ANALYSIS OF RENAL FUNCTION AFTER ON AND OFF PUMP CORONARY ARTERY BYPASS GRAFTING

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Cardiopulmonary bypass (CPB) is often associated with renal dysfunction, as measured by plasma creatinine levels and hemodialysis rates.

Aim. To compare creatinine clearance (CrCl), estimated with the Cockroft and Gault formula, between patients undergoing off-pump coronary artery bypass grafting (OPCAB) versus on-pump CABG (on-CAB).

Material and methods. Between April 2008 and April 2009, 119 patients underwent coronary bypass graft surgery. Fifty-eight (58) of these patients underwent OPCAB while 61 had on-CAB. Creatinine clearance, plasma creatinine levels, and clinical outcome were compared between the groups. A creatinine clearance value of 50 mL/minute was accepted as the lowest limit of normal renal function.

Results. There were two hospital deaths caused by sepses after pulmonary infection. Creatinine clearance (Preoperative OPCAB 73,64±33,72 x on-CAB 75,70±34,30mL/min; discharge OPCAB 75,73±35,07 x on-CAB 79,07±34,71 mL/min; p=0,609), and creatinine levels (Preoperative OPCAB 1,04±0,38 x on-CAB 1,13±0,53 mg/dL; discharge OPCAB 1,12±0,79 x on-CAB 1,04±0,29mg/dL; p=0,407) did not show statistically inter-group differences.

Conclusion. Deterioration in renal function is associated with higher rates of postoperative complications. No significant difference in CrCl could be demonstrated between the groups.

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Key words: coronary artery bypass, kidney, off-pump coronary artery bypass, bypass surgery, coronary artery.

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АНАЛИЗ ФУНКЦИИ ПОЧЕК ПОСЛЕ ON-PUMP И OFF-PUMP АОРТОКОРОНАРНОГО ШУНТИРОВАНИЯ

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Кардиопульмонарное шунтирование (CPB) часто ассоциируется с дисфункцией почек, как следует из анализа уровней креатинина в плазме и уровней гемодиализа.

Цель. Сравнить клиренс креатинина (CrCl), рассчитанного по формуле Кокрофта-Голта, у пациентов, перенесших off-pump коронарное шунтирование (OPCAB) и on-pump коронарное шунтирование (on-CAB).

Материал и методы. В период с апреля 2008 г. по апрель 2009 г., 119 пациентов, были подвергнуты коронарному шунтированию. Пятьдесят восемь (58) из этих пациентов прошли OPCAB, в то время как 61 — (on-CAB). Клиренс креатинина, уровень креатинина плазмы, и клинические результаты сравнивались между группами. Значение клиренса креатинина 50 мл/мин было принято в качестве минимального предела нормальной функции почек.

Результаты. Были два смертельных случая в больнице, вызванных сепсисом после легочной инфекции. Клиренс креатинина (предоперационная OPCAB 73,64±33,72 x on-CAB 75,70±34,30мл/мин; постоперационная величина OPCAB 75,73±35,07 x on-CAB 79,07±34,71 мл/мин; p=0,609) и уровни креатинина (предоперационная OPCAB 1,04±0,38 x on-CAB 1,13±0,53 мг/дл; постоперационное значение OPCAB 1,12±0,79 x on-CAB 1,04±0,29mg/дл; p=0,407) не имеют статистических различий между группами.

Заключение. Ухудшение функции почек ассоциируется с более высокой частотой послеоперационных осложнений. Существенной разницы в значениях уровня креатинина, не может быть продемонстрировано между группами.

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Ключевые слова: аорто-коронарное шунтирование, почки, off-pump аорто-коронарное шунтирование, хирургия, коронарная артерия.

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Introduction

Among cardiovascular surgeries, coronary artery bypass surgery, also coronary artery bypass graft (CABG) surgery, and colloquially heart bypass or bypass surgery is a surgical procedure performed to relieve angina and reduce the risk of death from coronary artery disease [1–4]. Deterioration of renal function after heart surgery is associated with increased morbidity and mortality. Its incidence may vary from 8% to 30% of cardiopulmonary bypass (CPB) operations and is associated with a mortality rate between 7% and 38% [5, 6]. Previous studies with patients undergoing CPB showed significant increases in plasma levels of creatinine, with consequent acute renal failure and need for hemodialysis [7, 8].

