ORIGINAL ARTICLE

Rev Bras Cir Cardiovasc 2013;28(3):391-400

Unstable angina does not increase mortality in coronary artery bypass graft surgery

Angina instável não aumenta mortalidade em cirurgia de revascularização miocárdica

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DOI: 10.5935/1678-9741.20130060

RBCCV 44205-1486

Abstract

Introduction: **Coronary artery bypass graft is often the treatment of choice for patients who suffer from unstable angina. We do not know whether this condition adds morbidity in this scenario.**

Objective: **To compare the outcomes of patients undergoing coronary artery bypass graft with unstable angina framework with patients who underwent coronary artery bypass graft showed no unstable angina.**

Methods: **Retrospective cohort study. Unstable angina was defined as acute coronary syndrome without ST elevation and without enzymatic alteration and/or class IV angina.**

Results: **Between February 1996 and July 2010, to 2,818 isolated coronary artery bypass graft performed, 1,016 (36.1%) patients had unstable angina. Multivariate analysis showed that patients with preoperative unstable angina used more medications such as acetylsalicylic acid, beta-blocker, heparin (anticoagulation), nitrate and less need for diuretics than patients without unstable angina. Patients with unstable angina used increased monitoring with Swan-Ganz and support with intra-aortic balloon than stable patients. On outcomes, required longer hospitalization (P=0.030) and had a lower death rate (P=0.018) in the post-coronary artery bypass graft alone.**

Conclusion: **Submit patients to coronary artery bypass graft in the presence of acute coronary syndrome such as unstable angina did not increase the mortality rate.**

Descriptors: **Angina, unstable. Myocardial revascularization. Mortality.**

Resumo

Introdução: **A cirurgia de revascularização do miocárdio muitas vezes é o tratamento de escolha de pacientes que sofrem angina instável. Não sabemos se essa condição acresce morbimortalidade nesse cenário.**

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Article received on June 25th, 2012
Article accepted on August 26th, 2012

Abbreviations, acronyms & symbols	
ASA	Acetylsalicylic acid
UA	Unstable Angina
BB	Beta-Blocker
preop IAB	Preoperative Intra-aortic balloon
CPB	Cardiopulmonary bypass
FC	functional class
DM	Diabetes mellitus
CKD	Chronic kidney disease
LVEF	Left ventricular ejection fraction
SAH	Hypertension
CI	confidence interval
ACE	inhibitor angiotensin converting enzyme
SL LCT	Severe lesion of the left coronary trunk
P	Statistical Significance
OR	Odds Ratio
ACSST	Acute coronary syndrome without ST elevation

Objetivo: **Comparar os desfechos dos pacientes submetidos a cirurgia de revascularização do miocárdio com quadro de angina instável com os pacientes submetidos a cirurgia de revascularização do miocárdio que não apresentaram angina instável.**

Métodos: **Coorte retrospectiva. A angina instável foi definida como síndrome coronariana aguda sem supradesnivelamento de ST e sem alteração enzimática e/ou angina classe IV.**

Resultados: **No período entre fevereiro de 1996 a julho de 2010, de 2.818 a cirurgia de revascularização do miocárdio isoladas realizadas, 1.016 (36,1%) pacientes apresentaram angina instável. A análise multivariada demonstrou que os pacientes com angina instável no pré-operatório utilizaram mais medicações como ácido acetilsalicílico, betabloqueador, heparina (anticoagulação plena), nitrato e menor necessidade de diureticoterapia, do que pacientes sem angina instável. Pacientes com angina instável utilizaram maior monitorização com Swan-Ganz e suporte com balão intra-aórtico do que os pacientes estáveis. Sobre os desfechos, necessitaram de maior tempo de internação (*P*=0,030) e apresentaram menor taxa de óbito (*P*=0,018) no pós-operatório de cirurgia de revascularização do miocárdio isolada.**

Conclusão: **Submeter pacientes a cirurgia de revascularização do miocárdio isolada na vigência de síndrome coronariana aguda como angina instável não elevou a taxa de mortalidade.**

Descritores: **Angina instável. Revascularização miocárdica. Mortalidade.**

INTRODUCTION

Unstable angina (UA) is a leading cause of hospital admission, and their occurrence is correlated with increased mortality in both the short- and the long-term [1]. Recent studies have shown that treatment with angioplasty or coronary artery bypass graft (CABG) have less favorable outcomes in the treatment of patients with unstable angina (UA) compared with those with stable angina. Advances in the treatment of coronary artery and the techniques tend to decrease the difference [2,3].

