



Prediction of clinical outcomes of patients treated with percutaneous coronary intervention for ST-Elevation myocardial infarction using familial history of premature coronary artery disease

Bahram Sohrabi¹ , Ahmad Separham², Hadi Habibolahi², Elgar Enamzadeh², Behnaz Ghamari³, Farid Karkon-Shayan*⁴

¹ Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

² Department of Cardiology, School of medicine, Tabriz University of Medical Sciences, Tabriz, Iran

³ Connective Tissue Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

⁴ Medical Philosophy and History Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Article info

Article History:

Received: 28 July 2018

Accepted: 25 Aug. 2018

ePublished: 15 Dec. 2018

Keywords:

Family Medical History,
Coronary Artery Disease,
Percutaneous Coronary
Intervention

Abstract

Introduction: ST-elevation myocardial infarction (STEMI) is a relatively common cause of mortality among patients. The effects of risk factors as predictors of mortality in patients has been shown in different studies. The present study was performed aiming to evaluate the association between a family history of premature coronary artery diseases (CADs) with clinical outcomes among patients treated with percutaneous coronary intervention (PCI) for STEMI.

Methods: This descriptive-analytical study was conducted in Shahid Madani Hospital of Tabriz University of Medical Sciences, Tabriz, Iran, on 200 patients with STEMI with a PCI. 100 out of these 200 patients had a family history of premature CAD. Patients were followed up within 48 hours after PCI, as well as one year after admission, and the secondary outcomes including myocardial infarction (MI), heart failure, ventricular arrhythmias (VAs), pulmonary edema, and death were evaluated.

Results: The mean age of the patients with positive and negative family history of premature CAD was 56.37 ± 8.20 and 61.72 ± 7.42 years, respectively. The mean age of the patients with a family history of a premature CAD was significantly lower than that of patients without a family history of a premature CAD ($P = 0.001$). There was no significant difference in the frequency of CAD risk factors, angiographic findings, and its complications, ST-segment resolution and frequency of secondary outcomes during 48 hours and one year after admission between the study groups ($P > 0.050$).

Conclusion: The present study showed that a family history of premature CAD does not predict the clinical outcomes in patients treated with PCI for STEMI which should be validated across future studies.

Citation: Sohrabi B, Separham A, Habibolahi H, Enamzadeh E, Ghamari B, Karkon-Shayan F. **Prediction of clinical outcomes of patients treated with percutaneous coronary intervention for ST-Elevation myocardial infarction using familial history of premature coronary artery disease.** J Anal Res Clin Med 2018; 6(4): 172-8. Doi: 10.15171/jarcm.2018.028

Introduction

Cardiovascular disease (CVD) is one of the most important causes of mortality in the United States and developed European countries and is one of the leading causes of death and disability in Iran.¹ Currently, the most commonly used therapeutic options are

coronary artery bypass grafting (CABG) and percutaneous transluminal coronary angioplasty (PTCA).² The latter is a less invasive and readily available method compared to the former.³

PTCA may be accompanied by several clinical adverse events during the procedure or

* Corresponding Author: Farid Karkon-Shayan, Email: faridkarkonshayan@yahoo.com



after it.⁴ Mortality, myocardial infarction (MI), cerebrovascular accidents, and emergency coronary artery bypass grafting (CABG) surgery are considered as major adverse clinical events (MACEs). Several studies have assessed risk factors for MACEs after PTCA.⁵⁻⁷ These risk factors are cerebrovascular disease, advanced age, cardiogenic shock, female sex, and treatment of the left main stem or graft lesions during PTCA.⁵ Identifying these risk factors help clinicians reduce the rate of MACEs in their patients.

The effects of these risk factors as predictors of mortality in patients with coronary artery disease (CAD) have been identified in several studies. However, the impacts of the positive family history of a premature CAD, as a major non-modifiable risk factor, on the clinical outcomes of these patients are not well-defined.⁸⁻¹⁰

It has been shown that a positive family history of premature CAD has a role in the impairment of the regulation of endothelium-dependent coronary blood flow. Evidence suggests that a positive family history of premature CAD genetically impairs the endothelium-dependent dilatation of the coronary arteries.¹¹ This association was found to be independent of other risk factors known to be involved in this regard such as hypercholesterolemia or advanced age. This may also have a role in the post-PTCA restenosis and its following MCAEs.¹² In addition, a link between positive family history and coronary artery calcification as well as its advancement was found in another study.¹³ These studies indicated the neglected importance of the positive family history of premature CAD in predicting clinical outcomes after PTCA. This study was carried out aiming to evaluate the association between a positive family history of premature CAD and clinical outcomes in patients with STEMI undergoing primary percutaneous coronary intervention (PPCI).

