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ARYA Atherosclerosis

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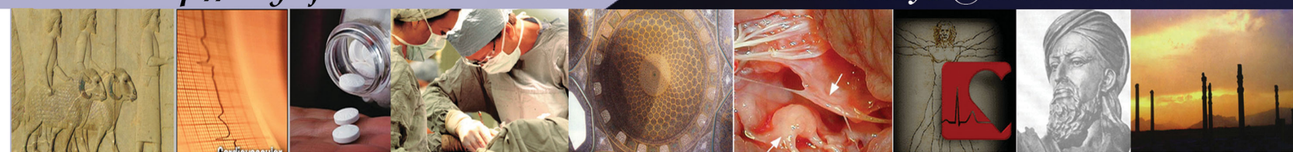

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Postal Code: 8166173414 Tel: + 98 31 36115206 Fax: +98 31 36115311
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* All the words of the article containing the references; each table is considered as 300 words.

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The effect of reflexotherapy and massage therapy on vital signs and stress before coronary angiography: An open-label clinical trial

Ali Khaledifar[(1)], Marzeih Nasiri[(2)], Borzoo Khaledifar[(3)], Arsalan Khaledifar[(2)], Ali Mokhtari[(4)]

Original Article

Abstract

BACKGROUND: Complementary medicine interventions are now successfully used to reduce stress as well as to stabilize hemodynamic indices within different procedures. The present study aimed to examine the effect of massage therapy and reflexotherapy on reducing stress in patients before coronary angiography.

METHODS: In this open-label clinical trial, 75 consecutive patients who were candidate for coronary angiography were randomly assigned to receive reflexotherapy (n = 25), or massage therapy (n = 25), or routine care (n = 25) before angiography. The Spielberger State-Trait Anxiety Inventory was used to determine the stress level of patients before and after interventions and vital signs were also measured.

RESULTS: Improvement in diastolic blood pressure, heart rate, and respiratory rate was shown in the reflexotherapy group, and similar effects were observed following other interventions including massage therapy and routine resting program. In subjects who received reflexotherapy the level of stress decreased slightly compared with the other two groups. However, following interventions the level of stress in reflexotherapy group was shown to be lower than other study groups.

CONCLUSION: Reflexotherapy before coronary angiography can help to stabilize vital sign as well as reduce the level of stress. The effect of massage therapy was limited to reducing stress.

Keywords: Reflexotherapy, Massage Therapy, Coronary Angiography, Vital Signs, Emotional Stress

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Introduction

Over the past 30 years, major advances have been made in the prevention, diagnosis, treatment, and rehabilitation of cardiovascular diseases. Despite the decline in mortality rate, heart diseases still have a great share in mortality and morbidity entire the world. At the beginning of the 20th century, heart diseases were cause of less than 10% of the total deaths in the world, while at the end of the 20th century, they were reported to be the main reason for half of all deaths in the developed countries and 25% of deaths in developing countries.[1] Also, 25 million annual deaths from cardiovascular diseases are expected by 2020.[2] Furthermore, about 50% of deaths due to cardiovascular events are associated with cardiac arrhythmias.[3,4] One of the most common diagnostic and therapeutic interventions in managing the patients with ischemic heart disease is angiography.[5] This procedure is the fourth common invasive intervention in Iranian patients.[6] According to the recent reports, about 80% of patients undergoing angiography have different levels of stress during the procedure[6] and fear of this procedure and its afterward revascularization have been reported in 60% of patients.[7] The main reasons for this fear include fear of death, potential problems, lack of knowledge of environmental change, and fear of changes in postoperative lifestyle.[8] Also, hospitalization and waiting for surgery are major sources of stress and tension in these patients.[9] Moreover, patients with preoperative stress experience more postoperative pain, less relief of symptoms, reduced physical capacity, dissatisfaction with treatment, more re-admission, lower improvement and lower level of quality of life after

1- Medical Intern, Student Research Committee, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
2- Associate Professor, Department of Cardiology, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
3- Associate Professor, Department of Surgery, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
4- General Practitioner, Department of Internal Medicine, School of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
Correspondence to: Arsalan Khaledifar, Email: khaledifar.ar.dr@gmail.com

surgery.[10] High stress before surgery also impairs the patient's coping mechanisms.[11,12] Hence, coronary angiography can be accompanied with psychological problems in addition to physical complications. Thus, it is necessary to reduce stress in these subjects using appropriate physical and psychological interventions. It is believed that medication might not to be the best way to reduce stress because of its related adverse events.[12,13]

In the past decade, interest in various forms of alternative medicine for patients, families, and health care professionals had been increasing. These complementary medicine interventions can be successfully used to reduce patient stress particularly in anxious patients undergoing interventional procedures.[14] Massage therapy and reflexotherapy are common interventions that are used in alternative medicine to facilitate health promotion and patient care in medical centers.[15] International Center for Complementary and Alternative Medicine has divided interventions in this medicine into five categories of replacement therapy, interventions in mind, body biologic therapy, energy therapy, and therapy based on manipulation of the body manually such as massage therapy and reflexotherapy.[16]

Considering the fact that non-pharmacological interventions are used in reducing symptoms of stress especially in patients who are candidate for cardiac interventions, we aimed to examine the effect of massage therapy and reflexotherapy on the management stress in this group of patients.

Materials and Methods

In this randomized clinical trial, 75 consecutive patients were included who were candidate for coronary angiography in Hajar hospital in Shahrekord, Iran, in August 2013. The main inclusion criteria were age older than 18 years, orientation in place, time, and environment, lack of mental retardation, blindness and deafness, absence of active psychological disorders or use of anti-stress drugs within recent 48 hours, absence of severe systemic illnesses, no previous history of hemorrhage, epilepsy, thrombosis, kidney or gall bladder stones, and no history of arthritis, burns, wounds and fractures in the limbs. All subjects provided written informed consent, and the Shahrekord University of Medical Sciences ethics committee approved our protocol.

The study subjects were randomly assigned to receive reflexotherapy, massage therapy, or no intervention as the control (with an ineffective massage and reflexotherapy) before angiography. In the first group, the procedure of reflexotherapy was first described to the patients and before the starting the procedure, vital signs were measured by a nurse who was aware of the type of the intervention. Reflexotherapy was done for each patient for 30 minutes, first for the left foot and then for the right foot (15 minutes each). Initially, the relaxation method was used from the footstalk toward the sole (plantar surfaces) at the beginning of the session. Then, four major plantar reflexology points (solar plexus, pituitary, heart and liver) were put under pressure using the thumbs.[17] Other reflexology parts of the plantar surface of the foot were also massaged and the intervention was put to an end with massaging the solar plexus by the researcher. The vital signs were measured again after finishing the intervention.[18] In the second group, massage therapy was done by similar physiotherapist throughout the protocol and consisted of neck, shoulder and back massages for 20 minutes. The massages were started with light compression by the inner regions of the fingers and progressed to hard compression. Manual kneading, friction (i.e., digital compression with the thumb) on trigger points, cervical traction, followed by organization in all planes (e.g., front, back, and sides). The massage was finished with light manual compression. Vital signs were also assessed at the beginning and the end of the maneuvers. The control group received only routine intervention including resting for 30 minutes before angiography. The study was registered in Iranian Randomized Control Trial (IRCT) (IRCT2016101719316N3).

The preoperative medical measurements consisted of obtaining information regarding the patients' demographics, personal characteristics, and duration of disease using a special questionnaire. The Spielberger State-Trait Anxiety Inventory was used to determine patient stress level before any intervention. The questionnaire included 20 items on the basis of 4-point scale with the scores ranging from 0 (absence) to 3 (severe). The cutoff scores for stress are as follows: < 20 no anxiety; 20-39 mild; 40-59 moderate, and > 60 severe.[19] The validity and reliability of the questionnaire were assessed by Hazavehei et al.,[20] and Rymazewska and Kiejna.[21] The test-retest reliability (r = 0.97) and validity of the Persian version of the questionnaire was described by Molavi Vardanjani et al.[22] The vital signs of the subjects (body temperature, pulse rate, respiratory rate, blood pressure were) were also measured immediately before and after angiography

and recorded in third study questionnaire.

Temperature was measured orally using classic glass thermometer. The heart rate was determined using a software peak detector. Blood pressure was measured through the catheter at cath lab. Respiratory rate was measured by counting breathes for 60 s using a timer.

Results were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) for quantitative variables and were summarized by frequencies and percentages for categorical parameters. Continuous variables were compared using one-way analysis of variance (ANOVA) or non-parametric Kruskal-Wallis test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the groups. Normal assumption was tested with Kolmogorov-Smirnov test. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with the expected value of less than 5 were observed. The difference in study variables after interventions was compared using the paired t-test or Wilcoxon test. The statistical software SPSS software (version 20.0, IBM Corporation, Armonk, NY, USA) was used. P-values of 0.05 or less were considered statistically significant.

Results

The study groups who received reflexotherapy, massage therapy, or routine intervention were similar in terms of baseline characteristics including male gender distribution (36.0%, 56.0%, and 60.0%, respectively, P = 0.215, Table 1). Regarding vital signs at baseline, the mean systolic blood pressure was significantly similar in the three study groups both before and after the interventions (Table 2). Although means of three indices of diastolic blood pressure, heart rate, and respiratory rate were significantly higher in those patients who received reflexotherapy compared with other two groups before interventions, but there were no differences in these parameters across the three groups after interventions. Improvement in vital parameters of diastolic blood pressure, heart rate, and respiratory rate was shown in the reflexotherapy group.

The mean body temperature was comparable in the three groups before interventions, while it was significantly lower in the two groups which received reflexotherapy or massage therapy compared with the control group (Table 2). With regard to the changes in stress level, the subjects who received reflexotherapy had higher level of stress compared with other two groups at the baseline, however, following interventions the level of stress in reflexotherapy group decreased slightly in comparison with other study groups (Table 2). Furthermore, applying reflexotherapy and massage therapy led to reduced stress level in the two groups (Figure 1).

Discussion

According to our findings of this study and regarding beneficial results of reflexotherapy on vital sign following angiography, improvement in some of vital parameters including diastolic blood pressure, heart rate, and respiratory rate was shown in the group that received reflexotherapy, while these effects were not clearly observed following other interventions including massage therapy and routine care.