Treatment of UA can vary from conventional strategy to an early invasive strategy and may be indicated both surgical and percutaneous revascularization [4]. Myocardial revascularization can control the persistent ischemia and progression to acute myocardial infarction, in addition to providing symptomatic relief as well as prevent ischemic complications [5].

There are different ways to define UA. According Braunwald, UA is angina pectoris (ischemic or equivalent) with at least one of three clinical characteristics: 1) occurs at rest (or with minimal effort), usually lasting longer than twenty minutes (if not interrupted by the nitroglycerin), 2) is described as an intense and frank pain and recent onset (less than 1 month), 3) occurs in a crescendo pattern (e.g., more intense, prolonged or frequent than previously), in the absence signs of myocardial necrosis (elevation of cardiac enzymes). On the ohter hand, the European System Risk in Cardiac Operations (EuroSCORE) defines UA as anginal pain at rest that requires treatment with intravenous nitroglycerin to the surgical procedure. For purposes of this study UA was defined as acute coronary syndrome without ST elevation (ACSST) and without enzyme and/or class IV angina [6,7].

According to current recommendations on UA, taking into account the patient's risk, CABG is indicated in cases of severe injury of the left main coronary artery, three-vessel disease with impaired left ventricular function (left ventricular ejection fraction < 0.5); two-vessel lesion with involvement of the proximal left anterior descending artery or decreased left ventricular function or provoked ischemia. Life expectancy, associated diseases, symptom severity and amount of viable myocardium at risk are also important factors [5,8,9].

It is not well defined which the real impact of UA on the prognosis of patients undergoing CABG in this context, or whether there is an optimal time interval between the acute event and revascularization. The aim of this study is to assess the characteristics of patients presenting UA and indication of CABG and compare with patients without UA in the preoperative of CABG as well as compare the in-hospital outcomes of these patients in this context.

METHODS

Population and sample

In the period from February 1996 to July 2010 2,818 isolated CABG were performed at Hospital São Lucas. Of these, 1,016 patients (36.1 %) showed UA preoperatively. UA was defined as acute coronary syndrome without ST elevation (ACSST) and without enzyme and/ or class IV angina.

Study design

Observational historical cohort study. Data were prospectively collected and entered into the database of the postoperative unit of cardiac surgery at the Hospital São Lucas at PUCRS.

Inclusion Criteria

Patients aged over 18 years led to cardiac surgery for coronary artery bypass graft (CABG) alone.

Exclusion Criteria

We excluded from the analysis valvular surgery alone or combined with CABG, urgent or emergency CABG, acute myocardial infarction with very recent (≤ 30 days) ST elevation preoperatively, acute myocardial infarction without very recent surgery (≤ 30 days) ST segment elevation in the preoperative.

Study variables

The variables included in the analysis were:

- Presence of UA in preoperative of CABG, making comparative analysis with CABG without UA preoperatively.
- Age calculated based on the average age and also divided into groups for analysis: less than 60 and greater than or equal to 60 years.
- Gender (male/female).
- Ejection fraction (LVEF) calculated by echocardiography, values divided for analysis in less than 40% and greater than or equal to 40%.
- Chronic kidney disease (CKD) - diagnosed by serum creatinine> 1.5 mg/dl.
- Diabetes Mellitus (DM).
- High blood pressure (HBP).
- Acute Myocardial Infarction (AMI) defined as acute coronary syndrome occurred in 30 to 90 days after surgery.
- Analysis of surgical risk by EuroSCORE.
- The need for intra-aortic balloon preoperatively (preop IAB).
- Presence of severe injury of the left main coronary artery (SL LCT) - considered as obstructive lesion greater than 50%.
- Previous use of drug: acetylsalicylic acid (ASA), beta blockers (BB), antiarrhythmics (amiodarone and propafenone), digoxin, corticosteroids, calcium channel antagonists, diuretics, statins, Heparin, angiotensin-converting enzyme inhibitors (ACEI), nitrates, oral hypoglycemic agents, insulin.
- Need for vasopressor and invasive monitoring with Swan-Ganz.
- Time of cardiopulmonary bypass (CPB), all CABG used CPB.
- Complete revascularization, considered when all vessels with a caliber greater than 1.5 mm and lesions with obstruction ≥ 50 % were revascularized.
- Use of revascularization (all used internal thoracic artery graft).
- AMI postoperatively.
- Stroke (CVA) postoperatively.
- Atrial fibrillation (AF) postoperatively.
- Acute renal failure (ARF) in the postoperative period, considered with a 50% increase in serum creatinine.
- Increased bleeding after surgery, it is considered excessive bleeding 200 ml/hr to 3 ml/h/kg during the first two hours postoperatively, or persisting around 100 ml/h or 1.5 ml/h/kg from the third hour.
- Need for multiple blood transfusions, need for transfusion to treat increased bleeding that triggers significant anemia (hemoglobin <8.0 mg/dl) or hemodynamic changes.
- Need for reintervention.
- Length of hospital stay.
- In-hospital mortality postoperatively.