Methods

This descriptive, analytical study was conducted in Shahid Madani Hospital of

Tabriz University of Medical Sciences, Tabriz, Iran, on 200 patients with STEMI with a PCI. Of these 200 patients, 100 had a family history of premature CAD. The duration of the study was 18 months from December 2015 to June 2017.

Inclusion and exclusion criteria: The inclusion criteria for this study included: 1. Patients with STEMI. STEMI was defined as an increase in the cardiac enzymes in an individual with typical chest pain and ST elevation of 1 mV in two adjacent limb or precordial leads, except in V2 and V3 leads. In V2 and V3 leads, ST elevations of ≥ 2 -2.5 mV in men and ≥ 1.5 mV in women were considered to be positive for STEMI. 2. Patients who were candidates for PCI, and 3. Patients with no positive family history of a premature CAD.

Moreover, every patient with the following characteristics was excluded from the study; 1. Patients with mechanical complications of MI, such as ventricular septal defect (VSD) or mitral regurgitation (MR), severe valvular disease, cardiomyopathy, cardiogenic shock, cardiopulmonary arrest, or an inexplicable electrocardiogram (ECG), 2. Failure to perform angioplasty due to the coronary artery anatomy (Multivessel or normal CAD), and 3. Patients who unwilling to participate in the study.

Of the 379 patients with STEMI, 182 (48.02%) patients had a family history of a premature CAD. Considering the inclusion and exclusion criteria of the study, 200 patients with STEMI (100 with a positive family history of premature CAD and 100 without CAD family history) were randomly selected using convenience sampling method and included in the study. Patients' demographic data including age as well as sex, risk factors for CAD and hemodynamic symptoms of the patients based on Killip Classification, were recorded at the time of admission to the emergency department. Patients were then divided into two groups based on the family history of premature CAD (a history of cardiovascular events including MI or a history of PCI in less

than 55 years of age in the father or brother of the patient or under 65 years of age in the mother or sister of the patient). Patients in both groups were evaluated for PCI findings during and after the procedure. These findings included final thrombolysis in myocardial infarction (TIMI) score, complications during angiography, including acute vessel closure, lack of reflow, and acute stent thrombosis. Furthermore, the percentage of drop of ST-segment elevations after PCI was calculated using ECG. Patients were evaluated for secondary outcomes including secondary MI, heart failure, ventricular arrhythmia (VA), pulmonary edema, and death 48 hours and one year after admission and the data were recorded (Figure 1).

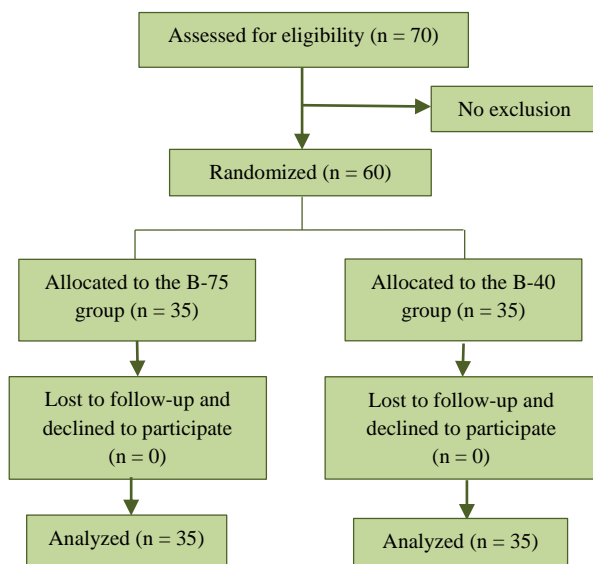


Figure 1. CONSORT chart of the studied population

The SPSS software (version 16, SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. The obtained data were expressed as mean \pm standard deviation (SD), frequency, and percentage. The normal distribution of data was evaluated using the Kolmogorov-Smirnov (K-S) test. Chi-square test was used to compare the qualitative variables, and independent t-test or Mann Whitney U test was applied to compare the quantitative variables. In all comparisons, $P \leq 0.050$ was considered as statistically significant. There was no previous study to be used in order for determining the sample size

of the study. Thus, the sample size was determined using the formula and considering $\alpha = 0.05$, the power of 80%, and the 95% confidence interval (CI). This yielded an initial sample size of 100 patients for each group.

