

Ischemic Preconditioning and Atrial Fibrillation after Coronary Artery Bypass Grafting Surgery

M Jannati, J Kojuri

Cardiovascular Research Center, , Shiraz University of Medical Sciences, Shiraz, Iran

Background: Atrial fibrillation is the most common arrhythmic complication after coronary artery bypass grafting. Ischemic preconditioning has proved to be a potent endogenous factor in suppressing ischemia-reperfusion induced arrhythmia.

Patients and Methods: In this prospective study, 101 patients were randomly selected and divided into two groups including 50 patients with ischemic preconditioning protocol and 51 patients in the control group. Data were collected from 24 hour electrocardiogram from 1 day before the operation to 3rd post-operative day. Atrial fibrillation was registered as positive, if it lasted longer than 30 seconds.

Results: The postoperative atrial fibrillation was significantly lower in the ischemic preconditioning group that was 8% in ischemic preconditioning and 23.52% in control groups ($P=0.033$). Control group had a longer stay in intensive care unit and longer mechanical ventilation support.

Conclusion: This study suggests that ischemic preconditioning is a useful prophylactic protocol to decrease the prevalence of post-cardiac surgery atrial fibrillation.

Keywords: Ischemic Preconditioning, Atrial Fibrillation, Coronary Artery Bypass Grafting

Introduction

Atrial fibrillation (AF) has been recognized as the most common arrhythmia after coronary artery bypass grafting (CABG). The reported incidence of AF after CABG varies between 15 to 40%.¹⁻⁵ This arrhythmia usually occurs between second and fourth post-operative days. Despite the fact that it is usually benign and self-limiting, it may result in hemodynamic instability, thrombo-embolic events, longer hospital stay and increased health care cost.^{6,7} Therefore, much more attention has focused on the prevention of this arrhythmia in high risk patients.⁸ Ischemic preconditioning is an adaptive biologic phenomenon in which

the heart becomes more tolerant to a period of prolonged ischemia.

This adaptation to ischemia was first described by Murray and colleagues and was defined as classic or early phase preconditioning. This increasing tolerance to ischemia is associated with a reduction in infarct size, apoptosis and reperfusion associated arrhythmias. It appears to persist as long as 1 to 2 hours after the ischemia.⁹ It became ineffective when the sustained ischemic insult exceeds longer than 3 hours. After disappearing the acute phase of preconditioning, a second phase of protection appears 24 hours later and is sustained for up to 72 hours. This has been referred to as second window of protection. Late-phase preconditioning protects against both infarction and stunning.¹¹⁻¹³ The aim of this study was to

Correspondence:

M Jannati

Cardiovascular Research Center, Faghihi Hospital, Shiraz, Iran

Tel: +98-711-2343529

E-mail: janatim@sums.ac.ir

evaluate the effect of ischemic preconditioning on prevalence of AF after CABG.

Patients and Methods

From June 2005 to June 2006, 101 candidates for CABG were randomized into 2 groups: control group (51 patients) and study group (50 patients) who received ischemic preconditioning protocol. Cardiopulmonary bypass (CPB) was established and the heart was vented. The aorta was then cross-clamped for 2 minutes followed by 3 minutes of reperfusion. The control group also had the pump running for 10 minutes before the routine operation. The

pre-operative characteristics of the patients in two groups were similar (Table 1). All patients had a continuous electrocardiographic monitoring for 3 days after CABG with memory monitoring (mind ray 9000 and 6000) and under supervision of ICU nurses. Electrocardiographic recordings were performed if irregular, and monitoring was done to detect supra-ventricular or ventricular tachyarrhythmia.

Patients with pre-operative atrial fibrillation, concomitant cardiac diseases, cardiac re-do operations, and emergency operations were excluded from the study.

Statistical Analysis

Statistical analysis was performed using SPSS for windows version 11.5. Categorical data were analyzed using the Fisher's exact test or Pearson Chi-square test. All other data were analyzed using independent sample t-tests for comparison continuous data. All data were presented as mean \pm standard deviation. P value less than 0.05 consider significance.

Results

Fifty-one patients (mean age was 66.47 ± 6.1 years) were selected as control group and 50 patients (mean age was 66.03 ± 8.74 years) were randomly selected to undergo cardiac surgery via ischemic preconditioning protocol. Demographic criteria and pre-operative factors are shown in Table 1. The overall incidence of post-operative AF was 8% among ischemic preconditioning group and 23.52% in control group ($P=0.033$). Effect of ischemic preconditioning on incidence of post-operative AF and other factors is shown in Table 2.

Discussion

AF has been recognized as the most common arrhythmia after coronary artery bypass grafting (CABG) with adverse outcome. The reported incidence of AF after CABG varies

Table 1. Population criteria and preoperative factor

	IP (n=50)	Control (n=51)	P value
Age (years)	66.03 ± 8.74	66.47 ± 6.10	0.978
Left ventricular ejection fraction	41.99 ± 10.31	43.61 ± 6.49	0.514
Diabetes mellitus	9	15	0.178
Preoperative beta-blocker	38	38	0.862
Preoperative amiodarone	1	1	1.000
Perfusion time (min)	85.16 ± 19.25	81.85 ± 12.35	0.232

IP=ischemic preconditioning protocol

Table-2. Post operative results

	IP (n=50)	Control (n=51)	P value
Postoperative AF	4 (8%)	12 (23.5%)	0.033
AF period (min)	21.91 ± 7.43	74.79 ± 8.53	0.001
ICU stay (hour)	21.63 ± 11.49	39.60 ± 16.78	0.002
Postoperative cardioversion	1(2%)	3 (5.88%)	0.617
Postoperative use of amiodarone	4 (8%)	6 (11.7%)	0.741

AF=atrial fibrillation

between 15 to 40%.^{1,4,5} This usually occurs between second and fourth post-operative day. The incidence of AF clearly increases with advance age, chronic obstructive pulmonary disease and higher preoperative heart rates. AF is usually well-tolerated, but tachycardia and loss of atrial contraction can cause heart failure which is associated with increasing risk of stroke,¹⁴⁻¹⁶ length of hospital stay^{14,17-22} and costs.^{21,23} Thus, although AF is rarely fatal, post CABG AF may lead to subjective discomfort and anxiety, systemic embolization,¹⁴⁻¹⁶ compromised hemodynamic function, hypotension, pulmonary edema, longer hospitalization,^{14,17-22} heart failure, costs²³ and a need for using post-discharge medication. AF is also associated with increased mortality 30 days and 6-months after CABG.^{24,25} Treatment of AF might fail or associated with potentially harmful side effects such as bleeding due to anticoagulation and recurrent hospital admissions.^{26,27} Therefore, research is clearly warranted for a suitable means to prevent AF following CABG.

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Myocardial ischemic preconditioning has been extensively studied in various experimental models as well as in human subjects.²⁸ Ischemic preconditioning has proved to be a potent endogenous factor in preserving high-energy phosphate, delaying myocardial infarction and improving post-ischemic functional recovery.^{24,28-30} Finally, ischemic preconditioning is a prophylactic method in prevention of AF after on-pump CABG especially in patients at high risk for developing AF.

In our study, ischemic preconditioning significantly suppressed AF after CABG, suggesting that it can be used as an effective prophylactic method for post-operative atrial fibrillation.

Ischemic preconditioning significantly suppresses AF after CABG.

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