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European Journal of Cardio-thoracic Surgery 37 (2010) 106—111

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Risk factors for deterioration of renal function after coronary artery bypass grafting

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Received 16 April 2009; received in revised form 23 June 2009; accepted 29 June 2009; Available online 20 August 2009

Abstract

Objective: Various definitions of impairment of renal function after coronary artery bypass grafting (CABG) are used in the literature. Depending on the definition, several risk factors are identified. We analysed our data to determine the risk factors for postoperative deterioration of the creatinine clearance of 10% or more. **Methods:** All patients undergoing isolated coronary surgery in a single centre between January 1998 and December 2007 are included. Clinical data, including demographics and renal risk factors, were prospectively collected in our database. The most recent preoperative serum creatinine level and the maximum serum creatinine level within the first week postoperatively were used to calculate the creatinine clearance. A deterioration of 10% or more was considered to be an endpoint for this study. **Results:** In 10 098 out of a total of 10 626 patients, the preoperative as well as the postoperative creatinine clearance could be calculated. In 1053 patients, the deterioration of the creatinine clearance was 10% or more. We could identify the following risk factors: advanced age, diabetes, chronic obstructive pulmonary disease, peripheral vascular disease, emergency operation, previous cardiac surgery, low preoperative haemoglobin level, high preoperative C-reactive protein level, perioperative myocardial infarction, re-exploration and the number of blood transfusions. **Conclusions:** Risk factors for the deterioration of renal function after revascularisation have been confirmed in this study. In addition, we found peripheral vascular disease, previous cardiac surgery, low preoperative haemoglobin, increased preoperative C-reactive protein level, perioperative myocardial infarction and the number of blood transfusions to be risk factors that have not been described earlier.

Keywords: Coronary artery bypass grafting; CABG; Database; Renal function

1. Introduction

Several risk factors for impairment of renal function after coronary artery bypass grafting (CABG) have been identified, of which female sex, age, diabetes mellitus, hypertension, preoperative creatinine clearance (CrCl) <50 ml min^{-1}, impaired left ventricular function, need for intra-aortic balloon pump (IABP) and re-exploration are most often mentioned [1—4]. Several studies state that deterioration of renal function occurs more often after conventional coronary artery bypass operation with the use of extracorporeal circulation (ECC) than after off-pump coronary artery bypass (OPCAB) [5—9] although others could not confirm this statement [3,4,10]. In addition, the use of aprotinin during CABG has been identified as another important risk factor for impairment of renal function [11,12]. Others could not support this finding [13,14]. Various definitions of impairment of renal function after CABG are used in the literature. Some authors use postoperative serum creatinine levels [5,6,10], some with a cut-off value of 1.5 mg dl^{-1} as an endpoint [6], while others use CrCl as a postoperative marker for renal function, with a cut-off point of 50 ml min^{-1} as an endpoint [4]. Sometimes, the postoperative CrCl is compared with the preoperative value to indicate change in renal function [4,15]. The Cockroft—Gault formula for CrCl [16] and the modification of diet in renal disease (MDRD) formula for estimated glomerular filtration rate (eGFR) [17] have been used to determine renal function. Recently, the deterioration of renal function has been described as a predictor of poor long-term survival [18]. We analysed our data to determine risk factors for the deterioration of CrCl after CABG, adding

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1010-7940/$ — see front matter
doi:10.1016/j.ejcts.2009.06.048

some variables which, to our knowledge, have not yet been described as such.

2. Materials and methods

2.1. Patients

In this retrospective study, we analysed the data of all patients undergoing isolated CABG with or without the use of ECC in a single centre (Catharina Hospital, Eindhoven, the Netherlands) between January 1998 and December 2007. Clinical data, including demographics and renal risk factors, were prospectively collected in our database. The study was approved by the local Medical Ethics Review Committee.

2.2. Operative techniques

In CABG surgery, all patients received short-acting anaesthetic drugs to facilitate early extubation. Normothermic ECC was performed using non-pulsatile flow. Cold crystalloid cardioplegia (St Thomas' solution) or warm blood cardioplegia was used to induce and maintain cardioplegic cardiac arrest, according to the surgeon's preference. All patients undergoing CABG received a low dose of aprotinin (2 million kallikrein inhibiting units) during ECC, administered to the prime solution. The anaesthetic management in OPCAB surgery was the same as in CABG surgery, but aprotinin was omitted.