Outcome

We assessed death rates, need for vasopressor support with intra-aortic balloon and length of stay in the postoperative of CABG.

Procedures

The anesthesia techniques of cardiopulmonary bypass (CPB) and cardioplegic solution (St. Thomas No. 2) were performed according to the standardization of the Hospital São Lucas, as previously described [10]. After surgery, all patients were transferred to the ICU postoperatively in cardiac surgery, under mechanical ventilation.

Statistical Analysis

The data were plotted on a spreadsheet Microsoft Access® and assessed in SPSS version 11.0. Descriptive statistics were performed, as well as the univariate tests: Chi

- square test for ordinal variables and quantitative data was used for analysis of variance or Student's t test (for unpaired variables) followed by *post hoc* test for Bonferroni data. Multivariate analysis was performed by logistic regression (backward conditional method). Statistical differences were considered when *P*<0.05.

Ethical Considerations

The research design of the study was submitted to the Research Ethics Committee of FAMED PUCRS, with protocol number 06003478.

RESULTS

In the period from February 1996 to July 2010 2,818 isolated CABG were performed, all using CPB. Of these, 1,016 patients (36.1%) showed UA preoperatively. The average age of the study population with UA preoperatively was 60.42 ± 10 years, left ventricular ejection fraction with average of 54.05±15%, CPB time of 85.54±34 minutes, average use of mammary graft in 74.1% and average rate of incomplete revascularization of 6.8%. All these characteristics were similar between the groups with UA and without UA in the preoperative of CABG.

Regarding the surgical risk analysis performed by logistic EuroSCORE, the average of surgical risk of patients with UA in preoperative of CABG was 5.19 compared with 3.30 for patients without UA in preoperative *P*=0.012. The mean hospital stay was 10.96±9.74 days, and waiting times for CABG in total was on the average 9.18 days, with longer interval for patients with UA (11.7 days) compared with no UA (7.8 days) (OR 1.30, 95% CI 1.29 to 6.41, *P*=0.003). Postoperative time was similar between groups, in total the average was 10.5 days, in patients with UA 10.99 days and without UA 10.27 days (OR:0.36, 95% CI 0.006 - 1.42, *P*=0.048). The longer length of stay in patients with UA preoperatively (10.96 days versus 10.27 days) was at the expense of longer waiting times for CABG.

The preoperative and postoperative characteristics with univariate analysis are described in Tables 1 and 2, respectively. Table 3 describes the characteristics and clinical outcomes in postoperative of CABG alone in patients with UA preoperatively, with statistical significance.

Univariate analysis showed that females were more prevalent among patients with UA in preoperative of CABG, in addition, these patients used more IAB preoperatively and medications such as aspirin, angiotensin-converting enzyme angiotensin nitrate, heparin and beta-blockers. But the use of diuretics were lower in this group of patients (Table 1).

On the evolution postoperatively, there was no difference in outcomes such as myocardial infarction, stroke or acute renal failure and need for vasopressor among patients with UA preoperatively and those who did not. Even with the highest rate of use of aspirin and heparin in patients with UA in preoperative of CABG, there was no difference between groups in relation to bleeding: 12 % in the group with UA and 10.7 % in the group without UA (OR: 1.14, 95% CI 0.89 to 1.45, *P*=0.29), need for reintervention: 4.1% in the group with UA and 5.3 % in the group without UA (OR: 0.77 95% CI 0.53 to 1.12, *P*=0.17), and need for multiple transfusions tended to be higher in patients with UA (OR: 1.22, 95% CI 1.02 to 1.45, *P*=0.027), not confirmed in the multivariate analysis. The CPB time was similar between the groups with values > 90 minutes in 37.9 % in the group with UA compared to 40.7% without UA (OR: 0.89, 95% CI 0.75 to 1.04; *P*=0.98), use of Swan-Ganz was higher in patients with UA preoperatively (Table 2).

