*Rev Bras Cir Cardiovasc 2011;26(3):373-9*

# The use of inhibitors of angiotensin-converting enzyme and its relation to events in the postoperative period of CABG

***O uso de inibidores da enzima conversora de angiotensina e sua relação com eventos no pós-operatório de cirurgia de revascularização miocárdica***

Graciane Radaelli[1], Luiz Carlos Bodanese[2], João Carlos Vieira da Costa Guaragna[3], Anibal Pires Borges[4], Marco Antonio Goldani[5], João Batista Petracco[6], Jacqueline da Costa Escobar Piccoli[7], Luciano Cabral Albuquerque[8]

DOI: 10.5935/1678-9741.20110011

RBCCV 44205-1292

***Abstract***

***Background:*** **Angiotensin-converting enzyme (ACE) inhibitors reduce the chance of death, myocardial infarction (MI) and cerebrovascular accident (CVA) in patients with coronary disease. However there is no consensus as to its indication in patients undergoing coronary artery bypass grafting (CABG).**

***Objective:*** **To assess the relationship between preoperative use of ACE inhibitors and clinical outcomes after CABG.**

***Methods:*** **Retrospective cohort study. We included data from 3,139 consecutive patients undergoing isolated CABG in Brazilian tertiary care hospital between January 1996 and December 2009. Follow-up was until discharge or death. Clinical outcomes after surgery were analyzed between users and nonusers of ACE inhibitors preoperatively.**

***Results:*** **Fifty-two percent (n=1,635) of patients received ACE inhibitors preoperatively. The use of ACE inhibitors was an independent predictor of need for inotropic support (OR 1.24, 95% CI 1.01 to 1.47, *P* = 0.01), acute renal failure (OR 1.23, 95% CI 1.01 to 1.73, *P* = 0.04) and progression to atrial fibrillation (OR 1.32, 95% CI 1.02 to 1.7, *P* = 0.03) postoperatively. The mortality rate among patients receiving or not preoperative ACE inhibitors was similar (10.3% vs. 9.4%, *P* = 0.436), as well as the incidence of myocardial infarction and stroke (15.6% vs. 15.0%, *P* = 0.694 and 3.4% vs. 3.5%, *P* = 0.963, respectively).**

1. Master; Pharmaceuticals.
2. PhD in Cardiology by the Institute of Cardiology of Rio Grande do Sul / Baylor College of Medicine, Houston / Texas, Professor of Postgraduate Medicine and Health Sciences at the Pontificia Universidade Catolica do Rio Grande do Sul (PUCRS), Porto Alegre, Brazil.
3. Doctor of Medicine from the Pontificia Universidade Catolica do Rio Grande do Sul, 2009; Head of Postoperative Cardiac Surgery HSL-PUCRS, Porto Alegre, Brazil.
4. Medical Resident of the Residency Program in Cardiology, Hospital São Lucas da PUCRS, Porto Alegre, Brazil.
5. Specialist in Cardiovascular Surgery, Chief of Cardiovascular Surgery of the HSL-PUCRS, Porto Alegre, Brazil.
6. Master of Cardiovascular Surgery, Chief of Cardiac Surgery of the HSL-PUCRS, Porto Alegre, Brazil.
7. PhD in Cell and Molecular Biology PUCRS, Adjunct Professor, Universidade Federal do Pampa - Campus Uruguaiana, Uruguaiana, RS, Brazil.
8. Doctor of Health Sciences, Federal University of Rio Grande do Sul, 2006, Cardiovascular Surgeon at HSL-PUCRS, Porto Alegre, Brazil.

Work performed at the Pontificia Universidade Catolica do Rio Grande do Sul, Porto Alegre, Brazil.

