Journal of Surgery and Trauma 2016; 4(3-4): 51-57.

www.jsurgery.bums.ac.ir

ORIGINAL ARTICLE

Associations between preoperative P-wave characteristics, C-reactive protein levels, and atrial fibrillation after coronary artery bypass graft surgery

Nahid Azdaki[1], Navid Ghodsi Nik[2], Navid Rabiee[2], Mahmood Zardast[3], Amir Rahmanian Sharifabad[4], Mahmood Hosseinzadeh Maleki[5]✉, Majid Jafarnezhad[1]

[1] *Assistant Professor of Cardiology, Atherosclerosis and Coronary Artery Research Center, Birjand University of Medical Sciences, Birjand, Iran*

[2] *Student of Medicine, Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran*

[3] *Assistant Professor of Pathology, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran*

[4] *Medical Doctor, Atherosclerosis and Coronary Artery Research Center, Birjand University of Medical Sciences, Birjand, Iran*

[5] *Associate Professor of Cardiac Surgery, Atherosclerosis and Coronary Artery Research Center, Birjand University of Medical Sciences, Birjand, Iran*

Received: May 13, 2017 ***Revised: July 2, 2017*** ***Accepted: July 5, 2017***

Abstract

Introduction: Atrial fibrillation (AF) is the most common complication of cardiac surgery which may cause remarkable morbidity and complications. Identifying predicting factors of this arrhythmia can help prophylactic therapy. The present study is designed to investigate the hypothesis that HsCRP level and P-wave characteristics are associated with the incidence of post-operative AF.

Methods: In this prospective study, 50 consecutive patients undergoing coronary artery bypass graft (CABG) operation during a 1-year period at Vali-e-asr Hospital, Birjand, Iran were enrolled. All the patients underwent electrocardiography (ECG) before surgery and P-wave duration and height were measured. In addition, blood samples were collected the day before surgery as well as 12, 24 and 72 hours after surgery to measure CRP serum levels. Patients were monitored after surgery to detect probable AF rhythm. Data was analyzed using SPSS 16.

Results: Of the 50 patients, 10 (20%) developed AF in the postoperative phase during days 1 to 5, while the other 40 patients (80%) had stable sinus rhythm. P-wave duration and height were significantly different in patients who subsequently developed postoperative AF with the mean values of 109.5±15.7 and 0.14±0.03, respectively. Mean HsCRP levels before and 12, 24, and 72 h after operation showed no significant difference.

Conclusions: Patients prone to AF arrhythmia can be identified by measuring P-wave duration and height in preoperative ECG. Hs.CRP levels before and after CABG surgery may not contribute to AF prediction.

Key Words: Coronary Artery Bypass; Atrial Fibrillation; Electrocardiogram; C - reactive protein

Tel: +985632381203
Fax: +985632440488
Po Box 97175-379
Email: jsurgery@bums.ac.ir

✉**Correspondence to:**
Mahmood Hosseinzadeh Maleki, *Associate Professor of Cardiac Surgery, Atherosclerosis and Coronary Artery Research Center, Birjand University of Medical Sciences, Birjand, Iran* ;
Telephone Number: +98 56 1443001-9
Email Address: mahmoodhosseinzadeh@yahoo.com

Introduction

Atrial fibrillation (AF) is the most common arrhythmia following cardiac surgery with an incidence of 25 to 60% (1-4). Even though it is not life-threatening and potentially self-limited, it has considerable medical and economic implications. This arrhythmia may impact cardiac function and lead to increased risks of stroke and thromboembolism as well as possible iatrogenic complications because of additional treatment efforts, prolonged length of hospitalization, and increased treatment costs (5, 6). While there exists effective pharmacological prophylaxis (7, 8), significant adverse events such as heart block and bradycardia, confine prophylactic therapy for patients who are at high risk of developing postoperative AF (POAF) (7). Prediction models have not been strong enough, according to clinical and paraclinical variables, to allow POAF prophylactic therapy (9). Thus, several studies have been performed to identify both the pathogenesis of POAF and the predisposing factors. Still, the exact etiologic pattern stands unclear. However, there has been an increasing number of variables suggested as predictors of POAF among which are inflammation and electrocardiographic changes that have recently been introduced and studied as risk factors and predictors of POAF (4, 5, 10-12).