Table 1. Baseline characteristics of the study participants stratified by intervention group

Characteristics	Reflexotherapy	Massage therapy	Routine method	P
Age (year)	67.2 ± 11.8	67.0 ± 11.1	64.7 ± 12.1	0.702
Disease duration (year)	4 (1.5-8.5)	3 (1.0-4.0)	4 (1.5-5.0)	0.273
Gender [n (%)]				0.215
Male	9 (36.0)	14 (56.0)	15 (60.0)	
Female	16 (64.0)	11 (44.0)	10 (40.0)	
Occupation state [n (%)]				0.057
Housekeeper	14 (56.0)	11 (44.0)	10 (40.0)	
Self-employed	3 (12.0)	12 (48.0)	8 (32.0)	
Employed	2 (8.0)	0 (0.0)	2 (8.0)	
Retired	6 (24.0)	2 (8.0)	5 (20.0)	
Education level* [n (%)]				0.073
Illiterate	17 (68.0)	14 (56.0)	10 (40.0)	
Sub-diploma	3 (12.0)	9 (36.0)	12 (48.0)	
Diploma	2 (8.0)	2 (8.0)	2 (8.0)	
College degree	2 (12.0)	0 (0.0)	1 (4.0)	

Analysis of variance and chi-square test were used; P-values of 0.05 or less were considered statistically significant

* Tukey's post hoc analysis was used

Table 2. The difference in the vital signs before and after study interventions

Characteristics		Reflexotherapy	Massage therapy	Control group	P
Systolic blood pressure	Before intervention	144.40 ± 27.60	140.80 ± 16.00	132.60 ± 16.70	0.129
	After intervention	139.60 ± 26.40	137.80 ± 15.20	132.60 ± 16.40	0.443
	Difference	4.80 ± 3.67	3.00 ± 3.22	0.00 ± 1.44	< 0.001
	P	< 0.001	< 0.001	> 0.999	
Diastolic blood pressure	Before intervention	86.60 ± 13.50	76.40 ± 12.10	77.80 ± 8.20	0.005
	After intervention	82.40 ± 13.00	75.40 ± 11.30	76.60 ± 8.38	0.064
	Difference	4.20 ± 5.89	1.00 ± 2.88	1.20 ± 3.61	0.017
	P	0.002	0.096	0.110	
Temperature	Before intervention	36.90 ± 0.27	36.90 ± 0.22	37.00 ± 0.14	0.068
	After intervention	36.80 ± 0.26	36.80 ± 0.22	37.00 ± 0.15	0.008
	Difference	0.70 ± 0.13	0.06 ± 0.11	0.02 ± 0.21	0.543
	P	0.009	0.016	0.574	
Respiratory rate	Before intervention	20.80 ± 2.10	20.10 ± 1.90	18.20 ± 0.80	0.608
	After intervention	18.60 ± 1.40	18.50 ± 1.30	18.20 ± 0.80	< 0.001
	Difference	-2.30 ± 1.30	-1.60 ± 1.10	-0.04 ± 0.90	< 0.001
	P	< 0.001	< 0.001	0.824	
Heart rate	Before intervention	82.40 ± 4.70	79.80 ± 4.40	78.20 ± 5.50	0.013
	After intervention	76.20 ± 4.80	75.00 ± 4.30	77.80 ± 5.50	0.163
	Difference	6.30 ± 2.56	4.76 ± 2.79	0.40 ± 2.50	< 0.001
	P	< 0.001	< 0.001	0.438	
Stress	Before intervention	60.60 ± 7.20	51.40 ± 6.80	47.80 ± 9.60	< 0.001
	After intervention	34.70 ± 4.70	39.70 ± 4.80	46.50 ± 9.20	< 0.001
	Difference	25.90 ± 5.94	11.70 ± 5.00	1.40 ± 1.80	< 0.001
	P	< 0.001	< 0.001	0.438	

P-values of 0.05 or less were considered statistically significant;

In fact, reflexotherapy could effectively reduce diastolic blood pressure, heart rate and also respiratory rate leading to higher level of relaxation in these patients as well as lower risk of hemodynamic instability during this procedure. However, the change in systolic blood pressure was not significant following reflexotherapy. Similar to our results, Molavi Vardanjani et al. showed reflexology can decrease the stress level before coronary angiography.[22]

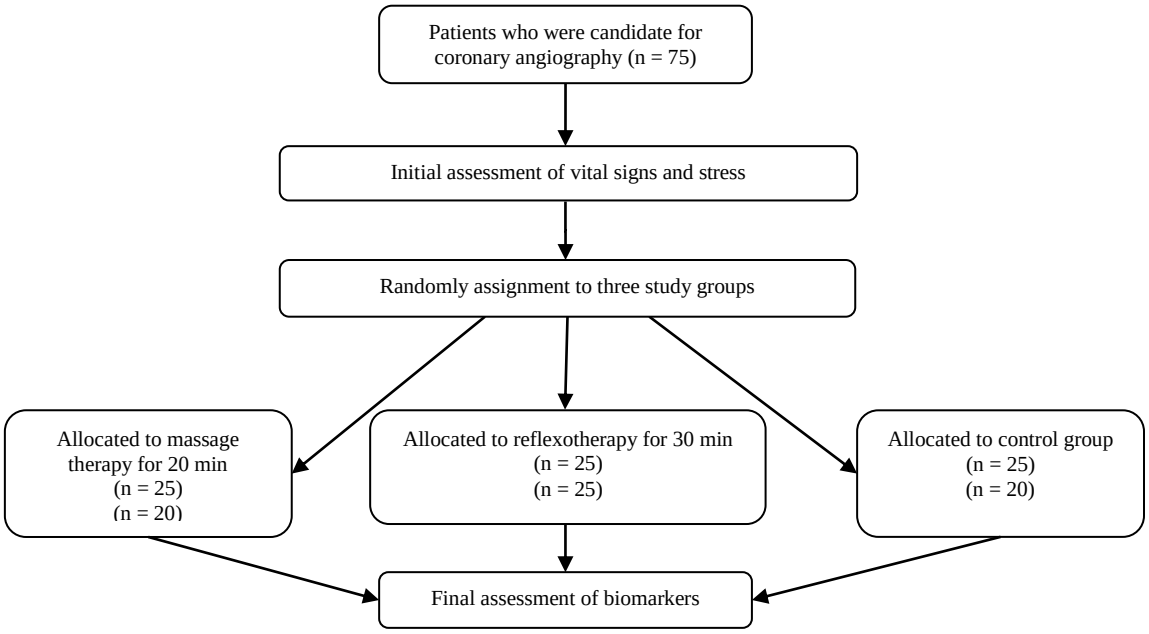

Figure 1. Consort chart for the study

The influence of reflexotherapy in hemodynamic parameters has been reported to be unclear. Moeini et al. similarly showed that the average heart rate and respiratory rate per minute had slightly decreased after reflexotherapy.[23] McVicar et al. indicated significant decrease in the systolic blood pressure and heart rate, but not diastolic blood pressure after reflexotherapy.[24] Park et al. also showed that reflexotherapy resulted in decreased systolic blood pressure but not diastolic blood pressure.[25] Besides, Quattrin et al. in a study on patients with cancer indicated significant decrease in all indices including systolic blood pressure, diastolic blood pressure, heart rate and respiratory rate after 30 minutes of reflexotherapy.[16] According to the central role of autonomic system on regulating vital signs in response to physical, psychological, and environmental stimulates, it is suggested that the effects of reflexotherapy on improvement of these vital parameters are via parasympathetic processes. Kuhn et al. believed that reflexotherapy causes relaxation in hyperactive areas of the body and stimulates the passive areas and consequently causes a balance and relaxation of the body.[26] Furthermore, Fritz revealed that manipulating foot in reflexotherapy induces the activity of the parasympathetic nervous system.[27] Moreover, the slight effects of massage therapy on improving vital signs can also be related to its impact on autonomic system. Results of Fritz study showed that massage therapy promotes a significant decrease in cortisol level from the baseline (31% on average) and increases active neurotransmitters such as serotonin (28% on average) and dopamine (31% on average).[27] Mean stress score was 60.6 ± 7.2 before intervention which is much less compared to the 91.4 ± 21.2 reported in a study done by Quattrin et al.[16] McVicar et al. demonstrated that reflexotherapy has an effect on anxiety and could be able to decrease the stress,[24] that was a predictable result, since anxiety, unlike state type, is not a short-term state and needs long-time intervention. In this research also the stress reduced after reflexotherapy. Another study was designed to evaluate the effect of reflexotherapy on mental stress. Their study revealed that there were significant decreases in blood pressure after reflexotherapy.[23]

Massage therapy may also promote parasympathetic activation,[28] which causes reductions in heart rate, blood pressure, and breathing, increase the release of hormones (e.g., endorphins), and decrease in stress level.[18,29] In this line, it seems that the effects of both reflexotherapy and massage therapy on reducing the level of stress is strongly associated with its effect as parasympathetic stimulator. Also, the physical effects of these interventions can mediate their beneficial effects on mental relaxation leading to reduction in stress.

Conclusion

In conclusion, our study demonstrates that scheduling reflexotherapy before coronary angiography can help to stabilize vital sign as well as reduce the level of stress within this procedure, and may lead to better outcome and lower rate of complications. However, the effect of massage therapy is limited to reducing the level of stress.

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Conflict of Interests

Authors have no conflict of interests.

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Healthy eating index and cardiovascular risk factors among Iranian elderly individuals

Nafiseh Rashidipour-Fard[(1)], Majid Karimi[(1)], Sahar Saraf-Bank[(2)], Mohammad Hassan Baghaei[(1)], Fahimeh Haghighatdoost[(2)], Leila Azadbakht[(3)]

Original Article

Abstract

BACKGROUND: Concurrent with increase in life expectancy, the prevalence of chronic diseases such as cardiovascular diseases (CVD) has also increased. Therefore, the aim of this study was to evaluate the association between healthy eating index (HEI) score and CVD risk factors among Iranian elderly.

METHODS: This cross-sectional study was performed on a sample of elderly persons from Isfahan, Iran, in 2013. Totally, 107 retired subjects were entered in statistical analysis. A semi-quantitative food frequency questionnaire was used to assess the dietary intake of participants. Anthropometric measurements and blood pressure of participants were determined. Fasting blood samples were taken for biochemical assessments.