Correspondence Address:
Graciane Radaelli
Avenida Ipiranga, 6690 - sala 300 – Serviço de Cardiologia
Porto Alegre, Brazil
E-mail: gracianeradaelli@yahoo.com.br

Article received on May 12th, 2011
Article accepted on July 14th, 2011

***Conclusion:*** **The use of preoperative ACE inhibitors was associated with increased need for inotropic support and higher incidence of acute renal failure and postoperative atrial fibrillation, not associated with increased rates of myocardial infarction, stroke or death.**

***Descriptors:*** **Angiotensin-converting enzyme inhibitors. Myocardial revascularization. Coronary disease. Coronary artery bypass.**

***Resumo***

***Fundamento:*** **Os inibidores da enzima conversora de angiotensina (IECA) reduzem o risco de óbito, infarto agudo do miocárdio (IAM) e acidente vascular encefálico (AVE) em portadores de doença coronariana. No entanto, não há consenso quanto à sua indicação em pacientes que serão submetidos à cirurgia de revascularização miocárdica (CRM).**

**Objetivo: Avaliar a relação entre uso pré-operatório de IECA e eventos clínicos após realização da CRM.**

***Métodos:*** **Estudo de coorte retrospectivo. Foram incluídos dados de 3.139 pacientes consecutivos submetidos à CRM isolada em hospital terciário brasileiro, entre janeiro de 1996 e dezembro de 2009. O seguimento dos pacientes foi realizado até a alta hospitalar ou óbito. Desfechos clínicos no pós-operatório foram analisados entre os usuários e os não-usuários de IECA no pré-operatório.**

***Resultados:*** **Cinquenta e dois por cento (1.635) dos pacientes receberam IECA no pré-operatório. O uso de IECA foi preditor independente da necessidade de suporte inotrópico (RC 1,24, IC 1,01-1,47; *P*=0,01), de insuficiência renal aguda (IRA, RC 1,23, IC 1,01-1,73; *P*=0,04) e de evolução para fibrilação atrial (FA, RC 1,32, IC 1,02-1,7; *P*=0,03) no pós-operatório. A mortalidade entre os pacientes que receberam ou não IECA no pré-operatório foi semelhante (10,3 vs. 9,4%, *P*=0,436), bem como a incidência de IAM e AVE (15,6 vs. 15,0%, P=0,694 e 3,4 vs. 3,5%, *P*=0,963, respectivamente).**

***Conclusão:*** **O uso pré-operatório de IECA foi associado a maior necessidade de suporte inotrópico e maior incidência de IRA e FA no pós-operatório, não estando associado ao aumento das taxas de IAM, AVE ou óbito.**

***Descritores:*** **Inibidores da enzima conversora da angiotensina. Revascularização miocárdica. Doença das coronárias. Ponte de artéria coronária.**

## INTRODUCTION

Inhibitors of angiotensin-converting enzyme (ACE) inhibitors have been shown to be beneficial in preventing death, myocardial infarction (AMI) and stroke (CVA) in patients with coronary artery disease (CAD). They additional effects of ACE inhibitors are the control of high blood pressure (HBP) and the reduction of morbidity and mortality in heart failure also, being a mainstay in the treatment of this disease [1-3]. In addition, they play an important role in minimizing the occurrence of ischemic events after coronary artery bypass grafting (CABG) [4].

The ACE inhibitors should be given early to all patients with ventricular dysfunction or myocardial infarction, for the advantages of these drugs in relation to cardiac remodeling and the hemodynamics improvement (vasodilatation and afterload reduction). The decrease in mortality was observed either in clinical studies that selected patients with AMI and concomitant ventricular dysfunction (studies SAVE, AIRE and TRACE) as in studies that did not select a specific group, using ACE inhibitors in all patients with AMI for up to 1-4 years after the event (studies ISIS 4 and GISSI 3). Prolonged use of ACE inhibitors also resulted in cardiovascular benefits (HOPE study) [5]. In addition to lowering blood pressure, ACE inhibitors act as anti-ischemic, through their protective effects of the vascular bed (antiatherosclerotic, antithrombotic and anti-inflammatory) [6,7].