High-sensitivity C-reactive protein (hsCRP) is an acute phase protein and an established marker of inflammation. Moreover, high CRP levels have been associated with the risk of coronary events, severity of atherosclerosis, and even long-term outcome following CABG. The role of CRP concentrations in identifying risks for complications after cardiac surgery has received increasing attention (5, 13, 14).

In addition, some studies have reported several P-wave characteristics that increase the risk of POAF (4, 15, 16). According to the Framingham Heart Study cohort, for instance, a significant correlation has been reported between maximum P-wave duration and incidence of AF (16).

The goals of the present study were to identify the role of HsCRP level and P-wave characteristics in predicting the incidence of POAF in order to promote prediction models and prophylactic treatment.

Methods

In this prospective, single-centered study, 50 consecutive patients undergoing coronary artery bypass graft operation (CABG) during a 1-year period at Vali-e-asr Hospital, Birjand, Iran, were enrolled upon approval from the Ethical Committee of Birjand University of Medical Sciences (code: Ir.bums.rec.1394.400) and provision of informed consent.

Indications for CABG surgery comprised of significant (>60%) disease of the left main coronary artery stem, ostial stenosis of left anterior descending artery, two- or three-coronary-vessel disease, and symptomatic coronary artery disease unsuitable for percutaneous coronary intervention.

Patients considered to be at high risk for the development of POAF, like those with a history of AF on anti-arrhythmic medical therapy, congestive heart failure at the time of preoperative evaluation, and/or concomitant valve surgery, those suffering from a chronic inflammatory condition, and/or those under medical treatment with amiodarone, corticosteroids, or non-steroidal anti-inflammatory drugs within 30 days prior to CABG surgery were excluded from the study.

All cases were operated on an elective basis. Based on the surgeon's preference, all operations were performed "On-Pump". The decision to use intra-aortic balloon pump, cardiac inotropic support, or temporary pacing was made by the anesthesiologist and/or the surgeon and was determined according to the patient's hemodynamic status and rhythm in the operating room and the postoperative heart surgical unit. Efforts were made to extubate patients within 24 hours after surgery. All patients underwent ECG before surgery using CARDIOTOUCH Machine at a rate of 25 under standard conditions. P-wave duration and height in all related ECG leads were measured with a ruler and the highest duration and height of P-wave in all the leads were used for analysis.

Blood samples were collected from all patients the day before surgery and 12, 24 and 72 hours after the operation. Sera samples were collected in clot vacutainer tubes and centrifuged within 30 minutes of vein puncture at 3500 rpm for 10 min and stored at −20ºC until measurement was completed. CRP serum levels were measured using human Hs.CRP Glory Kit.

POAF was defined as irregular arrhythmia lasting for ≥ 5 min before discharge. In our center, all patients were monitored in the intensive care unit after surgery with a 5-lead monitoring system using the standard lead II configuration. After

discharge from the intensive care unit, the patients were followed up 6–8 times daily in the service. Following surgery, if a patient manifested with symptoms of palpitations or an irregular pulse, a 12-lead ECG was performed to diagnose the arrhythmia.

Episodes of AF were treated according to clinical routines which included pharmacological interventions with intravenous amiodarone or, if contraindicated, with an oral β-blocker (metoprolol) and/or with electrical therapies like cardioversion.

All the data were analyzed using the Statistical Package for Social Sciences (SPSS) for Windows (version 16.0; SPSS Inc., Chicago, IL, USA). Continuous variables were tested for normal distribution using the Kolmogorov-Smirnov test and reported as means±standard deviations or median if not normally distributed. Continuous demographic data, CRP levels and P-wave duration and height were compared between groups using Student t test or Mann-Whitney if not normally distributed. Categorical demographic data were summarized as percentages and compared using the chi-square test. Cohen's d was calculated as the difference between the means divided by the pooled SD to indicate the standardized difference between two means (17). Precision (SD of difference between estimated and actual variable) was also calculated (18). All P-values < 0.05 were accepted as statistically significant.