RESULTS: The results of linear regression determined a significant inverse association between HEI score and homeostasis model assessment of insulin resistance [HOMA-IR, β = -0.238 (-0.426, -0.048)], fasting blood glucose [β = -0.194 (-0.383, -0.004)], and high-sensitivity C-reactive protein [hs-CRP, β = -0.196, (-0.386, -0.005)]. In addition, a significant positive association was observed between HEI score and high density lipoprotein cholesterol [HDL-C, β = 0.196 (0.006, 0.385)] levels. However, after adjusting for confounding variables, these significant associations were disappeared except for hs-CRP [β = -0.074 (-0.145, -0.003)].

CONCLUSION: Healthy eating index was associated with reduced risk of cardiovascular risk factors in old people. It seems that more adherence with healthy eating index could provide cardio-protective effects in elderly persons.

Keywords: Healthy Diet, Risk Factors, Cardiovascular Diseases, Iran

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Introduction

It has been reported that ageing (more than 60 years) is increasing rapidly worldwide and this increment is more than other age groups. It is estimated that from 1970 to 2025 a growth of 223% will occur in elderly subjects,[1] and the elderly population of the world will grow from 420 million to 973 million during 2000 to 2030.[2] Approximately, half of the elderly individuals live in developing countries. In Iran, the second largest country of the Middle East, the aging of population has become a concern. About 8.2% of Iranians are old and it is estimated that the elderly population will reach to 26% by 2050.[3]

Concurrent with increase in the life expectancy, the prevalence of chronic diseases such as cardiovascular diseases (CVD) has also increased.[4] Cardiovascular diseases are considered as the main cause of death throughout the world and about 30% of deaths are attributed to CVD.[1,5] To date, several risk factors have been identified for CVD, and it is well established that nutritional habits and dietary intakes are strongly related to CVD events.[4]

In this context, most of the previous studies have focused on macro-nutrients (carbohydrate and protein) or single foods (yogurt, rice, and legumes).[6-9] However, dietary intakes are complex and may have different effects on the risk of chronic diseases rather than single foods. Therefore, studying diet quality scores may be a practical approach in the

1- Shahid Motahari Hospital, Fooladshahr, Isfahan, Iran
2- Food Security Research Center AND Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran
3- Professor, Food Security Research Center AND Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan AND Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute AND Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences Tehran, Iran
Correspondence to: Leila Azadbakht, Email: azadbakht@hlth.mui.ac.ir

field of diet and health associations, particularly among elderly. So far, few studies have focused on diet quality of elderly and showed the protective effects of high quality diets against CVD risks and mortality rate.[4,10,11] Almost all earlier studies have shown that the diet of the majority of elderly persons needs improvement.[12,13] However, to the best of our knowledge, there is no report regarding the diet quality of Iranian elderly and its association with CVD risk factors whereas Iran would be the third fastest aging nation worldwide after United Arab Emirates and Bahrain between 2010 and 2050.[14]

Due to the direct link between ageing and suffering from a variety of chronic diseases like CVD, hypertension, stroke and dyslipidemia,[1] it is necessary to identify major health hazards in this population and inform public health policy makers to develop some strategies to reduce the economic burden of such preventable chronic diseases. Therefore, the aim of this study was to evaluate the association between healthy eating index (HEI) score and CVD risk factors among Iranian elderly.

Materials and Methods

This cross-sectional study was performed on a sample of elderly people from Isfahan, Iran, in 2013. Totally, 120 retired subjects (male and female) aged more than 60 years were enrolled from Shahid Motahari Hospital, Fooladshahr, Isfahan, using simple random sampling method during January 2014 to January 2015. Exclusion criteria were as follows: being on a specific diet, suffering from an inflammatory disease, and receiving hypoglycemic or hypolipidemic agents. Furthermore, those who reported daily energy intake out of range of 800-4200 kcal and those who did not complete more than 70 items of food frequency questionnaire (FFQ) were excluded from study. Finally, 107 retired persons (84.4% male) were included in the analyses. Enough sample size was calculated based on high-sensitivity C-reactive protein (hs-CRP) as the main dependent variable.[15] Ethics Committee of Isfahan University of Medical Sciences approved the study protocol. All participants completed a written informed consent before entering the study.

Using a validated 168-item semi-quantitative FFQ, dietary intake of participants were assessed.[16] The FFQ considered the frequency of consumption of each food item in scale of usual portion size. A trained dietitian completed all FFQs via face to face interview. The mean intake of each food item (in gram) was estimated through multiplying accurate portion sizes, obtained from household measures, by mean frequency intake. By using a modified version of Nutritionist IV software for Iranian foods (version 7.0, N-Squared Computing, Salem, OR, USA), the mean intake of macronutrients and micronutrients were calculated. To calculate HEI, 10 components were considered.[17] The frequency of consumption of cereals, vegetables, fruits, meats and total dietary diversity was scored 10 and 0 in the highest and lowest consumption, respectively. The frequency of consumption of total fat, saturated fatty acids, cholesterol and sodium was scored 10 and 0 in the lowest and highest consumption, respectively. Total HEI score was obtained from summing the scores of these 10 components. For dietary diversity score (DDS) calculation, several subgroups were considered for each five main food groups.[18] Grains were subdivided to refined bread, biscuits, macaroni, wholegrain bread, corn flakes, rice and refined flour. Vegetables were subdivided to vegetables, potato, tomato, other starchy vegetables, legumes, yellow vegetables and green vegetables. Fruits were classified as fruit and fruit juice, berries and citrus. Meats consisted of red meat, poultry, fish and eggs. Dairy products were subdivided to milk, yoghurt and cheese. If a person consumes at least once a day from each subgroup, he/she will get the full score of that subgroup.[19] The score of each main food group was calculated by summing the consumption frequency of each subgroup divided by the number of subgroups and then multiplied by 2. Total DDS score was obtained from sum of the scores of each 5 main food groups.

Body weight, waist circumference and height were measured by an expert. Weight was measured using a calibrated digital scale while participants wore light clothing and was recorded to the nearest 100 grams. Height was measured to the nearest 0.5 centimeter using an un-stretched tape while participants were barefoot. Waist circumference (WC) was measured to the nearest 0.5 centimeter at the narrowest level by an un-stretched tape without any pressure to body surface over light clothing. Body mass index (BMI) was calculated as body weight in kilogram divided by height squared in meter. For blood pressure measurement, a standard mercury sphygmomanometer was used. Blood pressure was measured in a sitting position and after 10 min rest. Blood pressure was measured twice with at least a 30 seconds interval and finally the mean of two measurements were entered to analysis.

By using a 3-day physical activity record, physical activity level of participants was measured and

presented in metabolic equivalent-hours per week (MET-hour/week). Socioeconomic status (SES) of participants was assessed through a validated Persian version questionnaire.[20] This questionnaire contained several questions about income, education, occupation, family number, house ownership, car ownership, the number of states, the number of traveling abroad in the last year, the number of traveling inside the country, the number of rooms at home, and having modern furniture at home. Based on completed physical activity questionnaires, tertiles of SES were used to classified participants into three groups: weak (score < 33%), moderate (33 < score < 66%) and strong (score > 66).

After 12-hours overnight fasting, blood samples were collected for biochemical analysis. Fasting blood sugar (FBS) was measured on the day of blood sampling using commercially available enzymatic reagents (Pars Azmoon, Tehran, Iran). Serum levels of total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) were quantified using commercially available enzymatic kits (Pars Azmoon, Tehran, Iran) by using an auto-analyzer system (Selectra E, Vitalab, Holliston, the Netherlands). Enzyme-linked immunosorbent assay (ELISA) method (Diagnostic Biochem Canada, Inc., Montreal, Canada) was used to assess serum insulin concentrations. By using fasting insulin and glucose levels, insulin resistance indices including homeostasis model assessment of insulin resistance (HOMA-IR)[21] and quantitative insulin sensitivity check index (QUICKI)[22] were estimated. Serum levels of hs-CRP were measured through an ultrasensitive latex-enhanced immunoturbidimetric assay (Randox Laboratory Ltd., Belfast, United Kingdom). Plasma levels of fibrinogen were determined by Clauss method which records the rate of fibrinogen conversion to fibrin by adding thrombin. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) were measured using commercially available enzymatic reagents (Pars Azmoon).

Kolmogorov-Smirnov test and histogram were used to determine normal distribution of all variables. The median cut point of HEI (77.19) was calculated and participants were stratified into two categories accordingly, participants in the low category (≤ 77.19) had lower adherence to HEI pattern in comparison with those in high category (> 77.19). To compare general characteristics of participants between low category and high category, chi-square and Student's independent t-test were performed. Analysis of covariance adjusted for age, sex and energy intake was run to compare dietary intakes and biochemical markers of participants between the two categories. In addition, to compare the biochemical factors between the median of HEI score, further adjustment for BMI was considered. Linear regression in crude and adjusted models (adjusted for age, sex, energy intake and BMI) was applied to determine the significant association between HEI score and CVD risk factors. Statistical analysis was performed by SPSS for Windows (version 18, SPSS Inc., Chicago, IL, USA). P-values less than 0.05 were considered as significant level.

Results

General characteristics of participants are presented in table 1. Participants in higher median of HEI were significantly older (P = 0.042) and had elevated systolic blood pressure than participants in lower median of HEI (P = 0.043).