There is growing evidence that ACE inhibitors should be used in all patients undergoing CABG. The Heart Outcomes Prevention Evaluation (HOPE) [5] demonstrated that therapy with ACE inhibitors benefits all patients with risk factors for cardiovascular disease as well as patients undergoing CABG. In the perioperative period, ACE inhibitors reduce inflammation and preserve endothelial function, improving long-term graft patency and minimizing the progression of existing atherosclerotic plaques.

There are still controversies over the preoperative use of ACE inhibitors in patients undergoing CABG. Studies suggest that the preoperative administration of ACE inhibitors in cases of CABG helps reduce systemic vascular resistance and the development of vasoplegia in the early postoperative phase, resulting in hypotension and renal dysfunction [8,9]. Other authors [10,11] suggest that preoperative use of ACE inhibitors does not cause hypotension and can be safely used in patients undergoing cardiac surgery.

The aim of this study was therefore to assess the relationship between the preoperative use of ACE inhibitors and clinical events after the completion of CABG.

## METHODS

We evaluated data from consecutive patients undergoing CABG at the Hospital São Lucas, Pontificia Universidade Catolica do Rio Grande do Sul (HSL-PUCRS) in Porto Alegre, Rio Grande do Sul, Brazil, between January 1996 and December 2009. We excluded those who had no information about the use or not preoperative ACE inhibitors or ARA2, and those undergoing concomitant valve replacement. In total, 3,139 patients met the inclusion criteria. Follow-up was during the period of hospitalization, or until hospital discharge or death.

After surgery, patients were admitted to the unit of Postoperative Cardiac Surgery (POCC) of the hospital. The information was taken from structured protocol completed by doctors or nurses of the unit in the pre-operative, perioperative and postoperative. The ejection fraction was measured by echocardiogram or radiocardiogram during hospitalization, and this data is available for more than 95% of patients. Patients were included in the ACE inhibitor group should be taking the drug or an angiotensin receptor antagonist 2 (ARA2) for at least 2 weeks.

The primary outcome assessed was the use of inotropic support after surgery, defined by need for vasopressor administration in the immediate postoperative period (24 to 48 hours). Secondary outcomes assessed were: acute renal failure (ARF), atrial fibrillation (AF), myocardial infarction, stroke and death. The preoperative use of ACE inhibitors or ARA2 was defined as the administration of medication in the same period to 24 hours before CABG. All outcomes, except for death were evaluated in the immediate postoperative period.

The diagnosis of ARF in the postoperative period was defined by an increase greater than or equal to 50% or serum creatinine greater than 0.5 mg/dL above the preoperative value. Postoperative AF was defined as the presence of AF of any duration observed in 12-lead electrocardiogram. The diagnosis of postoperative AMI was based on the current presence of subepicardial injury and the onset of Q wave, current of subendocardial injury with increased necrosis markers (troponin I or CK-MB), bundle branch block with new markers also high. Aiming to exclude the elevation of markers secondary to the procedure, it was only considered the increase of CK-MB of at least 5 times the reference value or greater than 10% of total CK or troponin I> 10 µg / dL after 12 hours of postoperative values as established by Nascente et al. [12] in the same population.

On the other hand, the diagnosis of stroke was defined as new neurological deficit consistent with findings on imaging (CT or MRI of the brain). The data were analyzed according to surgical priority: emergency (CABG should be done within a few hours), urgency (CABG should be performed during the same hospital) or elective (the patient's clinical status allowed readmission to hospital later to perform CABG).

As for the design, this was a retrospective cohort study.

The present study was assessed by the Research Ethics Committee of the Pontificia Universidade Catolica do Rio Grande do Sul (Registration 09/04811). Personal information obtained was kept confidential data being used exclusively for research. Because it is an observational study which evaluated only clinical and laboratory data of patients with no postoperative intervention or implication about the care provided, it was not applied the Informed Consent Form.