Results

Fifty patients fulfilled our criteria and were enrolled in the study. Regarding their demographic characteristics 62% were male and Mean±SD of the patients' mean age was 61.86±9.60 years. Half of them were hypertensive and one third were diabetic. Dyslipidemia had the same prevalence as diabetes. Smoking and addiction existed in 24 and 18 percent of patients, respectively. From among the participants, 26 percent had a family history of coronary artery disease (CAD) and 6 percent had a history of vascular accidents such as CVA.

Of the 50 patients, 10 (20%) developed AF in the postoperative phase during days 1 to 5, while the other 40 patients (80%) had stable sinus rhythm during the same period. Table 1 shows baseline characteristics and intra-operative parameters of patients, compared between AF and non-AF groups. Based on the table, the difference in mean age was statistically significant (Precision=6.29; p=0.013; Effect Size=0.49). Other baseline and intra-operative characteristics did not show a statistically significant difference between the groups.

Table 1: Baseline characteristics and intra operative parameters of patients

Variable	AF (N=10)	Non-AF (N=40)	P-value
Age	68.50±9.02	60.20±9.11	0.013[a]
Sex [n (%)]	7 (70)	24(60)	0.421
HTN[6]	7 (70)	18 (45)	0.145
DM[7]	3 (30)	14 (35)	0.539
DLP[8]	5 (50)	11 (27.5)	0.162
Smoking	3 (30)	9 (22.5)	0.449
Addiction	0 (0)	9 (22.5)	0.109
CAD[9] family history	4 (40)	9 (22.5)	0.229
CVA[10] history	1 (10)	2 (5.0)	0.496
Perfusion time	121.50±17.78	115.38±25.18	0.473[a]
Cross clamp time	71.10±13.86	22.17±3.15	0.504[б]

[a] independent T test
[б] Mann-Whitney test
$\chi 2$ test used for other comparisons
[1]Hypertension / [2]Diabetes / [3]Dyslipidemia / [4]Coronary artery Disease / [5]Cerebrovascular Accident

Concerning P-wave characteristics, P-wave duration and height were significantly different in patients who subsequently developed postoperative AF with the mean values of 109.5±15.7 and 0.14±0.03, respectively (Table 2).

HsCRP had the same trend in both AF and non-AF groups. It decreased 12h after operation, had a rise after 24h, and remained elevated until the third day after operation. Comparison of hsCRP levels at different time points using Friedman test showed statistically significant differences in both AF and non-AF groups (P <0.001) (Table 3, Figure 1). Bonferroni post-hoc test results showed that preoperative and 12h-postoperative hsCRP levels were significantly different from serum levels detected 24 and 48h after operation (P <0.001). Furthermore, Mean HsCRP levels at different time points (before and 12, 24, and 72 h after operation) were compared between AF and non-AF groups, which showed no significant difference (Table 3).

Table 2: P-wave characteristics in AF and non-AF patients

Variable	AF	Non AF	Effect size (Cohen D)	SD Error Precision	Independent T test results
P-wave duration	109.5±15.7	89.2±26.7	0.82	17.07	t=-2.32 p-value=0.025
P-wave height	0.14±0.03	0.11±0.04	0.72	0.03	t=-2.03 p-value=0.048

Table 3: CRP changes by postoperative AF status

Hs.CRP	Preoperative	12 h postop	24 h postop	72 h postop	Friedman test results
AF	0.613±1.181	0.481±0.875	6.865±3.918	7.088±3.416	Chi-square=23.16 df=3 p-value<0.001
Non-AF	0.625±1.445	0.476±0.961	6.340±2.608	6.534±4119	Chi-square=96.55 df=3 p-value<0.001
SD Error Precision	0.96	0.64	1.99	2.76	
Inter-group comparison	Z[ϭ]=-0.764 p-value=0.45 Cohen D=0.008	Z[ϭ]=-0.762 p-value=0.77 Cohen D=0.005	t[α] =-0.51 p-value=0.61 Cohen D=0.18	t[α] =-0.39 p-value= 0.69 Cohen D=0.14	