Table 1. Comparison of general characteristics of participants by median of healthy eating index*

Variables	HEI		
	Lower median (n = 53)	Higher median (n = 54)	P**
Male (%)	77.8	92.6	0.030
Age (year)	61.86 (1.02)	64.62 (0.87)	0.042
Height (cm)	166.85 (1.20)	168.58 (1.04)	0.277
Weight (kg)	71.74 (1.56)	74.88 (1.56)	0.159
BMI (kg/m^2)	25.64 (0.53)	26.31 (0.52)	0.379
WC (cm)	97.64 (1.35)	98.49 (1.20)	0.642
SBP (cmHg)	12.32 (0.19)	12.97 (0.24)	0.043
DBP (cmHg)	7.74 (0.13)	7.91 (0.11)	0.317

HEI: Healthy eating index; BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

* Data are means (SE) and percent (%); ** By using independent sample t-test and chi-square test

Table 2. Comparison of dietary intakes of participants by median of healthy eating index*

Variables	HEI		
	Lower median (n = 53)	Higher median (n = 54)	P†
Protein (g/d)	231.39 (14.55)	132.07 (14.12)	< 0.001
Carbohydrate (g/d)	256.37 (13.71)	387.45 (13.31)	< 0.001
Fat (g/d)	78.94 (2.32)	65.41 (2.26)	< 0.001
Cholesterol (mg/d)	589.66 (33.99)	280.49 (32.99)	< 0.001
Saturated fatty acids (g/d)	20.75 (0.79)	17.93 (0.77)	0.014
Total dietary fiber (g/d)	13.87 (0.76)	21.56 (0.74)	< 0.001
Fruits	362.20 (28.69)	535.36 (27.85)	< 0.001
Vegetables	286.45 (22.67)	441.98 (22.01)	< 0.001
Red meat	14.07 (2.27)	19.42 (2.21)	0.101
Legumes	12.25 (1.38)	16.71 (1.34)	0.025
Dietary diversity score	3.61 (0.41)	7.96 (0.27)	< 0.001

HEI: Healthy eating index

* Data are means (standard error); † By using analysis of covariance adjusted for age, sex and energy intake

Other general characteristics including height, BMI, waist circumference and diastolic blood pressure had no significant differences between two categories of HEI score (P > 0.050).

Table 2 shows dietary intakes of participants between two categories of HEI. Participants in top category of HEI consumed lower amounts of dietary protein, fat, cholesterol, (P < 0.001), and saturated fatty acids (P = 0.014) and higher amounts of carbohydrate, dietary fiber, fruit, vegetables, (P < 0.001), and legumes (P = 0.025). Furthermore, participants in higher category of HEI had greater dietary diversity score in comparison with lower category of HEI (P < 0.001).

Mean and standard errors (SE) of biochemical markers in crude and adjusted models are indicated in table 3. Participants in the top category of HEI score had marginally significant lower levels of hs-CRP and ALP in crude model (P = 0.052 and P = 0.076, respectively). However, after adjusting for age, sex, energy intake and BMI, this marginal association was disappeared. The mean values of other biochemical markers were not significantly different between the two categories of HEI score (P > 0.05).

The results of linear regression analysis are presented in table 4. There were significant inverse associations between HEI score and HOMA-IR [β in crude model = -0.238 (-0.426, -0.048); P = 0.015], fasting blood glucose [β in crude model = -0.194 (-0.383, -0.004); P = 0.047], ALP [β in model I = -0.156 (-0.256, -0.057); P = 0.002] and hs-CRP [β in crude model = -0.196 (-0.386, -0.005); P = 0.046, β in model I = -0.074 (-0.145, -0.003); P = 0.041]. A significant positive association was observed between HEI score and high density lipoprotein cholesterol (HDL-C) levels [β in crude model = 0.196 (-0.386, -0.005); P = 0.044]. Other CVD risk factors had no significant association with HEI score (P > 0.050).

Discussion

This cross-sectional study showed a desirable significant association between HEI score and some of cardiovascular risk factors including HOMA-IR, FBS, hs-CRP and HDL-C levels among elderly persons from Isfahan. However, other CVD risk factors were not statistically related to adherence to HEI score. According to our knowledge, this is the first time that the association of HEI score and CVD risk factors are assessed among Iranian old persons.

Nowadays, it is well established that those elderly persons who consumed high quality diets had lower risk for all-cause mortality, CVD mortality, coronary heart disease events or having at least one of the CVD risk factors including obesity, hypertension, hypercholesterolemia and diabetes mellitus.[1,4,10,23]

Consistent with our results, several previous studies have documented an association between higher scores of HEI and better control of glycemic indices.[24,25] Older men in the highest tertile of a modified-HEI had 75% decreased risk of incidence of impaired fasting glucose. In addition, a 52% reduction in the risk of 10-year incidence of impaired fasting glucose was observed by each 2-times increment in modified-HEI score among older men.[24] Furthermore, the results of a case-cohort study showed a tendency towards an inverse association between alternative-HEI and diabetes in countries with higher mean age.[25]

Table 3. Crude and adjusted means and standard errors of biochemical markers by median of healthy eating index in elderly subjects from Isfahan, Iran

Variables	HEI		
	Lower median (n = 53)	Higher median (n = 54)	P*
HOMA-IR			
Crude	74.09 (15.810)	71.22 (13.190)	0.889
Model I†	71.27 (15.370)	74.97 (14.910)	0.866
Model II‡	64.26 (14.270)	72.28 (13.660)	0.691
QUICKI			
Crude	0.34 (0.010)	0.33 (0.010)	0.680
Model I	0.34 (0.007)	0.33 (0.006)	0.663
Model II	0.34 (0.007)	0.34 (0.006)	0.616
Insulin (UIU/ml)			
Crude	12.84 (2.250)	13.69 (2.050)	0.780
Model I	12.35 (2.280)	14.22 (2.210)	0.565
Model II	12.35 (2.390)	14.17 (2.290)	0.591
Fasting blood sugar (mg/d)			
Crude	119.05 (8.960)	107.40 (4.060)	0.228
Model I	119.26 (7.180)	108.03 (6.960)	0.274
Model II	113.12 (5.850)	106.50 (5.600)	0.424
Triglyceride (mg/dl)			
Crude	156.31 (10.500)	178.23 (22.140)	0.385
Model I	157.86 (19.530)	179.30 (18.940)	0.441
Model II	157.50 (20.630)	179.46 (19.760)	0.452
Total cholesterol (mg/dl)			
Crude	194.74 (6.970)	193.10 (4.970)	0.847
Model I	194.41 (6.510)	195.26 (6.320)	0.928
Model II	196.79 (6.620)	196.96 (6.340)	0.985
LDL-C (mg/dl)			
Crude	99.31 (3.960)	97.05 (3.110)	0.653
Model I	99.53 (3.830)	98.16 (3.720)	0.802
Model II	100.92 (3.880)	99.65 (3.710)	0.816
HDL-C (mg/dl)			
Crude	49.07 (1.670)	49.87 (1.030)	0.683
Model I	49.34 (1.460)	49.79 (1.410)	0.827
Model II	50.49 (1.390)	50.42 (1.330)	0.975
hs-CRP (µg/ml)			
Crude	5.55 (1.800)	2.11 (0.200)	0.052
Model I	4.67 (1.210)	2.99 (1.180)	0.335
Model II	2.79 (0.500)	2.15 (0.470)	0.364
Fibrinogen (mg/dl)			
Crude	279.61 (8.580)	274.18 (6.580)	0.614
Model I	276.51 (7.850)	276.16 (7.610)	0.975
Model II	275.76 (8.260)	276.53 (7.910)	0.947
AST (IU/l)			
Crude	23.49 (2.750)	20.32 (0.770)	0.256
Model I	23.09 (2.000)	20.90 (1.930)	0.442
Model II	21.43 (1.450)	20.23 (1.390)	0.562
ALT (IU/l)			
Crude	21.76 (2.650)	18.18 (1.120)	0.205
Model I	21.64 (2.040)	18.68 (1.980)	0.310
Model II	20.10 (1.640)	17.92 (1.570)	0.350
ALP (IU/l)			
Crude	266.43 (40.110)	194.92 (9.430)	0.076
Model I	264.42 (30.010)	202.16 (29.100)	0.147
Model II	230.89 (16.420)	192.59 (15.730)	0.101

HEI: Healthy eating index; HOMA-IR: Homeostasis model assessment of insulin resistance; QUICKI: Quantitative insulin sensitivity check index; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; hs-CRP: High-sensitivity C-reactive protein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase

* P-values of crude model is resulted from independent sample t-test and P-values of model I and II are resulted from analysis of covariance (ANCOVA); † Model I is adjusted for energy intake, sex and age; ‡ Model II is adjusted for energy intake, sex, age and body mass index.

Table 4. Crude and adjusted correlation of healthy eating index scores and cardiovascular risk factors in elderly subjects from Isfahan, Iran

Variable[†]	HEI[*,†]	
	β[‡] (95% confidence interval)	P[§]
HOMA-IR	-0.238 (-0.426, -0.048)	0.015
Model I[‖]	-0.170 (-0.347, 0.006)	0.059
QUICKI	0.128 (-0.065, 0.320)	0.194
Model I	0.099 (-0.098, 0.297)	0.321
Insulin (UIU/ml)	-0.149 (-0.340, 0.044)	0.132
Model I	-0.128 (-0.330, 0.074)	0.212
Fasting blood sugar (mg/d)	-0.194 (-0.383, -0.004)	0.047
Model I	-0.122 (-0.277, 0.032)	0.120
Triglyceride (mg/dl)	0.142 (-0.049, 0.334)	0.146
Model I	0.149 (-0.057, 0.354)	0.154
Total cholesterol (mg/dl)	0.164 (-0.027, 0.355)	0.092
Model I	0.167 (-0.031, 0.365)	0.098
LDL-C (mg/dl)	0.119 (-0.074, 0.311)	0.226
Model I	0.116 (-0.083, 0.315)	0.249
HDL-C (mg/dl)	0.196 (0.006, 0.385)	0.044
Model I	0.164 (-0.017, 0.345)	0.076
hs-CRP (µg/ml)	-0.196 (-0.386, -0.005)	0.046
Model I	-0.074 (-0.145, -0.003)	0.041
Fibrinogen (mg/dl)	-0.083 (-0.276, 0.112)	0.406
Model I	-0.070 (-0.272, 0.133)	0.496
AST (IU/l)	-0.129 (-0.321, 0.063)	0.186
Model I	-0.120 (-0.252, 0.012)	0.074
ALT (IU/l)	-0.087 (-0.280, 0.106)	0.376
Model I	-0.071 (-0.220, 0.079)	0.350
ALP (IU/l)	-0.189 (-0.379, 0.001)	0.053
Model I	-0.156 (-0.256, -0.057)	0.002
Weight (kg)	0.013 (-0.181, 0.207)	0.893
Model I	0.005 (-0.197, 0.207)	0.959
BMI (kg/m^2)	-0.008 (-0.201, 0.186)	0.939
Model I	0.011 (-0.188, 0.210)	0.911
WC (cm)	-0.070 (-0.261, 0.124)	0.485
Model I	-0.045 (-0.242, 0.153)	0.654
SBP (mmHg)	0.048 (-0.145, 0.241)	0.625
Model I	0.019 (-0.176, 0.214)	0.846
DBP (mmHg)	0.019 (-0.174, 0.212)	0.848
Model I	0.010 (-0.170, 0.190)	0.914

HEI: Healthy eating index; HOMA-IR: Homeostasis model assessment; QUICKI: Quantitative insulin sensitivity check index; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; hs-CRP: High-sensitivity C-reactive protein; AST: aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; BMI: Body mass index; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

[*] HEI was considered as an independent variable for all cardiovascular risk factors.