Informed written consent was obtained from the patients or their first-degree relatives. All of the patients' information was confidential, and their personal information was not mentioned anywhere.

Results

The results showed that in the group with positive family history, 64 (64.0%) patients and 36 (36.0%) were men and women, respectively. Similarly, in the group without a prior family history of a premature CAD, 70 (70.0%) and 30 (30.0%) patients were men and women, respectively. The analysis showed no significant difference between the groups in gender ($P = 0.452$).

Moreover, the mean age of the patients with a family history of premature CAD was 56.37 ± 8.20 years ranging between 45 and 71 years. However, the mean age of the patients with no family history of premature CAD was 61.72 ± 7.42 years ranging between 50 and 74 years. The mean age of patients with positive history was significantly lower than that of those with negative family history ($P = 0.001$).

Lesion location: It was found that 69 (69.0%), 28 (28.0%), and 3 (3.0%) patients had respectively anterior STEMI, inferior STEMI, and lateral MI in the group with positive family history. However, in the other group, 68 (68.0%), 25 (25.0%), and 7 (7.0%) patients had anterior STEMI, inferior STEMI, and lateral MI, respectively. There was no significant difference in the location of STEMI between the two groups ($P = 0.411$).

CAD risk factors: There was no significant difference in the frequency of CAD risk factors including diabetes mellitus (DM) ($P = 0.414$), hypertension ($P = 0.249$), hyperlipidemia ($P = 0.293$), and smoking ($P = 0.395$) between the two study groups. In addition, there were no significant differences between the two groups in the

hemodynamics at the time of admission to the emergency department.

Killip classification: Analysis showed no significant difference in Killip classification between the two groups (Table 1).

Table 1. The comparison of the Killip classification of the patients in the two groups

Killip class	Positive history for premature CAD [n (%)]	Negative history for premature CAD [n (%)]	P
Class 1	58 (58)	62 (62)	0.194
Class 2	21 (21)	13 (13)	
Class 3	7 (7)	14 (14)	
Class 4	14 (14)	11 (11)	

CAD: Coronary artery disease

Angiographic findings: Analysis showed no significant difference in the angiographic findings and TIMI score between the two study groups (Table 2).

Complications of angiography: There was no significant difference in the complications of angiography between the two study groups (Table 3).

ST-segment elevation drop: The results of the present study showed that in the group with positive family history, ST-segment elevation drop was below 50%, 50-70%, and higher than 70% among 15 (15.0%), 21 (21.0%), and 64 (64.0%) patients, respectively. In the group without a family history of a premature CAD, the drop was under 50%, 50-70%, and higher than 70% among 15 (15.0%), 23 (23.0%), and 62 (62.0%) patients, respectively. There were no significant differences between the two groups in

ST-segment elevation drop ($P = 0.941$).

Secondary outcomes: No significant difference was found in the secondary outcomes in 48-hour and one-year follow-ups after PCI between the two study groups (Tables 4 and 5).

Discussion

There has been a controversy over the role of a positive family history of premature CAD in the prediction of cardiovascular risk.^{14,15} In some studies such as the Adult Treatment Panel III (ATP III) guidelines, there was no additive effects of positive family history on the risk prediction of CAD in individuals.¹⁶ On the other hand, other studies including the ones conducted by Assmann et al.,¹⁷ Hippisley-Cox et al.,¹⁸ and Ridker et al.¹⁹ consider it as a significant risk factor for all CVDs and not only CAD.

Here, the hypothesis that whether the positive family history of CAD predicts MACEs after PCI for STEMI, was tested. This study proved no significant association between a positive family history of premature CAD and secondary outcomes including secondary MI, heart failure, VA, pulmonary edema, as well as death in patients undergoing PCI for STEMI 48 hours and one year after the procedure.

In this regard, Rizzo et al. assessed the risk factors for CAD and their impacts on the outcomes of 135 patients who underwent PTCA in a one-year period of the study. This study showed a negative association between the presence of multivessel disease or DM with MACEs after PTCA.