2.3. Estimation of renal function

Creatinine clearance (CrCl) was determined using the Cockroft–Gault formula [15], which is different for men: $[(140 - \text{age}) \times \text{weight}/(\text{serum Cr} \times 72)]$ and women: $[(140 - \text{age}) \times \text{weight}/(\text{serum Cr} \times 72)) \times 0.85]$. The most recent preoperative serum creatinine level and the maximum serum creatinine within the first week postoperatively, or, if sooner, before discharge, were used to calculate the CrCl and the percentage change from the preoperative value. Patients with preoperative CrCl below 15 ml min^{-1} and those treated with dialysis were excluded from this study. A deterioration of 10% or more was considered to be an endpoint for this study.

2.4. Statistical analyses

Discrete variables were compared with the chi-square test and are presented as percentages. Continuous variables were compared with the Student's unpaired *t*-test and univariate logistic regression analyses were performed to investigate the impact of biomedical variables on renal function. If significant at $p < 0.05$, the variables were included into the multivariate logistic regression analyses for renal function. A *p*-value <0.05 was used for all tests to indicate statistical significance. Odds ratios (OR) with a confidence interval (CI) of 95% with *p*-values are reported. All statistical analyses were performed using SPPS version 15.0 (SPSS Inc., Chicago, IL, USA).

3. Results

Between January 1998 and December 2007, a total of 10 626 patients underwent isolated CABG surgery with or without ECC. Preoperative CrCl was not calculated in 432 patients due to emergency situation or missing records of patient's weight. Postoperative CrCl was not calculated in 277 patients due to mortality before renal function could be determined. Complete data were obtained in 10 098 patients. Mean preoperative CrCl was 74.5 ± 24.4 ml min^{-1} (range: 7–308) (Fig. 1) and the mean postoperative CrCl was 79.2 ± 28.4 (Fig. 2). Distribution of changes in CrCl is shown in Fig. 3. Eighty patients required some form of renal replacement therapy (continuous haemofiltration or dialysis). Deterioration of the CrCl of 10% or more was found in 1053 patients.

Patients' preoperative and perioperative demographic and clinical characteristics stratified by the degree of deterioration of CrCl are presented in Table 1.

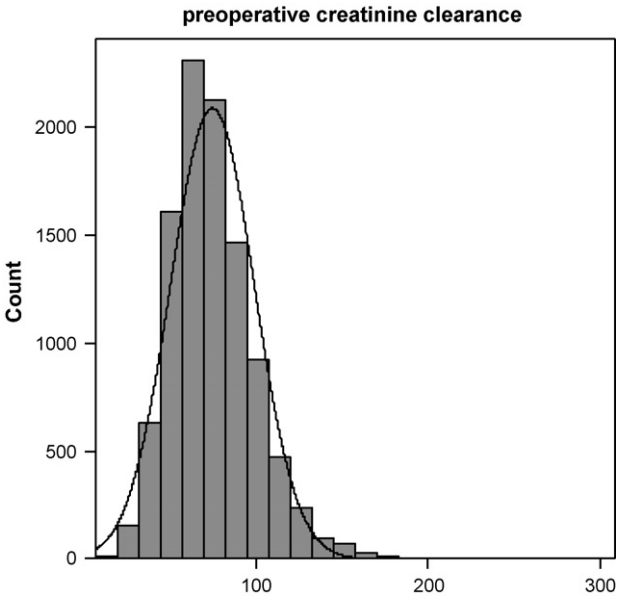

Fig. 1. Distribution of preoperative creatinine clearance (ml min^{-1}).

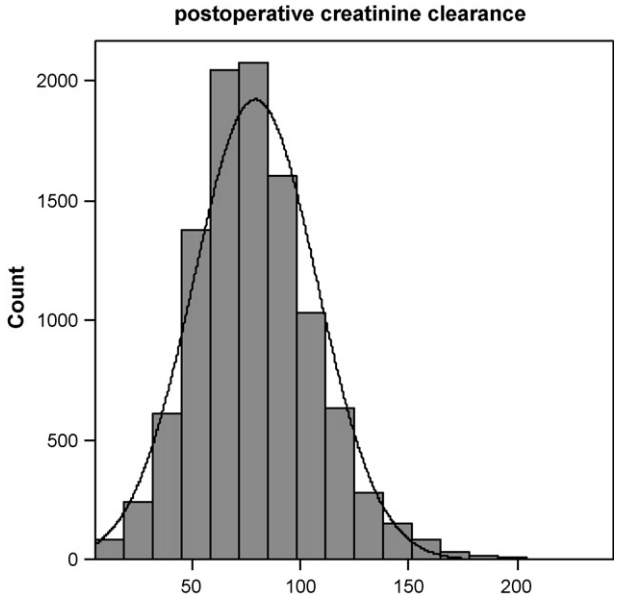

Fig. 2. Distribution of postoperative creatinine clearance (ml min^{-1}).