[†] Dependent variable; each cardiovascular risk was entered into separate regression models; [‡] Standardized β-coefficient; [§] Resulted from linear regression; [‖] Model I is adjusted for age, sex, energy intake and body mass index, except for weight, waist circumference and body mass index which were not adjusted for body mass index

It must be taken into account that due to relatively higher body fat mass and abdominal adiposity, Asian people have more risk for diabetes than white people in the same body mass index level.[26-28] Therefore, the findings of the present study are remarkable in this regard, since a previous study has shown that 22% of Iranian old persons have diabetes and 27.5% of diabetic patients are not aware of their disease.[3] Although we did not find any association between HEI score and body weight, BMI, and waist circumference, top category of HEI was inversely associated with FBS and insulin resistance that is shown by HOMA-IR. Lower glycemic load of healthy dietary patterns due

to high content of fruits and vegetables could modify β-cell function and reduce serum levels of blood glucose.[24] Furthermore, high content of fruits, vegetables and whole grains are associated with reduced levels of C-reactive protein (CRP).[24] It is shown that high levels of inflammatory markers are related to β-cell dysfunction and insulin resistance.[29] Moreover, healthy dietary patterns have high content of antioxidants due to higher amounts of fruits, vegetables and whole grains. The protecting effects of antioxidants against insulin resistance and elevated levels of blood glucose was reported previously.[30]

In the present study, higher score of HEI was related to the higher levels of HDL-C among elderly persons. The results of a cross sectional study on postmenopausal women indicated that women in high physical activity energy expenditure-high Canadian-HEI score had 10% higher amounts of HDL-C than women in the low physical activity-low Canadian-HEI group.[31] Other previous studies have determined beneficial association between HEI score and HDL-C levels among adults.[32,33] It had been shown that adults with better adherence to HEI were 21% less likely to have decreased levels of HDL-C.[33] However, two observational studies performed on Iranian adults could not detect impressive association between HEI score and HDL-C levels.[34,35] Higher adherence to healthy eating index is simultaneous with increased consumption of fruit, vegetables, whole grains, low-fat dairy foods, lean meats and legumes and lower intakes of total fat, saturated fatty acids and cholesterol. All these dietary factors are associated with improvement in lipid profile.[33,34]

In this cross-sectional study a negative association was found between HEI score and hs-CRP levels among elderly persons. Previous studies have documented inconsistent results. A study performed among elderly participants did not document an inverse association between HEI and CRP levels.[36] However, another study that was performed on overweight and obese postmenopausal women indicated 28% lower hs-CRP levels in high physical activity energy expenditure-high Canadian-HEI compared with low physical activity- low Canadian-HEI group.[31] However, other studies confirmed an inverse association between HEI score and hs-CRP levels among adults.[37,38] Recently, several studies have declared a significant inverse relation between HDL-C and hs-CRP concentrations. However, the underlying possible mechanism between HDL-C and hs-CRP is not clear.[39,40] In the current study HDL-C and CRP had significant positive and inverse association with HEI score, respectively. Previous studies have demonstrated negative association between fruit and vegetable,[41] legumes[42] and fiber intake[43] with CRP levels.

It is shown that 3.3% and 9.2% of old persons have abnormal tests of AST and ALP, respectively.[44] Fleming et al. demonstrated that elevated concentrations of AST and ALP were associated with increased risk of death from liver disease among elderly population. AST was associated with seven times increased risk of death and ALP was associated with six times increased risk of death from liver diseases.[44] In addition, it had been shown that high serum levels of AST, ALT and ALP was associated with increased risk of all-cause mortality among old subjects.[45] Based on our literature review, there is no previous study about the association of HEI score and hepatic enzymes. In the current study, an inverse association between HEI score and ALP and AST levels was observed. Higher scores of HEI are simultaneous with higher consumption of fruit and vegetables. It is well known that these food groups could be considered as a main source of antioxidants.[30] A previous study had shown an inverse association between total antioxidant capacity (TAC) and AST levels among obese adults.[46] Furthermore, healthy dietary patterns including Mediterranean dietary pattern could improve liver function by reducing insulin resistance and consequently reducing liver fat accumulation.[47] Now, it is established that HEI might be a beneficial approach for reducing insulin levels as well as insulin resistance.[48,49] In the present study, HEI score had a significant inverse association with HOMA-IR in crude model and a marginally inverse association in model I.

Previous studies have established that elderly peoples have several nutritional inadequacies and are malnourished or at risk of malnutrition.[50,51] Therefore, determining an applicable nutritional strategy among elderly people who are at great risk of dietary insufficiencies is of great interest. In the present study, participants with the most adherences with HEI score profited from cardio-protective effects of this dietary pattern. Higher scores of HEI with noticeable amounts of fruit, vegetables and whole grains provide a diet that has low density of energy. It has been declared that low-energy-dense diets have the capacity to provide dietary recommendations for macro- and micro-nutrients in elderly persons.[52]

In this cross-sectional study we presented the associations between HEI score and cardiovascular risk factors among Iranian elderly for the first time. We randomly included retired subjects from different socioeconomic status, which to some extent, could be a representative sample of elderly population in Isfahan. However, several limitations must be considered for the present study. First, due to cross-sectional nature of the study, the inference of causal association was impossible. Second, relatively small sample size of participants made it difficult to detect the exact associations between HEI score and CVD risk factors. Third, in this study dietary intakes of participants were assessed by a semi quantitative FFQ. Due to recall bias of this dietary tool, misclassification of participants is inevitable. At last, it is possible that there are unknown confounders that we did not enter as covariates in statistical analysis.

Conclusion

In conclusion, the results of this study showed a significant favorable association between HEI score and several CVD risk factors including HOMA-IR, FBS, hs-CRP and HDL-C levels among elderly persons from Isfahan. Large prospective cohort studies are needed to prove the observed relationship among Iranian old population.

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Conflict of Interests

Authors have no conflict of interests.

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The role of manual thrombectomy in cardiovascular outcome among patients with total cutoff vessel myocardial infarction undergoing primary percutaneous coronary intervention

Alireza Khosravi[1], Davoud Rajabi[2], Masoud Pourmoghaddas[2], Afzal Roohi[3], Masoumeh Esmaeili[4]

Original Article

Abstract

BACKGROUND: The applicability of manual aspiration thrombectomy in patients with ST-segment elevation myocardial infarction (STEMI) has been a challenging issue. This study aimed to compare the impact of additive manual thrombectomy on patients with myocardial infarction (MI) and total cutoff vessel with standard primary percutaneous coronary intervention (PPCI) with bailout thrombectomy.

METHODS: In this case-control study, 181 patients with acute STEMI were enrolled who referred to Chamran Hospital (Isfahan, Iran) between August to December 2014. The culprit lesion was treated with routine PPCI with bailout thrombectomy (111 patients) and routine primary thrombectomy then percutaneous coronary intervention [(PCI), 70 patients] during hospitalization and one month after discharge. Patients in the case group received manual thrombectomy before PPCI and patients in the control group received standard PPCI with bailout thrombectomy. Patients were followed during the study procedure, post-hospitalization and one month later for cardiovascular outcomes including death, recurrent MI, stroke, major bleeding, post PCI arrhythmia, no reflow, thrombolysis in myocardial infarction (TIMI)-flow and TIMI myocardial blush grade (TMBG), which were assessed and recorded.

RESULTS: Myocardial perfusion and angiographic outcomes had no significant differences in the two groups ($P = 0.730$). There was also no significant difference in no reflow prevalence between the two groups ($P > 0.990$). There were no significant differences for primary outcomes such as death, stroke, major bleeding and arrhythmia between the two groups ($P < 0.050$). In particular, outcomes were the same for both groups during hospitalization period and one month after discharge. Mortality rate during hospitalization was 5.7% for the control group and 4.5% for the case group ($P = 0.730$). However, one-month mortality rate was quite similar in both groups.

CONCLUSION: This study showed there is no significant difference in cardiovascular outcomes such as death, stroke, bleeding, arrhythmia, target vessel revascularization, and distal embolization during hospitalization and one month after discharge in patients with acute MI and total cutoff of the involved vessel, who underwent PPCI with and without primary Export® aspiration catheter direct thrombosuction.

Keywords: Cardiovascular Diseases, Myocardial Infarction, Percutaneous Coronary Intervention, Thrombectomy

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Introduction

Primary percutaneous coronary intervention (PPCI) had been known as one of the most effective therapeutic procedures for patients with ST-segment elevation myocardial infarction (STEMI) for restoring coronary flow to a normal thrombolysis in myocardial infarction (MI).[1,2] Poor myocardial reperfusion in some patients with STEMI causes large infarct size

1- Cardiologist, Hypertension Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
2- Cardiologist, Interventional Cardiology Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
3- Nurse, Chamran Hospital, Isfahan University of Medical Sciences, Isfahan, Iran
4- Nurse, Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
Correspondence to: Davoud Rajabi, Email: dvdrajabi@yahoo.com

and worse clinical outcomes.[1-4] Clinicians focused their studies on distal embolization as a major determinant of poor reperfusion and clinical outcome after primary angioplasty.[1-6] Manual thrombectomy was suggested as a useful procedure for preventing distal embolization and increasing reperfusion during PPCI.[2,5]

However, the impact of manual thrombectomy on cardiovascular events compared to target vessel revascularization (TVR) is not clear. Some studies have shown that manual thrombectomy with percutaneous coronary intervention (PCI) in STEMI patients has several benefits such as improvement of reperfusion microcirculation, ST-segment resolution (STR) and reduction in mortality.[1-3,6-10] Manual thrombectomy had significant impacts on mortality in patients with STEMI due to improved myocardial perfusion and reduced distal embolization.[5,11] Recent meta-analysis has shown that overall, thrombectomy with different technique did not reduce one-month mortality rate among STEMI patients.[12] Other studies showed that routine use of manual aspiration compared with PCI alone reduced the incidence of the primary outcome of impaired microvascular perfusion and reduced mortality by 52% annually,[6,13] whereas other studies on TVR in PPCI with manual thrombectomy showed no statistically significant reduction in cardiovascular mortality compared to without manual therapy.[6,11,14] Previous studies were performed on patients with MI regardless of whether the infarcted vessel is total cutoff or not.