Multivariate analysis showed that patients with UA in the preoperative of CABG were mostly female, used more medications such as aspirin, beta-blockers, heparin (anticoagulation), nitrate and needed less diuretics. More patients received monitoring with Swan-Ganz and support with intra-aortic balloon (Table 3). The overall rate of death in the study population was 5.4%, and the patients with UA had a lower death rate, 4.1% compared to the UA without preoperative rate of 6.1%, data with statistical significance (OR: 0.64, 95% CI 0.443 to 0.925, *P*=0.018), with a protective effect of 36% of deaths in patients with UA in preoperative of CABG. The hospitalization was higher in patients with UA requiring 10.96 days compared to 10.27 days for patients without UA (OR: 1.009, 95% CI 1.001 to 1.018, *P*=0.030), this difference was due to higher waiting time for CABG for patients with UA (Table 3).

Given the long period examined, from 1996 to 2010, and considering the changes in the management of acute coronary syndromes during this period, including UA, as the benefit of beta-blockers, statins, angiotensin-converting enzyme inhibitors and maintenance of acetylsalicylic acid for patients with UA undergoing CABG, we performed an analysis comparing two periods, as shown in Figures 1 and 2. Through this analysis, we conclude that patients with UA treated from 1996 to 2003 received more beta blockers, angiotensin-converting enzyme inhibitors, aspirin, Heparin and nitrate, less use of diuretics, and the death rate (3% versus 5.3%) was significantly lower in this group compared to those without UA, *P*=0.028. On the other hand, patients treated from 2004 to 2010 with UA received more aspirin, statins, Heparin and nitrate, and less use of diuretic, but no difference in the treatment of beta-blockers, angiotensin-converting enzyme inhibitors, showing similar mortality rate (6.4 % versus 7.7%) and higher in comparison with the previous period, perhaps for the greater complexity of patients undergoing CABG with the evolution of time (older, with more comorbidities).

Table 1. Preoperative characteristics of the study population and univariate analysis.

Variable	Total	UA	n UA	OR	CI 95%	*P*
	2794 (100%)	1007 (36,0%)	1787 (64,0%)			
Age						
>60	1482 (53%)	518 (51.4%)	964 (53.9%)	0.90	0.77 – 1.05	0.20
<60	1312 (47%)	489 (48.6%)	823 (46.1%)			
Gender						
Male	1912 (67.9%)	643 (63.3%)	1269(70.5%)	1.38	1.17 – 1.62	<0.01
Female	904 (32.1%)	372 (36.7%)	523 (29.5%)			
LVEF						
≤40%	538 (19.1%)	194 (19.2%)	344 (19.1%)	1.00	0.82 – 1.21	0.98
>40%	2272(80.9%)	818 (80.8%)	1454 (80.9%)			
CKD						
Yes	253 (9.0%)	101 (9.9%)	152 (8.4%)	1.19	0.92 – 1.56	0.18
No	2565 (91.0%)	915 (90.1%)	1650 (91.6%)			
DM						
Yes	866 (30.7%)	308 (30.3%)	558 (30.1%)	0.97	0.82 – 1.47	0.72
No	1952 (69.7%)	708 (69.7%)	1244 (69.0%)			
SAH						
Yes	2090 (74.2%)	754 (74.2%)	1336 (74.1%)	1.00	0.82 – 1.19	0.96
No	728 (25.8%)	262 (25.8%)	466 (25.9%)			
Recent AMI						
Yes	150 (5.3%)	59 (5.8%)	91 (5.0%)	1.16	0.83 – 1.62	0.39
No	2668 (94.7%)	957 (94.2%)	1711 (95.0%)			
FC						
1 and 2	321 (11.4%)	113 (11.1%)	208(11.5%)	0.95	0.75 – 1.22	0.73
3 and 4	2497(88.6%)	903(88.9%)	1594(88.5%)			
SL of LCT LCT						
Yes	649 (23.0%)	243 (23.9%)	406 (22.5%)	1.08	0.90 – 1.29	0.40
No	2169 (77.0%)	773 (76.1%)	1396 (77.5%)			
Preop IAB						
Yes	213 (7.6%)	97 (9.5%)	116 (6.4%)	1.53	1.16 – 2.03	0.003
No	2605 (92.4%)	919 (90.5%)	1686 (93.6%)			
AAS						
Yes	674 (23.9%)	303 (29.8%)	371 (20.6%)	1.63	1.37 – 1.95	<0.01
No	2144 (76.1%)	713 (70.2%)	1431 (79.4%)			
Statin						
Yes	1555 (55.2%)	543 (53.4%)	1012 (56.2%)	0.89	0.77 – 1.05	0.16
No	1263 (44.8%)	473 (46.6%)	790 (43.8%)			
ACE						
Yes	1521 (54.0%)	523 (51.5%)	998 (55.4%)	0.85	0.73 – 0.99	0.046
No	1297 (46.0%)	493 (48.5%)	804 (44.6%)			
Nitrate						
Yes	1847 (65.5%)	747 (73.5%)	1100 (61.0%)	1.77	1.49 – 2.09	<0.01
No	971 (34.5%)	269 (26.5%)	702 (39.0%)			
Diuretic						
Yes	655 (23.2%)	180 (17.7%)	475 (26.4%)	0.62	0.49 – 0.73	<0.01
No	2163 (76.8%)	836 (82.3%)	1327 (73.6%)			
Heparin						
Yes	932 (33.1%)	449 (44.2%)	483 (26.8%)	2.16	1.84 – 2.54	<0.01
No	1886 (66.9%)	567 (55.8%)	1319 (73.2%)			
BB						
Yes	1972 (70.0%)	749 (73.7%)	1223 (67.9%)	1.33	1.12 – 1.58	0.001
No	846 (30.0%)	267 (26.3%)	579 (32.1%)			