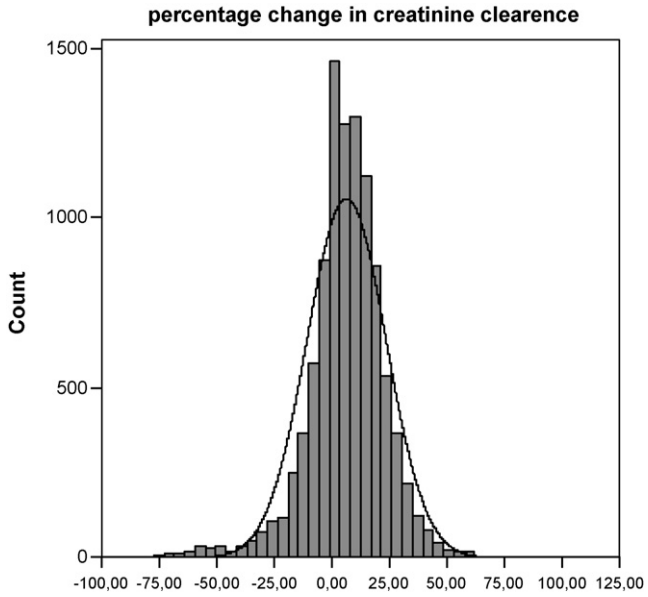

Fig. 3. Percentage change in creatinine clearance.

Table 1
Demographic characteristics stratified by deterioration of creatinine clearance.

	Deterioration of creatinine clearance		*p*-value
	<10%, *n* = 9045	≥10%, *n* = 1053	
Male gender	6998 (77.4)	799 (75.9)	0.146
Age	64.2 ± 9.5	67.8 ± 9.4)	<0.0001
Diabetes	1839 (20.3)	288 (27.4)	<0.0001
BMI >35 kg m^{-2}	192 (2.1)	44 (4.3)	<0.0001
BMI <20 kg m^{-2}	44 (0.5)	5 (0.5)	0.599
COPD	1088 (12.0)	172 (16.3)	<0.0001
Hypertension	3711 (41.0)	494 (46.9)	<0.0001
PVD	1004 (11.1)	151 (14.3)	0.001
CCS class	2.6 ± 1.2	2.5 ± 1.3	0.397
EF <35%	265 (3.0)	71 (7.2)	<0.0001
Emergency	227 (2.5)	139 (13.2)	<0.0001
Number of preop MI	0.48 ± 0.60	0.53 ± 0.63	0.005
Redo	468 (5.2)	134 (12.7)	<0.0001
Preop Hb (g dl^{-1})	13.9 ± 1.3	13.3 ± 1.6	<0.0001
Preop CRP (mg l^{-1})	10.4 ± 15.9	16.4 ± 28.9	<0.0001
Preop CrCl (ml min^{-1})	75.1 ± 23.9	69.6 ± 27.9	<0.0001
OPCAB	825 (9.1)	70 (6.6)	0.004
Crystalloid cardioplegia	3772 (41.7)	455 (43.2)	0.346
Blood cardioplegia	4090 (45.2)	478 (45.4)	0.346
ECC-time	57.0 ± 33.2	63.7 ± 38.9	<0.0001
Number of grafts	3.4 ± 1.1	3.4 ± 1.2	0.894
IABP	111 (1.2)	91 (8.6)	<0.0001
Periop MI	196 (2.2)	90 (8.5)	<0.0001
Re-exploration	374 (4.1)	162 (15.4)	<0.0001
Number of RBC units	0.75 ± 2.3	3.25 ± 6.2	<0.0001

Results in numbers (percentage) of mean ± standard deviation.
BMI: body mass index; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; CCS class: Canadian Cardiovascular Society Functional Classification of Angina; EF: left ventricular ejection fraction; preop MI: preoperative myocardial infarction; Redo: previous cardiac surgery; preop Hb: preoperative hemoglobin level; preop CRP: preoperative C-reactive protein level; preop CrCl: preoperative creatinine clearance; OPCAB: off-pump coronary artery bypass grafting; ECC-time: duration of extra-corporeal circulation; IABP: intra-aortic balloon pump support; periop MI: perioperative myocardial infarction; RBC: red blood cell.

