remained unchanged during the follow-up period in the off-pump group. In the on-pump CABG group, serum creatinine was increased significantly on the first postoperative day (POD) (p<0.001). However, there was a significant decrease in the serum creatinine values during the second POD (p=0.027; Figure 1). The mean increase in serum creatinine levels from the preoperative measures to two days after the surgery was significantly different between the two groups of patients (18.5% in the on-pump group and 0.7% in the off-pump group, p<0.001). Additionally, eGFR showed a significant decrease between the preoperative measures and those of the first day (p<0.001). Subsequently, however, we observed a significant increase in eGFR between the first and the second POD, reaching the preoperative levels (p<0.001; Figure 2). Glomerular filtration rate showed a mean increase of 5.2% in the off-pump group, and a mean decrease of 5.8% in the on-pump group. The overall change in eGFR from the preoperative measures to those 48 hours postoperatively was significantly different (p=0.039). When random effects regression analysis was conducted with serum creatinine as dependent variable, and after adjusting for Euroscore, NYHA class, hypertension, and diabetes, a significant interaction effect was found between time and the CABG surgery group (β=0.08, SE=0.04, p=0.048), indicating that the on-pump CABG group had a different change in serum creatinine levels during follow up compared with the off-pump CABG surgery group, even after adjusting for the patients' baseline clinical status. Similarly, multiple random effects regression analysis with dependent variable eGFR showed a significant interaction effect between time and CABG surgery group (β=-4.76, SE=2.13, p=0.025) after adjusting for Euroscore, NYHA, hypertension, and diabetes. No patient experienced acute renal failure and there were no deaths.

UrNGAL measurement

The mean UrNGAL measurements for the off-pump and on-pump CABG surgery groups are shown in Table 3. At both time points the UrNGAL levels were similar in the two surgery groups. UrNGAL decreased significantly 3 hours after the surgery in the on-pump group (p=0.001), while it only tended towards a significant reduction in the off-pump group (p=0.057). The mean decrease in the UrNGAL value was 26.6% and 27.2% in the off-pump and on-pump groups, respectively. The overall change in UrNGAL did not differ significantly between the groups, as indicated by the interaction term of the model (p=0.403).

Table 3. Changes in levels of urine neutrophil gelatinase-associated lipocalin (UrNGAL) during the follow-up period for the two groups.

	Preoperative	3 hours postoperative	% Change	p†	p‡
CABG surgery	Mean ± SD	Mean ± SD			
Off-pump	49.7 ± 151.6	36.5 ± 111.2	-26.6	0.057	0.403
On-pump	42.6 ± 64.5	31 ± 77.7	-27.2	0.001	
p*	0.360	0.901			

*p-value for group effect. †p-value for time effect. ‡Effects reported include differences between the two groups in the degree of change in UrNGAL (repeated measurements ANOVA). CABG – coronary artery bypass graft surgery.

Discussion

Renal function is an important determinant of early outcomes and quality of life after CABG. Even the superiority studies that compared on-pump versus off-pump bypass surgery initially focused on kidney sub-studies.[26] Although renal function may be reversible biochemically, the development of renal injury worsens long-term outcomes after CABG in patients with normal preoperative renal function, according to the risk, injury, failure, loss, end-stage renal disease (RIFLE) criteria.[27] These previous studies all focused on enhancing the maximal yield in CABG and avoiding preventable side effects such as renal injury.[26-27]

However, this is only possible using predictive markers that reveal damage in early periods with high sensitivity and specificity. NGAL has become a popular biomarker for detecting renal injury. It is a member of the functionally diverse lipocalin family, which generally binds to small, hydrophobic ligands.[28-30]

A recent review suggested the use of NGAL as a biomarker for the prediction of AKI after cardiac surgery; it also highlighted limitations, such as the lack of adherence of published studies to diagnostic study guidelines, heterogeneity in AKI definition, the lack of uniformly applicable cut-off values, and variability in the performance of commercially available NGAL assays.[31]

NGAL was originally identified as a 25kDa protein, covalently bound to matrix metalloproteinase-9 (MMP-9) from neutrophils,[32-33] and normally expressed in human neutrophils and in other cell types, such as epithelial cells, renal tubular cells and hepatic cells, during inflammation or injury.[33-34] Interestingly, it is also induced in a number of human cancers and is often a marker of poor prognosis. In the post ischaemic kidney, NGAL is upregulated in several nephron segments and accumulates predominantly in proximal tubules, where it co-localises with proliferating epithelial cells.[13] In addition, it has been identified as a regulator of epithelial morphogenesis in cultured kidney tubule cells.[35] During nephrogenesis, it serves as an iron transporting protein, a function that is crucial for cell growth and development.[36] These findings indicate that NGAL might be expressed by damaged tubules to induce re-epithelialisation and consequently might be important for renal regeneration after ischaemic injury.