### Statistical analysis

Continuous variables are described as mean ± standard deviation and categorical variables are described in percentages. The association between preoperative use of ACE inhibitors and clinical outcomes after surgery was evaluated by Student t test or chi-square as appropriate. Multivariate logistic regression analysis was performed to identify independent determinants of outcomes, and included those with $P$ <0.2. The results are presented in percentages and odds ratio (OR) with confidence interval 95% (CI). The level of significance alpha was 0.05.

All statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 12.0.

## RESULTS

### Patient characteristics

We evaluated 3,139 patients, being that in 1,635 (52.1%) we used ACE inhibitors or ARA2 in the pre-operatively (ACE inhibitors group) and in 1,504 (47.9%) we did not. Baseline characteristics of patients investigated are shown in Table 1. Apparently the ACE inhibitors group patients were more serious, because they had more comorbidities that were related to increased surgical risk as risk score of CABG recently published by our group [13]. The patients in the ACE inhibitor group had a higher number of females, higher prevalence of advanced heart failure (functional classes III and IV of the New York Heart Association) and systolic dysfunction. There was a tendency to increased number of individuals with chronic AF. There was no difference between groups regarding age and the prevalence of renal disease (ESRD) and chronic obstructive pulmonary disease (COPD). There was less need for emergency surgery / emergency in the ACE inhibitor group.

### Outcomes

The incidence of events evaluated in the post-CABG in patients who used and did not use ACE inhibitors in the preoperative period are shown in Figure 1. There was no

Table 1. Baseline characteristics of patients in the preoperative period.

| Variables | Using ACE inhibitors (n=1635) (%=52.1) | Not Using ACE inhibitors (n =1504) (%=47.9) | *P* |
|---|---|---|---|
| Age, mean (SD), years | 61.21(10.11) | 61.60 (10.35) | 0.294 |
| Female | 585 (35.8) | 467 (31.1) | 0.006 |
| Hypertension | 1361 (83.2) | 916 (60.9) | <0.001 |
| Smoking | 507 (31.0) | 574 (38.2) | <0.001 |
| Diabetes mellitus | 560 (34.3) | 369 (24.5) | <0.001 |
| Unstable angina | 571 (34.9) | 575 (38.2) | 0.059 |
| NYHA III and IV | 303 (18.5) | 180 (12.0) | <0.001 |
| Previous AMI | 766 (46.9) | 544 (36.2) | <0.001 |
| Ejection fractio | | | |
| n>50 % | 856 (52.6) | 995 (66.5) | <0.001 |
| 30-50% | 609 (37.5) | 429 (28.7) | |
| <30% | 161 (9.9) | 73 (4.9) | |
| History of AF | 67 (4.1) | 42 (2.8) | 0.058 |
| COPD | 296 (18.1) | 297 (19.7) | 0.259 |
| IRC | 158 (9.7) | 133 (8.8) | 0.465 |
| Previous heart surgery | 60 (3.7) | 43 (2.9) | 0.241 |
| Emergency surgery | 83 (5.1) | 147 (9.8) | <0.001 |
| Use of intra-aortic balloon | 176 (10.8) | 115 (7.6) | 0.003 |

*ACE: angiotensin-converting enzyme inhibitors; NYHA: classification of heart failure functional class according to the New York Heart Association, AMI: acute myocardial infarction, AF: atrial fibrillation, COPD: chronic obstructive pulmonary disease, ARF: acute renal failure*

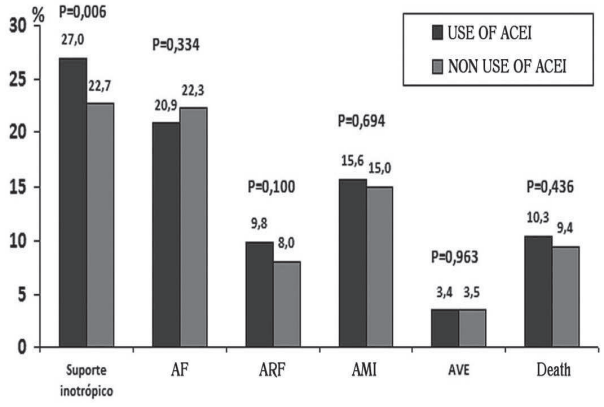


*Fig. 1 - Clinical outcomes after CABG by univariate chi-square.*
*ACEI: angiotensin-converting enzyme inhibitors*
*AF: atrial fibrillation*
*ARF: acute renal failure*
*AMI: acute myocardial infarction*