Complete obstruction of the infarcted vessel may have impacts on the thrombectomy results as well as its prognosis and cardiovascular disease events. So this study is the first study designed to assess and directly compare the frequency of cardiovascular outcomes and major adverse cardiac events (MACE) which consist of stroke, bleeding, MI, TVR among patients with acute MI and total occlusion of the involved artery, who underwent PPCI with and without primary Export® aspiration catheter direct thrombosuction.[4,6,10,11]

Materials and Methods

This study was designed as a case-control study in 181 patients with acute MI who referred to Chamran Hospital, Isfahan, Iran, between August 2014 and December 2014. The protocol was approved in research ethics committee of Isfahan University of Medical Sciences and written informed consent was obtained from all study participants. Inclusion criteria were having history of acute MI with ST-segment elevation in the past 24 hours with complete occlusion of infarcted artery evident in angiography. Exclusion criteria were subjects with cardiogenic shock, left main involvement, history or evidence of chronic occlusions, disturbance of consciousness, non-complete vessel occlusion, achievement of thrombolysis in myocardial infarction (TIMI) 3 after wire passage and death or other major cardiovascular event before starting the procedure. Patients were divided into two groups based on clinical condition and physician decision. In the first group (case group) PCI with manual thrombectomy was done and in the second group only PPCI was done. After enrolment of patients, a trained nurse measured weight and height (Seca, Germany). Blood pressure was measured by manual sphygmomanometer in sitting position with standard method. A questionnaire containing history of cardiovascular risk factors was filled out. In the case group, manual thrombectomy was done before PPCI and patients in the control group received standard PPCI with bailout thrombectomy. Patients were followed during the study procedure, post hospitalization and one month later for cardiovascular outcomes including death, recurrent MI, stroke, major bleeding, post PCI arrhythmia, no reflow, TIMI-flow and TIMI myocardial blush grade (TMBG), which were assessed and recorded by two cardiologists blind to study. In each visit ejection fraction was measured and recorded.

After one month, all study subjects were contacted and asked to attend the clinic visit. All cardiovascular outcomes such as recurrent MI, stroke, major bleeding, post PCI arrhythmia, no reflow, and TIMI-flow were assessed and the same cardiologist measured TMBG. Major bleeding was defined as any bleeding requiring hospitalization and/or causing 0.2 g/dl decrease in hemoglobin level and/or requiring blood transfusion that was not a hemorrhagic stroke. Hemorrhagic stroke was defined as a focal neurologic deficit of sudden onset caused by bleeding, diagnosed by a neurologist, and evident in computed tomography (CT) scan or magnetic resonance imaging (MRI), which lasted 24 hours.

TIMI-flow determination of angiographic blood flow (TIMI grade), arrhythmia, no reflow and TMBG were determined during angiography.[14]

All patients received oral aspirin (325 mg) and clopidogrel (600 mg) at the time of STEMI diagnosis. In the catheterization laboratory, intravenous boluses of unfractionated heparin (60 U/kg) and integrilin (10 mg) were administered. The PCI was performed with standard technique, with the femoral approach as the first choice. If TIMI 3 was achieved immediately after wire passage, the patient was excluded from the study. The thrombectomy was performed with Export® aspiration catheters (6 or 7 French). In the case group,

manual thrombectomy was performed first, and then the PCI was continued by balloon or stent. In the control group, firstly, primary PCI was begun and completed and thrombectomy was not performed for those who had large thrombus during procedure.

After the lesion was crossed with a guidewire, the thrombectomy catheter was inserted just proximal to the culprit lesion and was slowly pushed across the lesion for at least two passages while aspiration was done continually via thrombectomy catheter. Additional passages were performed until no further reduction in thrombus load could be obtained. If the operator was unable to cross the lesion with the thrombectomy catheter, predilatation was firstly performed with a small-diameter balloon and followed by other thrombectomy attempts. It was recommended that the guiding catheter be fully engaged with the coronary ostium during removal of the thrombectomy catheter in order to avoid embolizing thrombus to the systemic vasculature. After thrombectomy, the guiding catheter was aspirated to ensure removal of air or thrombus.[3,15] The PCI procedure was performed after thrombus aspiration was completed. Use of embolic protection devices was not allowed.

In control group we predilated the lesion and reevaluated the distal flow if the distal vessel was not appearing, and thrombectomy was done with the size of thrombus as in the case group before stenting.

Study data were entered into the SPSS software (version 15.0, SPSS Inc., Chicago, IL, USA) for statistical analysis. Qualitative and quantitative variables were presented with frequency/percentage and mean ± standard deviation, respectively. Study variables were compared between case and control groups with Student's independent t-test and chi-square tests for quantitative and qualitative variables, respectively. Logistic regression analysis was performed. All P-values less than 0.05 were considered as significant.

Results

Patient characteristics: A total of 188 patients were recruited and five patients were excluded due to TIMI 3 flow immediately after wire insertion. Furthermore, two patients were excluded due to death from perforation and stroke before initiation of the procedures. Finally, after exclusion 70 patients remained in the control group who received routine primary thrombectomy plus PCI and 111 patients remained in the case group and received PPCI and bailout thrombectomy. Table 1 shows the characteristics of the patients. Two groups were comparable except for smoking status that was higher in the control group.

Table 1. Characteristics of the patients at baseline

Characteristic	Primary thrombectomy (n = 70)	PPCI with bailout thrombectomy (n = 111)	P
Age (year)	58.5 ± 12.1	61.4 ± 14.0	0.140
Sex (male)	56 (80.0)	92 (82.9)	0.690
Medical history [n (%)]			
Diabetes mellitus	24 (34.5)	33 (29.7)	0.620
Hypertension	22 (31.9)	45 (40.9)	0.260
Smoking	22 (32.8)	49 (44.5)	0.150
CVD	16 (19.3)	24 (25.0)	0.370
Receiving thrombolytic therapy	13 (18.6)	11 (9.9)	0.110
Location of MI [n (%)]			0.110
Inferior	29 (41.4)	49 (44.1)	
Anterior	41 (58.6)	54 (48.6)	
Lateral	0 (0.0)	7 (6.3)	
Posterior	0 (0.0)	1 (0.9)	
Number of vessels involved [n (%)]			0.350
1	36 (51.4)	45 (40.5)	
2	23 (32.9)	45 (40.5)	
3	11 (15.7)	21 (18.9)	
Vessels involved [n (%)]			0.330
LAD	41 (58.6)	56 (50.5)	
CX	3 (4.3)	12 (10.8)	
RCA	26 (37.1)	42 (37.8)	
Other	0 (0.0)	1 (0.9)	
Ejection fraction < 30% [n (%)]	21 (30.0)	42 (37.8)	0.330

PPCI: Primary percutaneous coronary intervention; CVD: Cardiovascular disease; MI: Myocardial infarction; LAD: Left anterior descending artery; CX: Circumflex artery; RCA: Right coronary artery

Table 2. Study outcomes based on primary thrombectomy or primary percutaneous coronary intervention (PPCI) with bailout thrombectomy

Outcome	Primary thrombectomy (n = 70)	PPCI with bailout thrombectomy (n = 111)	P
Post primary thrombectomy TIMI flow grade			-
0	5 (7.1)	-	
1	10 (14.3)	-	
2	18 (25.7)	-	
3	37 (52.9)	-	
End TMBG [n (%)]			0.650
0	3 (4.3)	4 (3.6)	
1	8 (11.4)	20 (18.0)	
2	23 (32.9)	37 (33.3)	
3	36 (51.4)	50 (45.0)	
End TIMI flow grade [n (%)]			0.730
0	1 (1.4)	2 (1.8)	
1	3 (4.3)	5 (4.5)	
2	10 (14.3)	23 (20.7)	
3	56 (80.0)	81 (73.0)	
No reflow	6 (8.6)	11 (9.9)	> 0.990

PPCI: Primary percutaneous coronary intervention; TIMI: Thrombolysis in myocardial infarction; TMBG: TIMI myocardial blush grade

Myocardial perfusion and angiographic outcomes: There were no significant differences between the two groups regarding myocardial perfusion and angiographic outcomes such as death, stroke, bleeding, arrhythmia, TVR, and distal embolization. There was also no significant difference in no reflow prevalence between the two groups (Table 2).

Efficacy and safety: There were no significant differences for primary outcomes between the two groups. In particular, outcomes were the same for both groups during hospitalization period and one month after discharge. Mortality rate during hospitalization was 5.7% for the control group and 4.5% for the case group (P = 0.730). However, one-month mortality rate was quite similar in both groups (Table 3).

Results of logistic regression analysis: After entering demographic data into the model (age and sex), and after adjusting for known cardiovascular risk factors such as hypertension, smoking and number of involved vessels, major cardiac events were not associated with the success of manual thrombectomy during hospital stay and one month after PPCI (Tables 4 and 5).