α Independent T test ϭ Mann-Whitney Test

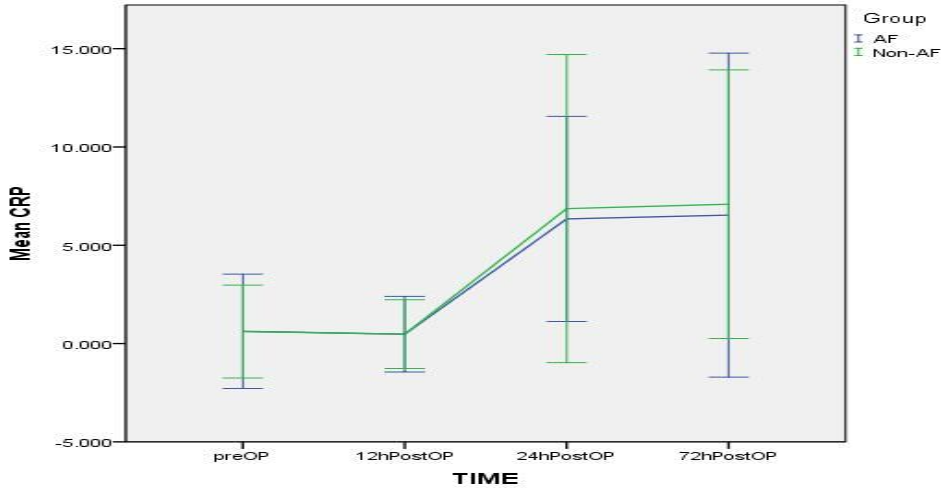

Figure 1: CRP levels before and after operation in AF and non-AF groups

Discussion

Predicting patients' risk of developing POAF stands as an important issue because it can help identify a group of cardiac surgery patients for whom prophylaxis would prove more beneficial than the risks. Several methods have been proposed for stratification of patient's risk of POAF, which do not have enough efficacies to predict major postoperative morbidity. The aim of our study was to investigate possible correlations of P-wave characteristics and CRP levels to postoperatively developed AF in patients undergoing CABG.

The post-CABG AF incidence of 20% in our study concurs with that reported by numerous groups (3, 13, 14, 19). The main finding of our study was that elevated preoperative P-wave height and duration in patients undergoing CABG are strongly associated with postoperative AF development. This is similar to the report by Hagjoo et al. about higher risk of postoperative AF in patients with abnormal P-wave morphology (20). It is also consistent with the report by Rader et al. where the authors found a significant association between P-wave amplitude and AF (21). Interestingly, Solak et al. recently showed that the P-wave index was significantly higher in a cohort of dialysis patients—a population with a high incidence of AF (22). Chandy et al. showed that increased P-wave duration is believed to be able to identify patients at risk of postoperative AF, but it is not powerful enough to predict POAF (23). Furthermore, P-wave duration > 25 ms in patients with anterior myocardial infarction has been found to be independently associated with AF (24). In contrast to our results, some studies have shown that P-wave duration was significantly shorter in patients with POAF. It is justifiable due to the fact that they evaluated postoperative ECGs which are affected by postoperative increased B-adrenergic tone (25, 26).

It seems that a group of cellular and electro-physical changes such as fibrosis, conduction disturbance, partly depolarized myocardial cells, etc. predispose patients to POAF and these abnormalities are best presented in electrocardiogram P-wave.

A notable finding in our study was the trend of CRP levels after CABG, which interestingly showed a decrease a few hours after operation before the expected rise which was observed 24h postoperatively. At any rate, there was no relationship between CRP levels and post-CABG AF, a finding widely documented in the literature (27, 28). For example, Gasparovic et al. in their study including 215 only "on-pump" cases, clearly reported that the magnitude of the inflammatory response does not influence the incidence of postoperative AF (13). Thus, the inflammation marker CRP cannot be used as a predicting factor for POAF.

One of the limitations of our study was that its data was derived from a single tertiary referral center; thus, the findings may not be easily generalizable. Furthermore, because patients were monitored for POAF only when they were in the hospital, patients who developed AF after discharge were not included in this study. A multicenter study with a longer follow-up period and assessment of long-term outcomes is suggested.

Conclusions

Patients prone to AF arrhythmia can be identified by measuring P-wave duration and height in preoperative ECG. Afterwards, anti-arrhythmic prophylaxis drugs such as Amiodarone can be administered to prevent POAF, hence reduce morbidity and mortality rates as well as treatment costs. HsCRP levels before and after CABG surgery may not contribute to AF prediction, although more comprehensive studies are required to answer this question.