Table 2. Multivariate analysis of predictors of inotropic support in post-CABG

| Variables | RC | IC 95% | *P* |
|---|---|---|---|
| Preoperative use of ACE inhibitors | 1.24 | 1.04-1.47 | 0.015 |
| Age | 1.03 | 1.02-1.04 | <0.001 |
| NYHA III and IV | 1.53 | 1.22-1.91 | <0.001 |
| Emergency surgery | 2.02 | 1.49-2.72 | <0.001 |
| Use of intra-aortic balloon | 1.51 | 1.15-1.99 | 0.003 |
| IRC | 1.61 | 1.23-2.09 | <0.001 |
| AF | 1.88 | 1.26-2.83 | 0.002 |
| Previous AMI | 1.27 | 1.07-1.51 | 0.006 |
| Previous heart surgery | 1.67 | 1.09-2.55 | 0.018 |

*ACE: angiotensin-converting enzyme inhibitors; NYHA: classification of heart failure functional class according to the New York Heart Association, AMI: acute myocardial infarction, AF: atrial fibrillation, COPD: chronic obstructive pulmonary disease, ARF: acute renal failure*

difference in mortality between the groups (10.3% of deaths in the group who used ACE inhibitors vs. 9.4% in the group who did not use ACE inhibitors, $P = 0.436$).

**Inotropic support**

The use of ACE inhibitors was the most used independent predictor of inotropic support in the postoperative period (OR 1.24, 95% CI 1.04 to 1.47, $P = 0.015$). Advanced age, heart failure functional class III or IV New York Heart Association (NYHA), urgent or emergency surgery, need for intra-aortic balloon and previous history of chronic renal failure, atrial fibrillation, myocardial infarction or cardiac surgery were also predictors of the need inotropic support after the procedure (Table 2).

**ARF**

Patients on ACE inhibitors had a higher risk of developing postoperative ARF (OR 1.23, 95% CI 1.01 to 1.73, $P = 0.042$), as well as elderly patients, patients with chronic obstructive pulmonary disease (COPD), heart failure, or CRF basal functional class III or IV heart failure patients, and those who required urgent or emergency surgery (Table 3).

**Postoperative AF**

The use of ACE inhibitors, after adjusting for age, was a predictor for the development of postoperative AF (OR 1.32, 95% CI 1.02 to 1.7, $P = 0.032$). In addition to age, COPD patients preoperatively also had a higher risk of AF (Table 4).

Table 3. Multivariate analysis of predictors of renal dysfunction after CABG.

| Variables | RC | IC 95% | *P* |
|---|---|---|---|
| Preoperative use of ACE inhibitors | 1.23 | 1.01-1.73 | 0.042 |
| Age | 1.06 | 1.05-1.08 | <0.001 |
| COPD | 1.7 | 1.26-2.29 | <0.001 |
| IRC | 3.8 | 2.76-5.24 | <0.001 |
| NYHA III and IV | 1.85 | 1.37-2.51 | <0.001 |
| Emergency surgery | 3.08 | 2.13-4.46 | <0.001 |

*ACE: angiotensin-converting enzyme inhibitors; NYHA: classification of heart failure functional class according to the New York Heart Association, AMI: acute myocardial infarction, AF: atrial fibrillation, COPD: chronic obstructive pulmonary disease, ARF: acute renal failure*

Table 4. Multivariate analysis of predictors of atrial fibrillation post-CABG.

| Variables | RC | IC 95% | *P* |
|---|---|---|---|
| Preoperative use of ACE inhibitors | 1.32 | 1.02-1.7 | 0.032 |
| Age | 1.07 | 1.06-1.09 | <0.001 |
| COPD | 1.8 | 1.36-2.39 | <0.001 |

*ACE: angiotensin-converting enzyme inhibitors; NYHA: classification of heart failure functional class according to the New York Heart Association, AMI: acute myocardial infarction, AF: atrial fibrillation, COPD: chronic obstructive pulmonary disease, ARF: acute renal failure*

The preoperative use of ACE inhibitors did not increase the risk of AMI, stroke or death in post-CABG.