UA: unstable angina, OR: odds ratio , CI: confidence interval, P: statistical significance, LVEF: left ventricular ejection, CKD: chronic kidney disease, DM : diabetes mellitus, Hypertension: hypertension, CF: functional class, preop IABP: preoperative intra-aortic balloon, SI of LCT: severe injury of the left coronary trunk, ASA: acetylsalicylic acid, ACE: angiotensin converting enzyme angiotensin BB: beta- blocker

Table 2. Postoperative evolution of the study population: univariate analysis.

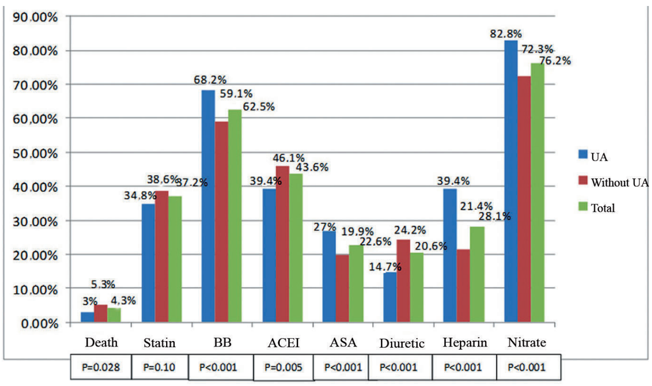
Variable	Total	UA	n UA	OR	CI 95%	*P*
	2794 (100%)	1007 (36.0%)	1787 (64.0%)			
AMI						
Yes	412 (14.6%)	158 (15.6%)	254 (14.1%)	1.12	0.90 – 1.39	0.29
No	2406 (85.4%)	858 (84.4%)	1548 (85.9%)			
Stroke						
Yes	82 (2.9%)	29 (2.9%)	53(2.9%)	0.97	0.61 – 1.53	0.89
No	2736 (97.1%)	987 (97.1%)	1749 (97.1%)			
AF						
Yes	572 (20.3%)	196 (19.3%)	376 (20.9%)	0.90	0.75 – 1.09	0.31
No	2246 (79.7%)	820 (80.7%)	1426 (79.1%)			
ARF						
Yes	203 (7.2%)	71 (7.0%)	132 (7.3%)	0.95	0.70 – 1.28	0.74
No	2615 (92.8%)	945 (93.0%)	1670 (92.7%)			
Vasopressor						
Yes	670 (23.8%)	245 (24.1%)	425 (23.6%)	1.03	0.86 – 1.23	0.75
No	2148 (76.2%)	771 (75.9%)	1377 (76.4%)			
CPB						
>90 min	1078 (39.7%)	373 (37.9%)	705 (40.7%)	0.89	0.75 – 1.04	0.98
≤90 min	1636 (60.3%)	610 (62.1%)	1026 (59.3%)			
Bleeding						
Yes	315 (11.2%)	122 (12%)	193 (10.7%)	1.13	0.89 – 1.44	0.29
No	2503(88.8%)	894 (88%)	1609 (89.3%)			
Reinterven.						
Yes	137 (4.4%)	42 (4.1%)	95 (5.3%)	0.77	0.53 – 1.12	0.17
No	2681(95.1%)	974 (95.9%)	1707 (94.7%)			
Tranfusions						
Yes	698 (24.8%)	276 (27.2%)	422 (23.4%)	0.02	1.02 – 1.45	1.22
No	2120 (75.2%)	740 (72.8%)	1380 (76.6%)			
Swan-Ganz						
Yes	47 (1.7%)	24 (2.4%)	23 (1.3%)	1.87	1.05 – 3.33	0.03
No	2771 (98.3%)	992 (97.6%)	1779 (98.7%)			
Death						
Yes	152 (5.4%)	42 (4.1%)	110 (6.1%)	0.66	0.46 – 0.95	0.026
No	2666 (94.6%)	974 (95.9%)	1692(93.9%)			