Acknowledgements

This study was supported by Deputy of Research & Technology of Birjand University of Medical Sciences. We wish to sincerely thank the officials for their financial support of this study.

Conflict of interests

The authors have no conflict of interests to declare.

References

1. Filardo G, Hamilton C, Hamman B, Hebeler RF, Adams J, Grayburn P. New-onset postoperative atrial fibrillation and long-term survival after aortic valve replacement surgery. Ann Thorac Surg. 2010 Aug 31;90(2):474-9.

2. Filardo G, Hamilton C, Hebeler RF, Hamman B, Grayburn P. New-onset postoperative atrial fibrillation after isolated coronary artery bypass graft surgery and long-term survival. Circulation: Cardiovascular Quality and Outcomes. 2009 May 1;2(3):164-9.

3. Attaran S, Shaw M, Bond L, Pullan MD, Fabri BM. Atrial fibrillation postcardiac surgery: a common

but a morbid complication. Interact Cardiovasc Thorac Surg. 2011 May 1;12(5):772-7.

4. Wong JK, Lobato RL, Pinesett A, Maxwell BG, Mora-Mangano CT, Perez MV. P-wave characteristics on routine preoperative electrocardiogram improve prediction of new-onset postoperative atrial fibrillation in cardiac surgery. J Cardiothorac Vasc Anesth. 2014 Dec 31;28(6):1497-504.
5. Pilatis ND, Anyfantakis ZA, Spiliopoulos K, Degiannis D, Chaidaroglou A, Vergou G, Kimpouri K, Cokkinos DV. The role of BNP and CRP in predicting the development of atrial fibrillation in patients undergoing isolated coronary artery bypass surgery. ISRN Cardiol. 2013 Dec 25;2013.
6. Bakir I, Casselman FP, Brugada P, Geelen P, Wellens F, Degrieck I, Van Praet F, Vermeulen Y, De Geest R, Vanermen H. Current strategies in the surgical treatment of atrial fibrillation: review of the literature and Onze Lieve Vrouw Clinic's strategy. Ann Thorac Surg. 2007 Jan 31;83(1):331-40.
7. Budeus M, Hennersdorf M, Perings S, Röhlen S, Schnitzler S, Felix O, Reimert K, Feindt P, Gams E, Lehmann N, Wieneke H. Amiodarone prophylaxis for atrial fibrillation of high-risk patients after coronary bypass grafting: a prospective, double-blinded, placebo-controlled, randomized study. Eur Heart J. 2006 Jun 7;27(13):1584-91.
8. Mitchell LB, Exner DV, Wyse DG, Connolly CJ, Prystai GD, Bayes AJ, Kidd WT, Kieser T, Burgess JJ, Ferland A, MacAdams CL. Prophylactic oral amiodarone for the prevention of arrhythmias that begin early after revascularization, valve replacement, or repair: PAPABEAR: a randomized controlled trial. JAMA. 2005 Dec 28;294(24):3093-100.
9. Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, Mazer CD, Barash PG, Hsu PH, Mangano DT. A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA. 2004 Apr 14;291(14):1720-9.
10. Gungor H, Babu AS, Zencir C, Akpek M, Selvi M, Erkan MH, Durmaz S. Association of preoperative platelet-to-lymphocyte ratio with atrial fibrillation after coronary artery bypass graft surgery. Med Princ Pract. 2017;26(2):164-8.
11. Xiong F, Yin Y, Dube B, Page P, Vinet A. Electrophysiological changes preceding the onset of atrial fibrillation after coronary bypass grafting surgery. PLoS One. 2014 Sep 23;9(9):e107919.
12. Ishii Y, Schuessler RB, Gaynor SL, Hames K, Damiano RJ. Postoperative atrial fibrillation: The role of the inflammatory response. J Thorac Cardiovasc Surg. 2017 Jun 30;153(6):1357-65.
13. Gasparovic H, Burcar I, Kopjar T, Vojkovic J, Gabelica R, Biocina B, Jelic I. NT-pro-BNP, but not C-reactive protein, is predictive of atrial fibrillation in patients undergoing coronary artery bypass surgery. Eur J Cardiothorac Surg. 2010 Jan 1;37(1):100-5.
14. Kangasniemi OP, Biancari F, Luukkonen J, Vuorisalo S, Satta J, Pokela R, Juvonen T. Preoperative C-reactive protein is predictive of long-term outcome after coronary artery bypass surgery. Eur J Cardiothorac Surg. 2006 Jun 1;29(6):983-5.
15. Perez MV, Dewey FE, Marcus R, Ashley EA, Al-Ahmad AA, Wang PJ, Froelicher VF. Electrocardiographic predictors of atrial fibrillation. Am Heart J. 2009 Oct 31;158(4):622-8.
16. Magnani JW, Johnson VM, Sullivan LM, Gorodeski EZ, Schnabel RB, Lubitz SA, Levy D, Ellinor PT, Benjamin EJ. P wave duration and risk of longitudinal atrial fibrillation in persons≥ 60 years old (from the Framingham Heart Study). Am J Cardiol. 2011 Mar 15;107(6):917-21.
17. Rosenthal R, Cooper H, Hedges LV. Parametric measures of effect size. The handbook of research synthesis. 1994:231-44.
18. Anderson NG, Jolley IJ, Wells JE. Sonographic estimation of fetal weight: comparison of bias, precision and consistency using 12 different formulae. Ultrasound Obstet Gynecol. 2007 Aug 1;30(2):173-9.
19. Filardo G, Ailawadi G, Pollock BD, da Graca B, Sass DM, Phan TK, Montenegro DE, Thourani V, Damiano R. Sex Differences in the Epidemiology of New-Onset In-Hospital Post–Coronary Artery Bypass Graft Surgery Atrial Fibrillation. Circ Cardiovasc Qual Outcomes. 2016 Nov 1;9(6):723-30.
20. Haghjoo M, Basiri H, Salek M, Sadr-Ameli MA, Kargar F, Raissi K, Omrani G, Tabatabaie MB, Sadeghi HM, Tabaie AS, Baghaie R. Predictors of postoperative atrial fibrillation after coronary artery bypass graft surgery. Indian Pacing Electrophysiol J. 2008 Apr;8(2):94.
21. Rader F, Costantini O, Jarrett C, Gorodeski EZ, Lauer MS, Blackstone EH. Quantitative electrocardiography for predicting postoperative atrial fibrillation after cardiac surgery. J Electrocardiol. 2011 Dec 31;44(6):761-7.
22. Solak Y, Gul EE, Kayrak M, Atalay H, Abdulhalikov T, Turk S, Covic A, Kanbay M. Electrocardiographic P-wave characteristics in patients with end-stage renal disease: P-index and interatrial block. Int Urol Nephrol. 2013 Apr 1;45(2):511-7.
23. Chandy J, Nakai T, Lee RJ, Bellows WH, Dzankic S, Leung JM. Increases in P-wave dispersion predict