Table 3. Association of major cardiac events (MACE) in subjects who underwent primary thrombectomy or primary percutaneous coronary intervention (PPCI) with bailout thrombectomy

Outcome	Thrombectomy (n = 70)	PPCI (n = 11)	P
During hospitalization [n (%)]			
Death	4 (5.7)	5 (4.5)	0.730
Stroke	0 (0.0)	2 (1.8)	0.520
Bleeding	2 (2.9)	3 (2.7)	> 0.990
Arrhythmia	3 (4.3)	5 (4.5)	> 0.990
TVR	0 (0.0)	0 (0.0)	-
Distal embolization	8 (11.4)	14 (12.6)	0.490
One month after discharge [n (%)]			
Death	1 (1.4)	1 (0.9)	> 0.990
Stroke	1 (1.4)	0 (0.0)	0.380
Bleeding	2 (2.9)	0 (0.0)	0.140
Arrhythmia	0 (0.0)	2 (1.8)	0.520
TVR	0 (0.0)	2 (1.8)	0.520
Distal embolization	0 (0.0)	0 (0.0)	-

PPCI: Primary percutaneous coronary intervention; TVR: Target vessel revascularization

Table 4. Odds of major cardiac events (MACE) during hospital stay in patients who underwent primary thrombectomy

Model	Odds ratio	95% CI	P
Crude Model	0.96	0.44-2.09	0.925
Adjusted Model 1	0.92	0.43-2.10	0.512
Adjusted Model 2	0.82	0.36-1.88	0.640

Model 1: Adjusted for age and sex; Model 2: Adjusted for age, sex, diabetes mellitus, hypertension, smoking and number of vessels; CI: Confidence interval

Discussion

This study showed there are no significant differences in cardiovascular outcomes such as death stroke, bleeding, arrhythmia, TVR, distal embolization during hospitalization and one month after discharge in patients with acute MI and total cutoff of the involved vessel, who underwent PPCI with and without primary Export® aspiration catheter direct thrombosuction. In the control group, patients received manual thrombectomy followed by PPCI with standard protocol and the case group received PPCI with bailout thrombectomy as needed when large thrombus was seen after balloon dilatation. Study findings suggest that major clinical outcomes such as stroke and major bleeding after PPCI did not change irrespective of adjunctive routine primary thrombectomy. The outcomes were similar within hospitalization period and one month after discharge. Furthermore, adding manual thrombectomy to the PCI did not significantly improve participants' outcomes. Although normal flow after PPCI is usually restored in epicardial vessels, in most patients, myocardial perfusion is not satisfactory due to distal embolization[1].

Table 5. Odds of major cardiac events (MACE) one month after primary thrombectomy in patients

Model	Odds ratio	95% CI	P
Crude Model	0.83	0.18-3.84	0.817
Adjusted Model 1	0.67	0.13-3.31	0.627
Adjusted Model 2	0.39	0.06-2.56	0.325

Model 1: Adjusted for age and sex; Model 2: Adjusted for age, sex, diabetes mellitus, hypertension, smoking and number of vessels; CI: Confidence interval

Therefore, a number of devices have been developed to reduce distal embolization. Several studies have been performed for assessing the impact of thrombectomy on PPCI outcomes and some of them had similar findings to our study.[8,16-28] Previous meta-analysis had similar results to our study and confirmed our findings.[1,4,11,29]

Generally, it is claimed that manual procedures are superior to mechanical procedures with respect to mortality, and markers of myocardial perfusion and mechanical procedures are recommended for management of patients who have heavy thrombus burden.[1,15] In a recent meta-analysis, Tamhane et al. reported that manual devices improved myocardial perfusion markers, where there was not a significant difference in one-month mortality between conventional PCI and PCI with thrombectomy.[30] Investigators reported that the risk of stroke increased in thrombectomy group. In contrast, we observed no difference in stroke risk; however, an insignificant reduction in myocardial perfusion markers was observed in thrombectomy group in our study. In another meta-analysis, De Luca et al. reported a significant increase in stroke risk in thrombectomy group and no differences in one-month mortality rate.[4] Another meta-analysis showed significant reductions in cardiac perfusion markers as well as mortality rate in STEMI patients who underwent both PPCI and adjunctive thrombectomy.[1] While analysis by Deng et al. showed no statistically significant differences in long-term mortality and reinfarction,[11] short-term reinfarction and long-term MACEs were significantly lower in thrombectomy group. The present study showed no significant differences between the study groups with respect to either mortality rate or cardiac perfusion markers. Subjects we considered here were total cutoff patients and the results provided new information on this group of patients. In total cutoff, distal part of vessel is not visible and thrombus burden is indistinguishable. We also compared all patients in whom thrombectomy was used (as routine primary or secondary during procedure) with patients in whom no thrombectomy was used according to above mentioned outcomes and observed no differences. Manual aspiration thrombectomy was not identified to result in notable benefits in PPCI patients. Nonetheless, the relatively short follow up period is a limitation of our study and extending this period could provide more information on long-term effects of both procedures in these patients. Use of thrombectomy remains challenging in STEMI, especially total cutoff patients and further research with larger sample sizes and longer follow-ups are warranted to give clear advice on medical practice in this regard.

For achieving accurate and interpretable results, we had to exclude some high-risk patients with cardiogenic shock. Large randomized trials are

needed for covering all patients. Although thrombosuction did not have benefit for patients, it can help operators to better visualize distal part of the artery and guide them for more precise decisions.

Our study also has limitations. First, our study is limited to a small sample size, and only applies to patients with STEMI who received PPCI. In addition, in this study, patients were followed for one month and in other similar studies, participants were followed for one year. It seems that some differences between findings of these studies and our study might be due to our short follow-up time. Moreover, most of the similar studies were performed on patients at the early hours of MI and with loose clots which are easily fragmented.

Conclusion

Findings of our study showed that adjunctive thrombectomy after PPCI did not have significant benefits to reduce cardiovascular outcomes in patients with STEMI and total cutoff culprit vessel.

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Conflict of Interests

Authors have no conflict of interests.

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Evaluation of pentraxin-3 level and its related factors in patients undergoing primary percutaneous coronary intervention

Saeed Alipour-Parsa[(1)], Habib Haybar[(2)], Mohammad Hasan Namazi[(3)], Morteza Safi[(3)], Isa Khaheshi[(4)], Mehdi Memaryan[(5)], Amir Mohammad Eghbalnejad-Mofrad[(6)]

Original Article

Abstract

BACKGROUND: Inflammation has an important role in the development and progression of atherosclerosis, and acute phase proteins such as pentraxin-3 (PTX3) can be deployed in determining the prognosis of coronary artery disease (CAD). So the purpose of this paper was to evaluate the PTX3 level and its related factors in patients undergoing primary percutaneous coronary intervention (PCI).

METHODS: In this cross-sectional study, the PTX3 levels were determined for 100 patients with ST-elevation myocardial infarction referred to the Modarres Hospital, Tehran, Iran. Checklist included demographic data [age, gender, history of myocardial infarction (MI)] and characteristics of heart disease (type of MI, culprit, and pre-dilation). PTX3 was measured for all patients before PCI.

RESULTS: In this study, the mean age of the participants was 58.7 (11.4). Global registry of acute coronary events (GRACE) score was higher in the group with abnormal PTX3 levels (P = 0.008). The number of the involved vessels (P = 0.005), MI type (P = 0.05), and the need for PCI all had a significant relation with abnormal PTX3 levels. The increased levels of PTX3 received higher Killip class, lower ejection fraction, and higher GRACE score. The group with abnormal PTX3 had a significant difference in platelet counts (P = 0.018) in comparison with the group with normal level of PTX3.

CONCLUSION: Currently, the biomarkers are highly important in the field of cardiovascular diseases. The diagnostic and prognostic importance of PTX3 as a new marker has been underscored in recent studies. Differentiating between high-risk patients with acute cardiac infarction and low-risk ones through their clinical signs is difficult.

Keywords: Pentraxin-3, Percutaneous Coronary Intervention, Atherosclerosis, Prognosis, Coronary Artery Disease

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Introduction

Inflammatory process plays a key role in the creation and development of atherosclerosis.[1] As a result of atherosclerosis process, the plaque formation of fibrosis-lipid (atheroma) grows gradually by aging and causes artery stenosis and inflammation, thus leading to the creation of coronary artery disease.[2]

Researchers have reported different factors involved in the instability and detachment of the plaque, which are as follows: factors associated with lipids such as low density lipoprotein (LDL) and lipoprotein (LP), those associated with oxidative stress such as glutathione peroxidase and myeloperoxidase, those associated with the acute phase of inflammation and the platelets and white blood cells (WBC) regulators as biomarkers, and proteolytic enzymes such as matrix metalloproteinase.[3] Pentraxin-3 (PTX3) is a multi-subunit glycoprotein in acute phase of inflammation

1- Associate Professor, Cardiovascular Research Center AND Department of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2- Assistant Professor, Cardiovascular Research Center AND Department of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3- Professor, Cardiovascular Research Center AND Department of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4- Assistant Professor, Cardiovascular Research Center AND Department of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5- Cardiologist, Cardiovascular Research Center AND Department of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6- Student of Medicine, Student Research Committee, Department of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
Correspondence to: Amir Mohammad Eghbalnejad-Mofrad, Email: amir_gforce69@yahoo.com

that can be synthesized by endothelial cells, monocytes, macrophages, and myeloid cells.[2] PTX3 is released from the platelet-activated neutrophils in coronary artery disease (CAD)[4] and through the process of inflammation, plays a role even as a prognostic factor for CAD.[5] The remarkable point is that PTX3 production has also been reported in the context of coronary atherosclerotic lesions.[6] A number of studies have indicated that high levels of serum PTX3 in unstable angina[5] have been associated with negative consequences after myocardial infarction (MI).[7] Compared with the high-sensitivity C-reactive protein (hs-CRP), PTX3 acts as a more specific factor of atherosclerosis and coronary vascular inflammation and has been independently associated with the progress of the atherosclerosis and coronary artery disease.[8] In one study by Wang et al. in 2014 on patients with angina who underwent percutaneous coronary intervention (PCI), the role of PTX3 was examined in predicting the elevation in cardiac troponin levels after the PCI. PTX3 levels were significantly high in patients whose troponin levels were three times higher than normal after 24 hours. In addition to the other risk factors, with logistic regression analysis, PTX3 was the most independent risk factor to increase the troponin levels after PCI.[9]

However, the accurate role of PTX3 in the pathogens of the inflammatory cardiovascular disease requires a comprehensive study. In patients with acute coronary syndrome (ACS) especially those under PCI, there are no clinically useful biomarkers for prognosis. Since inflammation has an important role in the development and progression of atherosclerosis, acute phase proteins such as PTX3 can be deployed in determining the prognosis of CAD. Nevertheless, thus far in ACS patients, particularly those who have been undergoing primary PCI, useful biomarkers have not been set clinically for the prognosis and outcome of PCI. Accordingly, the objective of this study was to evaluate the PTX3 level and its related factors in patients undergoing primary PCI.