UA: unstable angina, OR: odds ratio, CI: confidence interval, P: statistical significance, AMI: acute myocardial infarction, Stroke, AF: atrial fibrillation, ARF: acute renal failure, CPB: cardiopulmonary bypass, min.: minutes

Table 3. Multivariate analysis of preoperative factors and associated outcomes in patients with unstable angina during preoperative period of isolated CABG.

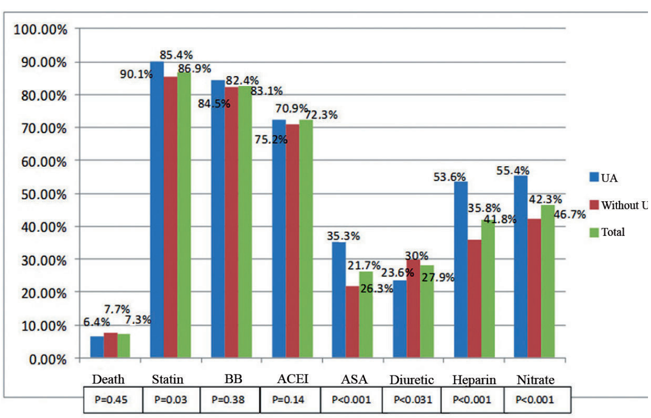
VARIABLE	OR	CI 95%	*P*
Female	1.41	1.19 – 1.67	<0.001
AAS	1.62	1.35 – 1.95	<0.001
BB	1.19	0.99 – 1.43	0.055
Diuretic	0.57	0.47 – 0.70	<0.001
Full Heparin	2.01	1.69 – 2.38	<0.001
Nitrate	1.63	1.37 – 1.94	<0.001
Swan-Ganz	1.93	1.03 – 3.61	0.039
Preop IAB	1.52	1.12 – 2.07	0.007
Length of hospital stay	1.01	1.01 – 1.02	0.030
Death	0.64	0.44 – 0.93	0.018

OR: odds ratio, CI: confidence interval, P: statistical significance ASA: acetylsalicylic acid, BB: beta-blocker, IABP: preop intra-aortic balloon



P: statistical significance

Fig. 1 - Rates of death, use of statins, beta-blockers (BB), angiotensin converting enzyme inhibitors (ACEI), acetylsalicylic acid (ASA), diuretic, Heparin (heparin) and nitrate in patients with unstable angina (UA) and without preoperative surgical myocardial revascularization. Analysis of the period between 1996 - 2003, total of 1799 patients



P: statistical significance

Fig. 2 - Rates of death, use of statins, beta-blockers (BB), angiotensin converting enzyme inhibitors (ACEI), acetylsalicylic acid (ASA), diuretic, Heparin (heparin) and nitrate in patients with unstable angina (UA) and without preoperative surgical myocardial revascularization. Analysis of the period 2004 - 2010, total of 1019 patients

DISCUSSION

The risk scores that estimate the risk of operative mortality and morbidity of heart surgery in adults based on demographic and clinical variables, such as the European System Risk in Cardiac Operations (EuroSCORE) and the Society of Thoracic Surgeons (STS), consider the UA as additional risk to patients undergoing CABG, deserving score in their scores, but when alone does not alter the risk, so when presenting this feature as an isolated risk factor it remains as low risk. On the other hand, score developed at the Hospital São Lucas/PUCRS found no increased risk of operative mortality and in-hospital postoperative of CABG in patients with signs of UA, not receiving score [11].