## DISCUSSION

Some studies have shown that blocking the renin-angiotensin system (RAS) with ACE inhibitors improves ventricular function, prolongs survival and decreases the size of the infarct in patients after AMI [14] or patients with heart failure [15]. However, it is unclear the role of ACE inhibitors in patients undergoing CABG. Surgeons attributed the beneficial effects of ACE inhibitors to their antihypertensive and antiatherogenic properties. Lazar et al. [16] concluded that all patients undergoing CABG should receive ACE inhibitors preoperatively.

The results of this study suggest that preoperative use of ACE inhibitors as an independent predictor of the need for inotropic support postoperatively, consistent with previously published data [17-20].

Perioperative hypotension, for generating a reduction in renal perfusion pressure is a known risk factor for the development of ARF in surgical patients. However, the association between therapy with ACE inhibitors and renal failure after cardiac surgery remains controversial [21]. The effect of ACE inhibitors on renal function after surgery may depend on the prior exposure time. Rady & Ryan [11] found no significant association between use of ACE inhibitors and renal failure in post-cardiac surgery in patients chronically treated with medication. In contrast, Arora et al. [22] in a large observational study, showed significant association between preoperative use of ACE inhibitors and acute renal failure in the postoperative period of cardiac surgery and abdominal aortic surgery [23]. In addition, there are reports that treatment with ACE inhibitors may increase the adverse effects during the first 3 months after surgery did not improve clinical outcome up to 3 years of follow up [24]. On the other hand, the study APRES [25] showed that the use of long-term ramipril reduced the composite endpoint of cardiac death, myocardial infarction and heart failure in clinical treatment with revascularization. Our study suggested that use of ACE inhibitors in the pre-CABG increases the risk of ARF. As the follow-up occurred during the hospital stay, not have time to test whether there was a potential benefit of treatment as clinically important events.

A study by White et al. [26] in patients undergoing cardiac surgery (CABG and valve) showed a statistically significant association between the use of ACE inhibitors before surgery and reduce postoperative AF. Although we only evaluated patients undergoing CABG, our results are contradictory to the study cited, since there was an increased chance of developing postoperative AF. The blockade of the RAS in patients undergoing CABG contributes to the reduction of systemic vascular resistance

and the vasoplegia in the immediate postoperative period, resulting in hypotension, which often requires volume and / or vasoactive drugs [17-20]. It is known that both the hypotension and volume overload are factors that contribute to the development of AF postoperatively [27].

Our study showed that preoperative use of ACE inhibitors did not increase the risk of AMI, stroke or death in post-CABG. In contrast, Miceli et al. [28] demonstrated that preoperative therapy with ACE inhibitors has increased at twice the risk of death in patients undergoing coronary artery bypass grafting. However, it is believed that other studies [29,30] did not show similar results due to small sample size to detect differences in mortality.

Interrupting the use of ACE inhibitors, or reducing the dose in the immediate postoperative period, and their reintroduction into the postoperative period, may be reasonable alternatives to minimize the acute effects, without loss of their chronic cardioprotective effects. Therefore, our work raises the hypothesis to be tested in future studies.