Patients with a deterioration of CrCl of more than 10% were older, more often had diabetes, a body mass index (BMI) of more than 35 kg m^{-2}, chronic obstructive pulmonary disease (COPD), hypertension, peripheral vascular disease (PVD), a left ventricular ejection fraction (EF) of less than 35%, an emergency operation, previous cardiac surgery and more preoperative myocardial infarctions. The preoperative haemoglobin (Hb) level as well as the preoperative CrCl was lower whereas the preoperative C-reactive protein (CRP) level was higher. Off-pump CABG was performed less often, whereas the duration of ECC was longer. Complications such as the need for intra-aortic balloon pump support, perioperative infarction and re-exploration for any cause were more frequent. The number of red blood cell (RBC) units transfused was higher.

3.1. Univariate analyses

Results of univariate logistic regression analyses to identify risk factors for deterioration in CrCl of 10% or more are shown in Table 2.

Preoperative significant risk factors were: advanced age, diabetes, BMI >35 kg m^{-2}, COPD, hypertension, PVD, number of preoperative myocardial infarctions, EF <35%, emergency operation, previous cardiac surgery, lower preoperative Hb

Table 2
Univariate logistic regression analysis for deterioration of creatinine clearance of more than 10%.

Risk factor	Odds ratio (95% CI)	*p*-value
Preoperative risk factors		
Male gender	0.92 (0.79–1.06)	0.275
Age*	1.044 (1.036–1.051)	<0.0001
Diabetes	1.47 (1.27–1.70)	<0.0001
BMI >35 kg m^{-2}	2.02 (1.44–2.82)	<0.0001
BMI <20 kg m^{-2}	0.98 (0.38–2.47)	0.965
COPD	1.42 (1.19–1.70)	<0.0001
Hypertension	1.27 (1.11–1.41)	<0.0001
PVD	1.34 (1.11–1.61)	0.002
CCS class*	0.978 (0.929–1.030)	0.397
Number of preop MI*	1.157 (1.046–1.280)	0.005
EF <35%	2.48 (1.89–3.26)	<0.0001
Emergency	5.90 (4.73–7.37)	<0.0001
Redo	2.67 (2.18–3.27)	<0.0001
Preop Hb (g dl^{-1})*	0.753 (0.719–0.788)	<0.0001
Preop CRP (mg l^{-1})*	1.013 (1.009–1.016)	<0.0001
Preop CrCl (ml min^{-1})*	0.990 (0.987–0.993)	<0.0001
Peri- and postoperative risk factors		
OPCAB	0.71 (0.55–0.91)	0.008
Crystalloid cardioplegia	1.03 (0.90–1.18)	0.648
ECC-time*	1.005 (1.003–1.007)	<0.0001
Number of grafts*	0.996 (0.941–1.054)	0.894
IABP	7.61 (5.72–10.12)	<0.0001
Periop MI	4.21 (3.25–5.46)	<0.0001
Re-exploration	4.21 (3.46–5.13)	<0.0001
No of blood transfusions*	1.196 (1.173–1.220)	<0.0001

CI: confidence interval; BMI: body mass index; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; CCS class: Canadian Cardiovascular Society Functional Classification of Angina; preop MI: preoperative myocardial infarction; EF: ejection fraction; Redo: previous cardiac surgery; preop Hb: preoperative hemoglobin level; preop CRP: preoperative C-reactive protein level; preop CrCl: preoperative creatinine clearance; OPCAB: off-pump coronary artery bypass; ECC: extra-corporeal circulation; IABP: intra-aortic balloon pump; periop MI: perioperative myocardial infarction.
* Entered as a continuous variable.

Table 3
Multivariate analysis of preoperative risk factors.