postoperative atrial fibrillation after coronary artery bypass graft surgery. Anesth Analg. 2004 Feb 1;98(2):303-10.

24. Jazi MH, Amirpour A, Zavvar R, Behjati M, Gharipour M. Predictive value of P-wave duration and dispersion in post coronary artery bypass surgery atrial fibrillation. ARYA Atheroscler. 2012;8(2):59.

25. Tsikouris JP, Kluger J, Song J, White CM. Changes in P-wave dispersion and P-wave duration after open heart surgery are associated with the peak incidence of atrial fibrillation. Heart & Lung: The Journal of Acute and Critical Care. 2001 Dec 31;30(6):466-71.

26. Cheema AN, Ahmed MW, Kadish AH, Goldberger JJ. Effects of autonomic stimulation and blockade on signal-averaged P wave duration. J Am Coll Cardiol. 1995 Aug 1;26(2):497-502.

27. Cosgrave J, Foley JB, Kelly R, McGovern E, Bennett K, Young V, Tolan M, Crean P, Kelleher D, Walsh MJ. Perioperative serum inflammatory response and the development of atrial fibrillation after coronary artery bypass surgery. Heart. 2005 Nov 1;91(11):1475-6.

28. Ishida K. Relation of inflammatory cytokines to atrial fibrillation after off-pump coronary artery bypass grafting. European Journal of Cardio-Thoracic Surgery. 2006 Apr 1;29(4):501-5.