Our study has some limitations. The fact that it prevents the best observational evaluation of the intervention, making a hypothesis-generating study, whose results need further investigation with controlled trials. Patients who were using ACE inhibitors in the preoperative period had a higher number of comorbidities. We have no information of the real reason for not prescribing ACE inhibitors in the preoperative period. The use or nonuse of ACE inhibitors before surgery was an option of the doctor who referred the patient to the implementation of CRM. Even with an indication if we consider the underlying disease that caused the procedure, nearly half of the sample was not in use. In these patients, the ACE inhibitor was not prescribed in the hospital for a short period before surgery. In addition, we did not perform a separate analysis of treatment with ACE inhibitors or ARA2. During the study period, all revascularization procedures were performed by the same group of cardiac surgeons, with no significant changes in surgical technique. However, there was this period changes in the pharmacological treatment of ischemic heart disease that could be related to the incidence of outcomes.

## CONCLUSION

The preoperative use of ACE inhibitors was associated with increased need for inotropic support postoperatively, and the higher incidence of ARF and AF not associated with an increased rate of myocardial infarction, stroke and death.

## REFERENCES

1. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med. 2000;342(3):145-53.

2. EURopean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease Investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). Lancet. 2003;362(9386):782-8.

3. Mill JG, Milanez MC, Busatto VCW, Moraes AC, Gomes MGS. Ativação da Enzima conversora de angiotensina no coração após infarto do miocárdio e suas repercussões no remodelamento ventricular. Arq Bras Cardiol. 1997;69(2):101-10.

4. Anderson TJ, Elstein E, Haber H, Charbonneau F. Comparative study of ACE-inhibition, angiotensin II antagonism, and calcium channel blockade on flow-mediated vasodilatation in patients with coronary disease (BANFF study). J Am Coll Cardiol. 2000;35(1):60-6.

5. Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet. 2000: 355(9200):253-9.

6. Miyazaki M, Sakonjo H, Takai S. Anti-atherosclerotic effects of an angiotensin converting enzyme inhibitor and an angiotensin II antagonist in Cynomolgus monkeys fed a high-cholesterol diet. Br J Pharmacol. 1999;128(3):523-9.

7. Brasier A, Recinos A 3rd, Eledrisi MS. Vascular inflammation and the renin-angiotensin system. Atherioscler Thromb Vasc Biol. 2002;22(8):1257-66.

8. Tuman KJ, McCarthy RJ, O'Connor CJ, Holm WE, Ivankovich AD. Angiotensin-converting enzyme inhibitors increase vasoconstrictor requirements after cardiopulmonary bypass. Anesth Analg. 1995;80(3):473-9.

9. Arora P, Rajagopalam S, Ranjan R, Kolli H, Singh M, Venuto R, et al. Pre-operative use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers is associated with increased risk for acute kidney injury after cardiovascular surgery. Clin J Am Soc Nephrol. 2008;3(5):1266-73.

10. Pigott DW, Nagle C, Allman K, Westaby S, Evans RD. Effect of omitting regular ACE inhibitor medication before cardiac surgery on haemodynamic variables and vasoactive drug requirements. Br J Anaesth. 1999;83(5):715-20.

11. Rady MY, Ryan T. The effects of preoperative therapy with angiotensin-converting enzyme inhibitors on clinical outcome after cardiovascular surgery. Chest. 1998;114(2):487-94.

12. Nascente RB, Guaragna JCVC, Franca AS, Spiandorello RM,

Werutski G, Azevedo E, et al. Estabelecimento do ponto de corte da troponina I como marcador de infarto do miocárdio em cirurgia de revascularização miocárdica. Sci Med. 2005;15(3):142-7.

13. Cadore MP, Guaragna JCVC, Anacker JFA, Albuquerque LC, Bodanese LC, Piccoli JCE, et al. Proposição de um escore de risco cirúrgico em pacientes submetidos à cirurgia de revascularização miocárdica. Rev Bras Cir Cardiovasc. 2010;25(4):447-56.

14. Pfeffer MA, Greaves SC, Arnold JM, Glynn RJ, LaMotte FS, Lee RT, et al. Early versus delayed angiotensin-converting enzyme inhibition therapy in acute myocardial infarction. The healing and early afterload reducing therapy trial. Circulation. 1997;95(12):2643-51.

15. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N Engl J Med. 1991;325(5):293-302.

16. Lazar HL. All coronary artery bypass graft surgery patients will benefit from angiotensin-converting enzyme inhibitors. Circulation. 2008;117(1):6-8.

17. Tuman KJ, McCarthy RJ, O'Connor CJ, Holm WE, Ivankovich AD. Angiotensin-converting enzyme inhibitors increase vasoconstrictor requirements after cardiopulmonary bypass. Anesth Analg. 1995;80(3):473-9.

18. Argenziano M, Chen JM, Choudhri AF, Cullinane S, Garfein E, Weinberg AD, et al. Management of vasodilatory shock after cardiac surgery: identification of predisposing factors and use of a novel pressor agent. J Thorac Cardiovasc Surg. 1998;116(6):973-80.

19. Raja SG, Fida N. Should angiotensin converting enzyme inhibitors/angiotensin II receptor antagonists be omitted before cardiac surgery to avoid postoperative vasodilation? Interact Cardiovasc Thorac Surg. 2008;7(3):470-5.

20. Deakin CD, Dalrymple-Hay MJ, Jones P, Monro JL. Effects of angiotensin converting enzyme inhibition on systemic vascular resistance and vasoconstrictor requirements during hypothermic cardiopulmonary bypass. Eur J Cardiothorac Surg. 1998;13(5):546-50.

21. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. Clin J Am Soc Nephrol. 2006;1(1):19-32.

22. Arora P, Rajagopalam S, Ranjan R, Kolli H, Singh M, Venuto R, et al. Preoperative use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers is associated with increased risk for acute kidney injury after cardiovascular surgery. Clin J Am Soc Nephrol. 2008;3(5):1266-73.

23. Cittanova ML, Zubicki A, Savu C, Montalvan C, Nefaa N, Zaier K, et al. The chronic inhibition of angiotensin-converting enzyme impairs postoperative renal function. Anesth Analg. 2001;93(5):1111–5.

24. Rouleau JL, Warnica WJ, Baillot R, Block PJ, Chocron S, Johnstone D, et al; IMAGINE (Ischemia Management with Accupril post-bypass Graft via Inhibition of the coNverting Enzyme) Investigators. Effects of angiotensin-converting enzyme inhibition in low-risk patients early after coronary artery bypass surgery. Circulation. 2008;117(1):24-31.

25. Kjøller-Hansen L, Steffensen R, Grande P. The Angiotensin-converting Enzyme Inhibition Post Revascularization Study (APRES). J Am Coll Cardiol. 2000;35(4):881-8.

26. White CM, Kluger J, Lertsburapa K, Faheem O, Coleman CI. Effect of pre-operative angiotensin converting enzyme inhibitor or angiotensin receptor blocker use on the frequency of atrial fibrillation after cardiac surgery: a cohort study from the atrial fibrillation suppression trials II and III. Eur J Cardiothorac Surg. 2007;31(5):817–20.

27. Echahidi N, Pibarot P, O'Hara G, Mathieu P. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. J Am Coll Cardiol. 2008;51(8):793-801.

28. Miceli A, Capoun R, Fino C, Narayan P, Bryan AJ, Angelini GD, et al. Outcome in patients undergoing coronary artery bypass grafting effects of angiotensin-converting enzyme inhibitor therapy on clinical. J Am Coll Cardiol. 2009. Disponível em: http://content.onlinejacc.org/cgi/content/full/j.jacc.2009.07.008v1

29. Rady MY, Ryan T. The effects of preoperative therapy with angiotensin-converting enzyme inhibitors on clinical outcome after cardiovascular surgery. Chest. 1998;114(2):487-94.

30. Weightman WM, Gibbs NM, Sheminant MR, Whitford EG, Mahon BD, Newman MA. Drug therapy before coronary artery surgery: nitrates are independent predictors of mortality and beta-adrenergic blockers predict survival. Anesth Analg. 1999;88(2):286-91.