According to our study, UrNGAL levels were reduced 3 hours after CABG surgical procedures. In the on-pump group, they decreased significantly, while in the off-pump group only a tendency towards a significant reduction was observed. In contrast, a significant increase in serum creatinine and a significant decrease in eGFR values were observed after on-pump CPB. Off-pump coronary artery bypass has no significant influence on postoperative serum creatinine levels and eGFR. Interestingly, Lipcsey et al[25] found that, although plasma-NGAL was higher postoperatively in on-pump patients ($p<0.001$), there were no differences in UrNGAL; this suggests that plasma-NGAL acts as a neutrophil activation biomarker and UrNGAL as a tubular injury marker, and that on-pump patients had greater neutrophil activation.[25]

We believe that the decrease in UrNGAL levels is firstly related to the systematic hydration applied to our patients, as part of the preparation protocol, by administration of fluids and electrolytes. This obviously resulted in an increased intravascular volume status favouring renal function. Secondly, the systematic use of inotropes in the preparation regimen probably contributed to the improvement in the glomerular filtration. Thus, the boosted cardiac output, in combination with the increase of the total circulating blood volume, might be the reason for this significant upgrading of kidney perfusion. Moreover, prolonged postoperative high vasopressor requirements and haemodynamic instability are not common among

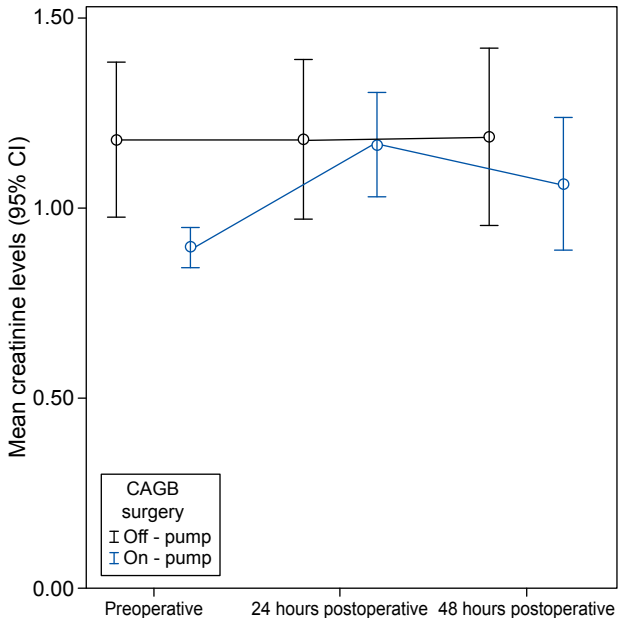

Figure 1. Mean serum creatinine levels preoperatively and 24 hours and 48 hours postoperatively for the on-pump and off-pump CABG groups. CABG – coronary artery bypass graft surgery.

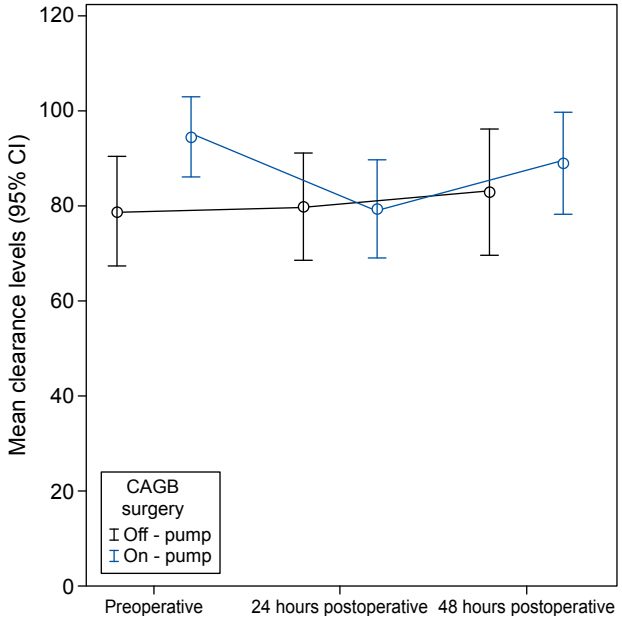

Figure 2. Mean clearance (estimated GFR) levels preoperatively and 24 hours and 48 hours postoperatively for the on-pump and off-pump CABG groups. CABG – coronary artery bypass graft surgery.

these patients, so UrNGAL declines rapidly, reaching levels lower than the preoperative ones. The type of operative technique, on-pump versus off-pump, did not influence the UrNGAL levels, which were similar pre- and post-operatively in both cases.