Preoperative risk factors	Odds ratio (95% CI)	*p*-value
Age*	1.044 (1.029–1.060)	<0.0001
Diabetes	1.59 (1.28–1.98)	<0.0001
BMI >35 kg m^{-2}	1.62 (0.94–2.79)	0.079
COPD	1.28 (0.99–2.79)	0.056
Hypertension	1.19 (0.97–1.45)	0.083
PVD	1.33 (1.03–1.74)	0.029
Number of preop MI*	1.159 (0.991–1.356)	0.065
EF <35%	1.53 (0.96–2.45)	0.070
Emergency	4.57 (2.44–8.57)	<0.0001
Redo	2.51 (1.76–3.58)	<0.0001
Preop Hb (g dl^{-1})*	0.858 (0.799–0.921)	<0.0001
Preop CRP (mg l^{-1})*	1.007 (1.003–1.012)	0.001
Preop CrCl (ml min^{-1})*	0.999 (0.993–1.004)	<0.0001

CI: confidence interval BMI: body mass index; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; EF: left ventricular ejection fraction; Redo: previous cardiac surgery; preop Hb: preoperative hemoglobin level; preop CRP: preoperative C-reactive protein level; preop CrCl: preoperative creatinine clearance.
* Entered as a continuous variable.

level, higher CRP and lower preoperative CrCl. On the other hand, sex, BMI of <20 kg m^{-2} and functional angina class (CCS) were not identified as risk factors. Significant peri- and postoperative risk factors were CABG versus OPCAB, duration of ECC, the need for IABP, perioperative myocardial infarction, re-exploration for any cause as well as the number of perioperative RBC unit transfusions. The type of cardioplegia and the number of grafts were not identified as risk factors.

Table 4
Multivariate logistic regression analyses including peri- and postoperative risk factors.

	Odds ratio (95% CI)	*p*-value
Preoperative risk factors		
Age*	1.048 (1.032–1.065)	<0.0001
Diabetes	1.70 (1.36–2.13)	<0.0001
BMI >35 kg m^{-2}	1.60 (0.92–2.79)	0.095
COPD	1.36 (1.04–1.78)	0.024
Hypertension	1.22 (0.99–1.50)	0.059
PVD	1.35 (1.03–1.78)	0.028
Number of preop MI*	1.162 (0.989–1.366)	0.067
EF <35%	1.53 (0.94–2.51)	0.086
Emergency	2.19 (1.061–4.53)	0.034
Redo	2.05 (1.39–3.02)	<0.0001
Preop Hb (g dl^{-1})*	0.887 (0.824–0.954)	0.001
Preop CRP (mg l^{-1})*	1.008 (1.003–1.012)	0.001
Preop CrCl (ml min^{-1})*	1.002 (0.996–1.008)	0.499
Peri- and postoperative risk factors		
OPCAB	1.04 (0.70–1.57)	0.817
ECC-time*	1.000 (0.997–1.003)	0.879
IABP	1.77 (0.88–3.57)	0.105
Periop MI	2.83 (1.82–4.39)	<0.0001
Re-exploration	2.49 (1.69–3.65)	<0.0001
No of RBC units*	1.152 (1.107–1.199)	<0.0001

BMI: body mass index; CI: confidence interval; COPD: chronic obstructive pulmonary disease; ECC-time: duration of extra-corporeal circulation; EF: ejection fraction; IABP: intra-aortic balloon pump support; OPCAB: off-pump coronary artery bypass grafting; PVD: peripheral vascular disease; preop MI: preoperative myocardial infarction; Redo: previous cardiac surgery; preop Hb: preoperative haemoglobin level; preop CRP: preoperative C-reactive protein level; preop CrCl: preoperative creatinine clearance; periop MI: perioperative myocardial infarction; RBC: red blood cells.
* Entered as a continuous variable.

3.2. Multivariate analyses

All statistically significant preoperative risk factors identified with univariate regression analyses were entered into a multivariate logistic regression analysis. Results of these analyses are shown in Table 3.

Independent preoperative risk factors were advanced age, diabetes, PVD, emergency operation, previous cardiac surgery, lower Hb level, higher CRP level and lower preoperative CrCl. Peri- and postoperative risk factors were added to the multivariate model when identified to be significant using the univariate logistic regression analyses. The following factors were identified as independent risk factors (Table 4): advanced age, diabetes, COPD, PVD, emergency operations, previous cardiac surgery, lower preoperative Hb level, higher preoperative CRP level, perioperative myocardial infarction, re-exploration for any cause and the number of RBC unit transfusions.