Plasma creatinine values may not represent a specific marker of renal dysfunction, since it can be affected by muscle mass and sex. Moreover, we can see significant reductions in glomerular filtration rates with normal plasma creatinine levels [9,10]. Creatinine clearance (CrCl) can be estimated by the formula developed by Cockroft and Gault; its value is more associated with renal dysfunction and morbidity and postoperative mortality [11,12].

In 2007, Sajja LR et al. published a study comparing coronary artery bypass grafting (CABG) with and without CPB in patients with renal failure not on dialysis preoperatively and demonstrated a favorable effect on renal function in the off-pump operation, with more benefits pronounced in patients with diabetes mellitus (DM), hypertension (HBP), and those with greater impairment of ventricular function [13]. Other studies have compared CABG with and without CPB in order to demonstrate the deleterious effect of CPB on renal function; however, many did not use CrCl as a marker of renal dysfunction [14,16]. The increase in severity of cases referred for CABG makes surgery without CPB a useful tool to decrease morbidity and operative mortality.

The objective of this study is to test the effect of CPB on renal function in patients undergoing coronary artery bypass grafting (CABG), with and without cardiopulmonary bypass, through creatinine clearance calculated by the Cockcroft and Gault formula.

Material and methods

Between April 2007 and April 2009, 119 patients with heart failure and indication for CABG were divided into two groups (off-pump and on-pump groups, which were randomly selected). The randomization was based on a random number generator. The measurement parameters needed to calculate the CrCl preoperatively and at discharge were done. The study protocol was approved by the institutional Ethics and Research Committee and the patients agreed to participate by signing an informed consent.

Exclusion criteria were: chronic renal failure requiring dialysis, left ventricular ejection fraction (LVEF) below 30%, associated cardiac surgery beside CABG, minimally invasive operation, and urgent or emergency operation.

Clinical and demographic pre-operative characteristics are shown in Table 1.

Anesthesia and surgical technique

The operation began with hemodynamic monitoring, with measurement of mean arterial pressure, central venous pressure and urine output, and respiratory monitoring with pulse oximetry.

Anesthetic induction was performed with midazolam (100–200μg/kg), fentanyl (150–200mg), and pancuronium (50–100 mg/kg), and maintained with propofol (5–10 mg/kg/hour). The operation was carried out as usual, the means of access being by median sternotomy with cannulation of the aorta and inferior vena cava through the right atrium after systemic heparinization (300UI/Kg), obtaining an activated clotting time (ACT) above 480s, with mild hypothermia to 34 °C. In patients operated without CPB, systemic heparinization was done (150UI/Kg) with ACT above 250s and use of mechanical suction stabilizer during construction of anastomoses.

The method of myocardial protection used was controlled hypoxia with intermittent aortic clamping, which was done to perform the anastomoses between the coronary arteries and bypass grafts that would likely be chosen (left internal mammary artery or saphenous vein).

At the end of surgery, the patients in normothermia were taken to the postoperative unit, where they were continuously monitored.

Patient follow-up was done by a single member of the surgical team, who followed a protocol for pre- and post-operative comparison.

Calculation of creatinine clearance

The creatinine plasma levels were routinely obtained in all patients in the preoperative period and before hospital discharge. These values were used to estimate CrCl by the Cockroft and Gault formula, with correction for sex and weight of the patient. The Cockroft and Gault equation is expressed as follows: male- [140 — age (years)] x weight (kg) /72 x serum creatinine, and female-140 — age (years)] x weight (kg) /72 x 0.85 x serum creatinine. The age is in years, weight in kilograms and plasma creatine in micomoles per milliliter. The value of 50ml/min CrCl was accepted as the lower limit of normal renal function.