The use of Swan-Ganz catheter was significantly higher in patients with UA in preoperative of CABG. Most invasive monitoring was not associated with higher rates of cardiogenic shock, postoperative infarction or sepsis, since the use of diuretics was significantly lower in this group of patients (OR 0.57), possibly due to the use of this tool. The increased use of Swan-Ganz could be related as a marker of severity for this group of patients. Nevertheless, obtaining specific hemodynamic parameters, contributed to lower outcomes postoperatively.

Monitoring of fluid replacement is a fundamental aspect to be avoided complications caused by overload or lack of volume in the intravascular space. The use of invasive hemodynamic monitoring in the postoperative period of cardiac surgery in patients with hemodynamic instability is useful in guiding the control of plasma volume, use of vasoactive drugs, requiring circulatory assistance. Another fact to be noted is that there is no reliable correlation between central venous pressure (CVP) and pulmonary capillary pressure (PCP), and the control of blood volume according to CVP is not safe [12]. However, studies show that these values are somewhat inaccurate with respecti to assessment of blood volume, especially in patients on mechanical ventilation due to changes in systolic volume induced by preload also which depend on contractility and afterload, which are not assessed by these parameters.

Other methods such as echocardiography and transesophageal Doppler with measurements of aortic flow and end-diastolic volume are interesting options with drawback of relying on experienced operator and can not be used continuously for a long period of time. Another sensitive indicator of response to blood volume in mechanically ventilated patients is the change in systolic blood pressure and its ddown, with good correlation with negative deflection and fluid infusion and concomitant improvement in cardiac output and increase in atrial filling pressures [13].

The need for intra-aortic balloon was also significantly higher in the group with UA, which may represent the most severity of these when compared to the group without acute event in the preoperative of CABG alone. The indication of intra-aortic balloon in our service is limited to low ejection fraction (< 30 %), cardiogenic shock, severe injury to the left main coronary (> 50 %) and intractable angina, the latter being the main reason for using this study. Even needing this support preoperatively, death rates were lower.

The benefits of intra-aortic balloon were studied by Santarpino et al. [14], which assessed the use of intra-aortic balloon in the preoperative period of CABG of high risk (EuroSCORE>12) and found similar outcomes to low risk CABG (EuroSOCORE<5) without the device, with low rates of associated complications, advocating a more liberal use of intra-aortic balloon, especially in high-risk CABG. Macruz et al. [15] retrospectively assessed the early (intraoperative) and late (postoperative) use of intra-aortic balloon. 130 patients were studied at Texas Heart Institute. Data from this study suggest that the intra-aortic balloon is effective as a method of circulatory support in patients with low cardiac output after cardiopulmonary bypass, with a tendency to better results when used early; it was observed influence of age and CPB time, suggesting that more efficient methods of circulatory support should be used in elderly patients and in patients with low cardiac output syndrome after cardiac surgery with CPB times greater than 120 minutes.

Females had an odds ratio of 1.4 for UA in the preoperative of CABG. It is believed that the behavior of coronary heart disease is different between genders. Campbell et al. [16] compared the histological structure of the myocardium and coronary microvasculature of men and women and found differences in the arterioles wall and the ratio of the cardiac myocyte and body surface area that can justify the presence of ischemic symptoms in more frequent in females, although not always correlating with more severe coronary artery disease than in males. Hasdai et al. [17] assessed the outcome of 10,000 patients after ACS in relation to gender and observed in this record that females had older age, no association with increased mortality, lower use of antiplatelet agents (such as glycoprotein IIbIIIa) and less use of less beta blockers, antiplatelet and statin, and more diuretics and digoxin at discharge [17]. Although studies suggest female as a risk indicator for CABG and being part of the scores [18], others did not confirm this risk in the context of ACS [19-21], as well as the present study.