4. Discussion

In this retrospective single-centre study of more than 10 000 patients, we found several independent risk factors for the deterioration of renal function after CABG. Some of them are in agreement with the previously reported findings whereas others are not. This might be explained by the different definitions of deterioration of renal function.

4.1. Definition of the study endpoint

The need for dialysis [14,20], a postoperative creatinine level of >2.1 mg dl^{-1} [19] or a postoperative CrCl less than 50 ml min^{-1} [4] are examples of study endpoints commonly used. However, in patients with preoperative impaired renal function, only a small extra damage is needed to reach the study endpoint. Patients with preoperative normal renal function may experience severe damage of the kidneys before they reach the study endpoint. Consequently, in all of these studies, the preoperative renal function, whether defined by the creatinine level or CrCl, has been identified as a risk factor for reaching the study endpoint. In studying renal impact factors, changes in renal function not reaching the previously described endpoints might be important as well.

Creatinine clearance (CrCl) calculated by the Cockroft–Gault formula has been described as a better indicator for renal function than serum creatinine level in patients undergoing CABG [21]. Therefore, we defined renal impairment as a 10% or more deterioration of the preoperative CrCl. Thus, we were able to describe risk factors for minor changes in renal function. Even minor deterioration of renal function in patients with already impaired renal function might lead to clinical problems [18]. The clinical significance of the 10% deterioration in renal function is possibly only obvious in patients with preoperative renal impairment. Furthermore, it seems reasonable to assume that the same risk factors may also play a role in more pronounced deterioration of renal function.

4.2. Risk factors

In agreement with others, we found several independent preoperative risk factors: age used as a continuous variable [4,15,19,20], diabetes [15,20], COPD [20], emergency operations [20] and re-exploration for any cause [4]. Other independent risk factors, which, to our knowledge, have not been described, were PVD, previous cardiac surgery, the preoperative Hb and CRP levels, perioperative myocardial infarction and the number of blood transfusions. Risk factors described by others that could not be confirmed in this study were EF [6,15], preoperative CrCl [4,6,15,19], preoperative angina class [19], BMI <20 kg m^{-2} [4], the need for IABP [4], duration of ECC [19], the number of grafts [6] and female sex [4]. In contrast with other investigators [5–8], OPCAB was not superior to CABG in preserving renal function in our study. This is in agreement with the findings of others [3,4,10]. The use of aprotinin could have even exaggerated the negative effect of ECC on postoperative renal function [11]. As stated earlier, discrepancies in identified risk factors might at least partly be explained by different definitions of renal dysfunction. Already impaired renal function is mentioned in most studies [4,6,15,19] as a risk factor for developing renal insufficiency after cardiac surgery. This seems logical when renal insufficiency is defined as the need for dialysis or a CrCl of less than 50 ml min^{-1}. In our study, using a 10% or more deterioration of the preoperative CrCl as an endpoint, we could not identify the preoperative CrCl as an independent risk factor. We also noticed an improvement in the mean value of CrCl in comparison with the preoperative value. Only 10.4% of the whole patient population had postoperative deterioration of CrCl. In the rest of the patients, CrCl either deteriorated with $<10\%$ or even improved postoperatively. This can possibly explained by haemodilution that is usually observed in the perioperative period [9]. Some of the risk factors that were identified in this study, for example, diabetes and peripheral vascular disease, cannot be corrected preoperatively. These risk factors can be used for risk stratification and informing the patients. Others, such as preoperative Hb and CRP level and the number of blood transfusions, can be corrected. Further studies are needed to investigate whether measures to correct preoperative Hb and CRP level and avoidance of blood transfusions will lead to better preservation of renal function.

5. Conclusions

In this retrospective single-centre study of more than 10 000 patients, we could identify the following risk factors for a deterioration of 10% or more of the preoperative CrCl: advanced age, diabetes, COPD, peripheral vascular disease, emergency operation, previous cardiac surgery, low preoperative Hb, high preoperative CRP, perioperative myocardial infarction, re-exploration and the number of blood transfusions.

5.1. Limitations of the study

This study had a retrospective design. Some patients were lost to follow up and some data were unobtainable, making results less accurate. The use of intra-operative and postoperative medications that can affect the renal function such as diuretics and inotropic support was not registered.

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