Statistical analysis

In order to verify the minimal number of patients investigated to provide statistical or no statistical significance, we applied the power analysis that provided a minimal number of 100 subjects. The choice of measures of central tendency and dispersion of the values that make up the samples and the statistical tests for comparison between them were based on the type of distribution, defined as parametric by the Kolmogorov-Smirnov test, according to the statistical program SPSS® version 13.0 (SPSS ® Inc, Illinois, USA). The values obtained for the study of each continuous variable were organized and expressed as means and standard deviations. For the categorized variables, absolute and relative frequencies were used. To compare the means of two sample populations, we used the Student "t" test and, between the paired means, we used the paired t-test. To verify the existence of correlation between two continuous variables, we used the Pearson correlation test.

Results

There were two deaths due to lung infection followed by sepsis. The groups were homogeneous in the comparison between the clinical and demographic pre-operative characteristics. The mean CPB time was 49,90±17,98 minutes and anoxia was 49,83±18,45 minutes. Deterioration in renal function was associated with higher rates of postoperative complications.

The CrCl (preoperative OPCAB 73,64±33,72 x on-CAB 75,70±34,30mL/min; discharge OPCAB 75,73±35,07 x on-CAB 79,07±34,71 mL/min; p=0,609) and creatinine plasma levels (preoperative OPCAB 1,04±0,38 x on-CAB 1,13±0,53 mg/dL; discharge OPCAB 1,12±0,79 x on-CAB

Table 1

Demographic and clinical characteristics of patients

Variables	Group W/OUT CPB (n=58)	Group W/CPB (n=61)	p
Gender			0,408
Male	55,2%	75,4%	
Female	44,8%	24,6%	
Age	66,9± 9,10	60,9± 9,5	0,102
HTN	96,6%	93,4%	0,438
COPD	6,9%	11,5%	0,389
DM	53,4%	47,5%	0,519
DLP	48,3%	39,3%	0,326
Smoking	41,4%	65,6%	0,080
Obesity	22,4%	32,8%	0,206
Non-dialytic CRF	13,8%	23,0%	0,198
Previous AMI	62,1%	59,0%	0,733
Uni/biarterial lesion	66,6%	33,4%	0,318
Triarterial lesion	47,6%	52,4%	0,415
LVEF>45%	56,4%	64,7%	0,424
45< LVEF >35	28,2%	23,5%	0,614
LVEF <35%	15,4%	11,8%	0,617

Abbreviations: CPB – cardio pulmonary bypass, HTN – hypertension, COPD – chronic obstructive pulmonary disease, DM – diabetes mellitus, CRF – chronic renal failure, AMI – acute myocardial infarction, LVEF – left ventricular ejection fraction.

Table 2

Creatinine clearance and plasma creatinine levels

Variables	Group W/OUT CPB (n=58)	Group W/CPB (n=61)	p
Cr/Cl (ml/min)			
Preoperative	73,64±33,73	75,70±34,0	0,746
Discharge	75,74±35,07	79,07±34,1	0,609
Plasma creatinine (mg/dL)			
Preoperative	1,04±0,39	1,13±0,54	0,258
Discharge	1,12±0,80	1,04±0,29	0,447

Abbreviations: CPB – cardio pulmonary bypass, CrCl – creatinine clearance.

1,04±0,29mg/dL; p=0,407) showed no statistically significant difference between the two groups during both observation periods (pre-operative and discharge) (Table 2).

Discussion

This investigation was undertaken to evaluate creatinine clearance (CrCl), estimated with the Cockroft and Gault formula, between patients undergoing off-pump coronary artery bypass grafting (OPCAB) versus on-pump CABG (on-CAB). As a main result, we suggest that CABG with CPB did not produce changes in renal function, which was estimated by calculation of CrCl in comparison with the procedure done without CPB.

Renal disorders are recognized as an independent risk factor for increased cardiovascular morbidity and mortality in subjects with heart failure [17, 18]. Previous evidences also suggest that subjects with damaged kidney function are at increased risk for heart failure development [19, 20].