The length of stay was longer in patients with UA in preopearative of CABG, at the expense of longer wait times for CABG, and not due to prolonged ventilation, need for vasopressors, sepsis and delirium. There are no clear recommendations on which the ideal timeout for conducting CABG after UA. The advantages of early CABG for the treatment of UA include limiting the area of ischemia and left ventricular remodeling, however, it can lead to reperfusion injury and further damage to the myocardium, thereby increasing the systemic inflammatory response [22].

The optimal time interval between the ACS and CABG is still controversial. The PL-ACS registry included 2028 patients with acute coronary syndrome (ACS), in which 55% had UA and indication for CABG, 60% underwent surgery at different time intervals. They concluded that after 12 months of waiting for CABG the risk of death rises in twice and CABG performed during the first month after ACS is associated with increased prevalence of mortality, considering the ideal interval to wait between 1-3 months [22]. This result is different compared to the found in this study, in which the average waiting time was 11.7 days; unrelated to increased mortality, probably due to not including patients with acute transmural myocardial infarction.

Weiss et al. [23], in a study with analysis of records of more than 40,000 patients with ACS, including transmural infarction, observed that patients undergoing CABG in 2 days of hospitalization had higher mortality rates than those who were taken to surgery with waiting time of three or more days of hospitalization in non-emergency cases, suggesting that the optimal time interval between CABG after ACS should be greater than or equal to 3 days. Costa et al. [24] found similar conclusion after comparing outcomes between two groups of patients waiting for less than 30 days and more than 30 days undergoing CABG: overall mortality was 5.9 % (1 death in 15 patients in Group I and 1 death in 19 patients in group II - P=1.0); they argue that CABG can be performed safely, especially after the first 72 hours of the ischemic event.

The UA in preoperative of CABG alone, different from the expected, showed a lower rate of in-hospital mortality in this study, compared with the group without UA, even with higher surgical risk by assessing the logistic EuroSCORE in this group (5.19 compared with 3.30 of the patients without preoperative UA P=0.012). Possibly by the fact that this sample of patients with signs of UA has received optimized medical treatment, compared with the group with no UA, such as greater use of acetylsalicylic acid, beta-blockers, full-dose heparin and nitrate (OR 1.62; 1.19, 2.01, 1.63 , respectively) compared with those who did not have the acute event. But the use of diuretics was significantly lower in this group of patients (OR 0.57). This fact reveals the great importance in medical management for all groups.

The average mortality rate was 5.4 %. Mortality in patients with preoperative UA undergoing isolated CABG was 4.1 %, versus 6.1% in the group without acute event in this study. The death rate is similar to that presented by other authors as Kaul et al. [18] (5.9%), Hochman et al. [25] (4.3%), Howard et al. [26] (4.3%) and Jatene et al. [21] (4.1%), in the context of ACS. However, when we compared the mean death for periods, we observe that there is a significant difference when assessing the period 1996-2003 (4.3%) and 2004-2010 (7.3%) P=0.001, despite advances in treatment and management of ischemic patients undergoing CABG, with greater use of statins, beta-blockers, angiotensin-converting enzyme inhibitors and acetylsalicylic acid, which can be explained by the increased complexity of patients undergoing CABG, with more comorbidities, age and more complex pathologies.

When assessing patients with UA undergoing isolated CABG in the period 1996-2003, we found that this group of patients showed a lower mortality rate compared to those without UA and that there was no significant difference in death rate between the patients with and without UA in the period 2004-2010. In this period, the optimal medical treatment did not appear to reduce mortality, perhaps because both groups of this period present more uniform clinical treatment and management, particularly regarding the use of beta-blockers and angiotensin converting enzyme angiotensin.

Limitations

Although the data collection was performed prospectively, the data analysis was performed retrospectively, and data were not collected for the specific purpose of this analysis. Thus, some important issues were not raised as a risk assessment according to the scores of acute coronary syndrome as TIMI score or GRACE, which would enable a more detailed assessment regarding the severity of patients preoperatively. Another limitation is the monitoring of the patient, performed until hospital discharge of which we have no data on outcomes after this time.

CONCLUSION

The present study showed that patients with UA undergoing isolated CABG showed no increased mortality. Rather, possibly because they have received better medical treatment, and invasive monitoring and hemodynamic support more frequently, patients with UA had lower death rates than those considered stable.

Authors' roles & responsibilities	
CPS	Main author
JCG	Coauthor
RSC	Coauthor
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MAG	Coauthor
JBP	Coauthor
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