Mishra et al[37] studied NGAL levels in 71 children undergoing cardiopulmonary bypass and reported that urine and serum NGAL concentrations have higher sensitivity and specificity for early detection of acute renal injury after CABG. Bennett et al[38] found an elevation of UrNGAL within 2-6 hours after CPB in children. Both studies referred to paediatric patients who were undergoing general cardiac surgery, and there were no confounding variables or comorbid conditions.

Wagener et al[39] found that patients demonstrated an increase in UrNGAL levels after cardiac surgery, which preceded AKI. Again, this study referred to patients undergoing general cardiac surgical procedures. When the measurements of UrNGAL levels were limited to patients undergoing CABG surgery, the results were different. In accordance with our study, Wagener et al[40] showed that UrNGAL decreased within 3 hours after cardiac surgery and that it was not different in patients undergoing off-pump and on-pump CABG.

Fadel et al[41] also suggested that plasma NGAL levels may be helpful for the detection of early renal injury following CABG. Shaw et al[42] studied the economic impact and cost effectiveness of urine NGAL determination after CABG and indicated that NGAL appears to be cost-effective in the early diagnosis of acute renal damage after CABG.

Demitras et al[20] showed that postoperative NGAL levels were significantly different after only 6 hours ($p=0.045$). Furthermore, there were no significant differences between the groups according to basal and postoperative 24-hour and 72-hour values of NGAL ($p>0.05$).[20] Additionally, the NGAL level was not correlated with serum creatinine levels[20] and the elevated NGAL levels were present at low serum creatinine levels. The authors concluded that NGAL is not a stable predictive biomarker for acute renal injury after cardiac bypass surgery.[20] Similar results were shown in a recent study that investigated the role of NGAL as a predictive biomarker for AKI after transcatheter aortic valve implantation.[43]

As far as novel biomarkers for the evaluation of renal function after cardiac surgery are concerned, the role of cystatin C (Cys C) should be highlighted. Cys C as a marker of renal failure has been shown to be of prognostic value; however, a wide range has been reported for its predictive accuracy. Kiessling et al[44] recently showed that an early (24-hour) postoperative serum Cys C increase appears to be a moderate biomarker in the prediction of AKI, whereas a preoperative and intraoperative Cys C increase has on-

ly limited diagnostic and predictive value. The combined use of NGAL and Cys C in urine and plasma as early predictors of AKI after cardiac surgery is not well-studied in the literature. Gohnemy and Amro[45] recently showed that plasma NGAL and plasma Cys C may be considered as early predictors of AKI (at 3 and 6 hours postoperatively) after cardiac bypass operations. They allow the diagnosis of AKI up to 24 hours prior to a clinical diagnosis based on conventional definitions of AKI. High-risk patients may potentially have benefits from early therapies that can be started before irreversible injury occurs.[44]

Conclusions

Many studies collectively support the use of NGAL as a biomarker for the prediction of AKI after cardiac surgery. However, there are some limitations, including a lack of published studies that adhere to diagnostic study guidelines, heterogeneity in AKI definition, the lack of uniformly applicable cut-off values and variability in the performance of commercially available NGAL assays.

Our study has several strengths. Firstly, it is based on a homogeneous patient sample, which was studied prospectively using a unified preparation and operation protocol, in the same centre and by the same surgeon group, which is a difficult target to achieve. Additionally, the method used for the measurement of UrNGAL (ARCHITECT i 2000 SR analyzer-Abbott Diagnostics Division) is characterised by higher accuracy when compared to previously used methods (Western blotting, Elisa).

However, this study also has limitations, including the relatively small number of patients, and the limited number of postoperative UrNGAL measurements. Another potential weak point is the fact that patients were not assigned randomly to each surgical technique, but were selected according to the decision of the surgical team.

All in all, UrNGAL measurements show no superiority of either of the two CABG operative techniques concerning their influence on postoperative renal function. Large randomised clinical trials should be designed to help demonstrate the superiority of one technique or the other with adequate statistical power.

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