The evaluation of renal function solely by plasma creatinine has limitations, because this parameter may vary according to age, sex, muscle mass, metabolism, and hypertension [21]. The CrCl is a useful alternative for measurement of the glomerular filtration rate and its direct measurement is not available in clinical practice, so the adoption of formulas for estimating these values is an acceptable solution [22]. Among these formulas, the Cockcroft-Gault equation uses the available clinical data and can be related to heart disease [11, 23]. Renal function remains an important factor that can contribute to hospital mortality rates following open heart surgery, since in more serious situations, which may require dialysis, morbidity and mortality increase significantly regardless of the intensive support offered to patients in this severe clinical condition [24]. Chertow et al. demonstrated a mortality rate of 63% in 30 days in patients who required dialysis, versus 4,3% in the absence of renal dysfunction [25]. Most of the factors responsible for deterioration of renal function postoperatively are inherent to the patient and difficult to control; probably the only preventable factor is whether or not CPB are used.

Despite the continued interest in off-pump CABG techniques, their benefits regarding the degree of renal dysfunction remains controversial. Studies show reduced risk of renal failure, especially in high risk patients, although other studies failed to demonstrate this favorable effect [13, 26, 27]. Shroff GR et al., analyzing the results of hemodialysis patients undergoing CABG, found a modest increase in survival for patients operated without CPB; this increase is more pronounced in the early periods and tends to decrease over the years [28, 29].

In this study, we evaluated the possible deleterious effects of CPB on the renal function of patients undergoing CABG by the estimated CrCl instead of measuring plasma creatinine levels, as previously published studies have shown a higher relationship of CrCl with renal dysfunction (especially in patients with normal serum creatinine) [5, 12]. Our initial hypothesis was that patients operated upon without CPB would have a lower degree of renal dysfunction, as assessed by CrCl. However, our results showed no significant difference when comparing the groups and the same trend ocurred with plasma levels of creatinine. This finding is in agreement with other previously published works; this suggests the need for other markers to determine the impact of CPB on renal function, since the CrCl may be normal despite the presence of renal dysfunction, especially when the change in plasma creatinine is mild or moderate [5, 9, 18, 30].

In 2009, Felicio et al. proposed the estimation of the glomerular filtration rate by measurement of serum cystatin C instead of estimated CrCl; major changes of this marker were found post-surgically when CPB was compared with the values of plasma creatinine and estimated CrCl [31].

Against to our data, a previous study [32] reported that acute renal injury after CABG was related to increased long-term risk of heart failure onset. The authors also found that acute renal injury was an independent predictor of hospitalization for heart failure, even after adjustment for confounders that are usually involved in heart failure. We believe that the use of CABG with CPB was able to attenuate a possible acute renal injury. On the other hand, Nezami and coworkers [33] reported that renal function evaluated with CrCl and Cr after CABG was not significantly distinct between subjects undergoing off-pump and on-pump methods. The alterations in renal function after the both procedures were not associated with the levels of high-sensitivity nor C-reactive protein tumor necrosis factor-α.

Our study presents some limitations that are worth to be addressed. For instance, the potential of a type II statistical error in a negative study with relatively small number of patients. We investigated only heart failure patients; there were no other cardiovascular disorder, since that was not the purpose of our study.

Our surgeon team considered the strategy to proceed with off-pump CABG procedure only when the hemodynamic situation was unstable. All of the procedures were performed in our group is through a median sternotomy approach and under general anesthesia. Previous studies indicated that surgeon experience plays a role and emphasized the importance of surgeon volume in establishing favorable outcomes for off-pump CABG [34, 35]. Based on our experience, we observe a significant surgeon volume–result connection for mortality after off-pump CABG, indicating that high volume of procedures presents better mortality outcomes, we believe that this is due to the experience of the surgeon.

This study investigated the relationship between cardiac surgery procedures and the kidney in the context of CABG with CPB. This is a clinically relevant issue due to the great number of patients that undergo CABG with CPB and due to the high incidence of acute renal function as a perioperative complication. Our study collaborates to the comprehension of cardiac and renal interaction by indicating that acute injury to the renal activity may be induced by cardiac surgery.

Conclusion

We suggest that CABG with CPB did not produce changes in renal function estimated by calculation of CrCl in comparison with the procedure done without CPB.

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