Table 2. The comparison of angiographic findings and thrombolysis in myocardial infarction (TIMI) score between the two groups

Angiographic findings/TIMI score	Positive history for premature CAD [n (%)]	Negative history for premature CAD [n (%)]	P
1 vessel disease	44 (44)	45 (45)	> 0.999
2 vessel disease	56 (56)	55 (55)	
TIMI score = 0	54 (54)	54 (54)	0.194
TIMI score = 1	7 (7)	13 (13)	
TIMI score = 2	3 (3)	5 (5)	
TIMI score = 3	36 (36)	28 (28)	

CAD: Coronary artery disease; TIMI: Thrombolysis in myocardial infarction

Table 3. The frequency of angiographic complications of the patients in two study groups

Complication	Positive history for premature CAD [n (%)]	Negative history for premature CAD [n (%)]	P
No reflow	7 (7)	9 (9)	0.584
Slow flow	12 (64)	8 (8)	
Acute stent Thrombosis	0 (0)	0 (0)	-
Acute vessel closure	0 (0)	0 (0)	-

CAD: Coronary artery disease

Table 4. The comparison of the frequency of secondary outcomes within 48 hours of admission in the two groups

Secondary outcomes	Positive history for premature CAD [n (%)]	Negative history for premature CAD [n (%)]	P
Secondary MI	4 (4)	5 (5)	0.586
Heart failure	2 (2)	3 (3)	
VA	5 (5)	3 (3)	
Death	2 (2)	0 (0)	

CAD: Coronary artery disease; MI: Myocardial infarction; VA: Ventricular arrhythmia

This study also proved the strong predictive value of the family history of CAD in clinical outcomes after PTCA during one-year follow-up of the study. The authors concluded that patients with this feature have the highest risk of developing adverse outcomes after angiography and special care should be given to this set of patients.⁴

Table 5. The comparison of the frequency of secondary outcomes after one year of admission in the two groups

Secondary outcomes	Positive history for premature CAD [n (%)]	Negative history for premature CAD [n (%)]	P
Secondary MI	6 (6)	5 (5)	0.756
Heart failure	2 (2)	5 (5)	
VA	1 (1)	2 (2)	
Death	3 (3)	2 (2)	

CAD: Coronary artery disease; MI: Myocardial infarction; VA: Ventricular arrhythmia

In another study, Kim et al. evaluated the effects of positive family history on the manifestations and outcomes of coronary heart disease in 11612 patients with acute MI. Patients in the group with a positive family history were often men and younger.

Positive family history was also associated with a higher total cholesterol level, triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) among men. However, no differences were found between

patients with positive and negative family history in MACEs.²⁰ In the present study, similar to the study by Kim et al.,²⁰ the mean age of patients with positive family history was significantly less than that of patients without a family history, however there was no significant difference in the risk factors of CAD and MACEs after PCI between the two groups.

In another study, Padilla et al. examined the incidence of MACEs after PTCA in a group of Hispanic patients. In this study, a marginally significant relationship was found between positive family history with MACEs during admission. However, the association was shown to be weak after discharge.²¹ Differences in the reported results may be due to the variations in the sample selection, the duration of follow-up of the patients, and the cases under investigation.

Conclusion

Few studies have assessed the relationship between family history of premature CAD and clinical outcomes after PTCA among patients with STEMI. As appears, these studies have shown a lower age of onset of CAD in patients with a positive family history of premature CAD and a higher incidence of post-PTCA MCAEs. In this study, a lower age of onset of CAD was also found among these patients. However, the link between positive family history and MACEs was not found to be significant. In addition, none of the assessed parameters including lesion location, CAD risk factors, Killip classification, and angiographic findings were different between the two study groups. Due to the clinical significance of the subject and the interference of other factors in this field, further studies are necessary for better decision making.

Acknowledgments

The authors would like to appreciate all the patients for their contribution to the study and patience throughout the work.

Authors' Contribution

Study concept and design: Bahram Sohrabi, Ahmad Separham

Acquisition of data: Hadi Habibolahi, Elgar Enamzadeh, Behnaz Ghamari, Farid Karkon Shayan

Analysis and interpretation of data: Farid Karkon Shayan

Drafting of the manuscript: Hadi Habibolahi, Elgar Enamzadeh, Behnaz Ghamari, Farid Karkon Shayan

Critical revision of the manuscript for important intellectual content: Bahram Sohrabi, Ahmad Separham

Statistical analysis: Farid Karkon-Shayan
Administrative, technical, and material support: Bahram Sohrabi, Ahmad Separham
Study supervision: Bahram Sohrabi, Ahmad Separham.

Funding

This study was based on a dissertation by Hadi Habibollahi submitted to and supported by the cardiovascular research center of Tabriz University of Medical Sciences.

Conflict of Interest

Authors have no conflict of interest.

Ethical Approval

This study was implemented after approval by the Medical Ethics Committee of Tabriz University of Medical Sciences.

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