Materials and Methods

In this cross-sectional study, 100 patients with typical chest pain with ST-elevation on their electrocardiogram (ECG), were considered as the research statistical population who referred to Shahid Modarres Hospital, Tehran, Iran, from September 2014 to September 2015. After initial assessments, patients who underwent angiography and angioplasty were included in the study. PTX3 level was measured upon arrival (within 20 minutes of admission) in this population and patients were divided into two groups based on the level of PTX3 (with and without normal level, normal level is less than 3.1 and abnormal level is more or equal to 3.1), and then during hospitalization the associated factors according to the variables were evaluated. The variables of the questioner were age, gender, high blood pressure, hyperlipidemia, diabetes, history of PCI, coronary artery bypass grafting (CABG), MI, cigarette smoking and global registry of acute coronary events (GRACE) score. GRACE scoring system includes parameters such as age, history of congestive heart failure (CHF), history of MI, heart rate during rest, systolic blood pressure at the time of hospital admission, ST-segment deviation captured in ECG, initial serum creatinine level, and elevated cardiac enzyme level in the hospital, place of lesions on angiography, number of involved vessels, contrast nephropathy, in-hospital death, PCI candidate, and left ventricle ejection fraction (LVEF).

All patients with chest pain who had ST-elevation on ECG and underwent angiography and angioplasty were enrolled in the study and those persons who did not fill their information completely, candidates for CABG, patients with cardiogenic shock, positive cancer history, chronic kidney disease (CKD), psoriasis, treated by statins drugs, and patients without any intervention programs after triage in hospital were excluded and not used in the final analysis.

In this cross-sectional study, a check list was filled by cardiology resident for each patient. Cardiovascular assessments were also recorded and the location of the MI lesion was determined based on the ECG detected features. PTX3 was measured for all patients before PCI. The sampled blood was approximately 10 cc. Sample was measured by laboratory expert with human PTX3 enzyme linked immunosorbent assay (ELISA) kit (Cusabio Biotech Co., Japan). During hospitalization, patients were evaluated in terms of associated factors.

Categorical data are reported as number (percentage). Continuous variables are presented as mean [standard deviation (SD)]. The Shapiro-Wilks test was used to examine the normality assumption of quantitative variables. To compare demographic and baseline characteristics of groups, independent samples t-test was used for continuous variables and Pearson chi-square tests were conducted for nominal variables. P-values less than 0.05 were considered statistically significant. All tests were two-sided. The SPSS for Windows (version 18.0, SPSS Inc., Chicago, IL, USA) was used for all data analyses.

Informed written consent was obtained from all participants and the ethical committee of Shahid Beheshti University of Medical Sciences, Iran, (ethical code: IR.SBMU.RAM.REC 13940229) approved this study in 2015. The study protocol conforms to the ethical guidelines of the 2008 Declaration of Helsinki.

Results

In this study, patients were divided into two groups based on the level of PTX3 (with and without normal level of this factor). Cut-off for normal value was 3.1 ngr/ml, based on the manufacturer kit. Accordingly, 30 persons had normal levels of PTX3 and 70 persons had abnormal levels.

In this project, 100 patients with acute ST-elevated MI (STEMI) who were candidate for primary PCI were enrolled, with the mean age of 58.7 (11.4) years. Eighty-nine (89%) participants were male which shows that male sex was a significant and meaningful risk factor. Smoking cigarette 42 (60%) (P = 0.660), high blood pressure 29 (41.4%) (P = 0.110), diabetes 20 (28.6%) (P = 0.460) and hyperlipidemia 3 (4.3%) (P = 0.360) were other statistically significant risk factors in group with abnormal PTX3 (Table1). The distribution of cases with and without normal level of PTX3 is shown in table 1 based on quantitative variables. It was found that the difference between the groups with and without normal PTX3 level (Table 1) in terms of heart rate (P = 0.002), GRACE score (P = 0.008), lactate dehydrogenase (P = 0.026), total creatine phosphokinase (P = 0.013), duration of hospitalization (P = 0.004), platelet count (P = 0.018), platelet/lymphocyte ratio (P = 0.001) has been statistically significant.

In table 2 the statistically significant and meaningful items were, type of MI (P = 0.050), the culprit vessel (P = 0.030), and the other terms like Killip class (P = 0.010), stage PCI requirement (P = 0.005) and left ventricular function (P = 0.007) were statistically significant.

Table 1. Baseline characteristics of the participants

Characteristics	Normal PTX3 (n = 30)	Abnormal PTX3 (n = 70)	P
Male [n (%)]*	27 (90.0)	62 (88.6)	> 0.990
Smoking (yes) [n (%)]*	16 (53.3)	42 (60.0)	0.660
Hypertension (yes) [n (%)]*	7 (23.3)	29 (48.4)	0.110
Diabetes (yes) [n (%)]*	6 (20.0)	20 (28.6)	0.460
Affected with HLP (yes) [n (%)]*	3 (10.0)	3 (4.3)	0.360
Familial history of CAD (yes) [n (%)]*	14 (46.7)	28 (40.0)	0.660
Age (year)	55.4 ± 12.5 (40.0-91.0)	60.1 ± 10.7 (44.0-89.0)	0.070
Triglyceride (mg)	148.9 ± 58.0 (38.0-266.0)	130.3 ± 86.4 (37.0-552.0)	0.210
Cholesterol total (mg/dl)	177.0 ± 34.7 (114.0-249.0)	180.8 ± 32.4 (110.0-284.0)	0.630
Low density lipoprotein(mg/dl)	105.6 ± 32.4 (49.0-160.0)	103.7 ± 30.0 (50.0-190.0)	0.780
High density lipoprotein (mg/dl)	40.7 ± 12.3 (5.1-69.0)	43.4 ± 12.5 (23.0-79.0)	0.310
Uric acid (mg/dl)	5.5 ± 1.4 (2.2-7.9)	6.8 ± 11.6 (2.5-100.0)	0.360
Door to balloon (min)	65.5 ± 28.7 (30.0-180.0)	77.3 ± 35.7 (30.0-240.0)	0.080
Symptom to balloon (min)	241.5 ± 171.1 (72.0-2656.0)	274.1 ± 346.7 (90.0-2880.0)	0.530
Stents diameter (cm)	2.9 ± 0.4 (2.2-3.5)	3.0 ± 0.4 (2.5-4.0)	0.260
Creatinine (mg/dl)	1.1 ± 0.1 (0.8-1.3)	1.1 ± 0.2 (0.09-1.5)	0.300
Hemoglobin (Hb) (mg/d/l)	13.4 ± 1.4 (8.9-16.3)	12.7 ± 2.2 (7.3-16.8)	0.058
Systolic blood pressure (mmHg)	124.0 ± 20.1 (95.0-185.0)	124.1 ± 17.7 (90.0-165.0)	0.980
Heart rate	74.6 ± 10.5 (50.0-93.0)	82.9 ± 13.8 (45.0-119.0)	0.002
GRACE score	148.0 ± 25.2 (98.0-215.0)	177.0 ± 80.1 (120.0-798.0)	0.008
Lactate dehydrogenase (LDH)(u/l)	551.0 ± 249.0 (284.0-1153.0)	745.1 ± 611.4 (268.0-3561.0)	0.026
Creatine phosphokinase-MB (IU/l)	71.6 ± 124.4 (5.0-542.0)	127.4 ± 138.3 (10.0-550.0)	0.052
Total creatine phosphokinase (IU/l)	491.5 ± 720.7 (32.0-2800.0)	994.2 ± 1239.9 (53.0-5250.0)	0.013
Hemoglobin A1c (mmol/mol)	6.2 ± 1.9 (4.3-13.8)	6.1 ± 1.4 (4.0-11.8)	0.079
Duration of hospitalization (d)	6.2 ± 2.6 (4.0-18.0)	8.2 ± 3.7 (5.0-26.0)	0.004
Platelet count (10^9/l)	191.0 ± 27.0 (122.0-250.0)	216.1 ± 76.4 (117.0-666.0)	0.018
Platelet/lymphocyte ratio	84.6 ± 26.3 (30.0-139.0)	136.8 ± 67.0 (11.8-3561.0)	0.001
Troponin (ng/ml)	66.1 ± 37.5 (3.0-172.0)	74.5 ± 60.9 (2.0-193.0)	0.120

PTX3: Pentraxin-3; HLP: Hyperlipidemia; CAD: Coronary artery disease; GRACE: Global registry of acute coronary events; SD: Standard deviation

Data are expressed as mean ± SD (range) and P-values are based on independent Student's t-test unless otherwise stated

* P-values based on Fisher's exact test

Table 2. Characteristics of heart disease in two groups of patients with normal and abnormal level of pentraxin-3

Variables	Normal PTX3 (n = 30)	Abnormal PTX3 (n = 70)	P*
Type of myocardial infarction [n (%)]			0.050
Anterior	7 (23.3)	35 (60.0)	
Lateral	4 (12.3)	1 (1.4)	
Inferior	9 (30.0)	17 (24.3)	
Posterior	0 (0)	1 (1.4)	
RV Inferior	8 (26.7)	13 (18.6)	
Inferoposterior	2 (6.7)	3 (4.3)	
Culprit [n (%)]			0.030
LAD	7 (23.3)	38 (54.3)	
RCA	18 (60.0)	23 (32.9)	
LCX	5 (16.7)	8 (11.4)	
LM	0 (0)	1 (1.4)	
Pre-dilation [n (%)]			> 0.990
Yes	7 (23.3)	17 (24.3)	
No	23 (76.7)	53 (75.7)	
Post-dilation [n (%)]			0.180
Yes	9 (30.0)	32 (45.7)	
No	21 (70.0)	38 (54.3)	
Thrombectomy [n (%)]			0.080
Yes	22 (73.3)	62 (88.6)	
No	8 (26.7)	8 (11.4)	
Killip class [n (%)]			0.010
I	29 (96.0)	35 (50.0)	
II	1 (4.0)	33 (47.1)	
III	0 (0)	2 (2.9)	
Need to repeat PCI [n (%)]			0.005
Yes	7 (23.3)	38 (54.3)	
No	23 (76.7)	32 (45.7)	
Left ventricle function [n (%)]			0.007
Normal	15 (50.0)	13 (18.6)	
Mild dysfunction	6 (20.0)	17 (35.7)	
Moderate dysfunction	7 (23.3)	25 (35.7)	
Severe dysfunction	2 (6.7)	15 (21.4)	
Quantitation of mitral regurgitation [n (%)]			0.070
Without problem	11 (36.7)	10 (14.3)	
Trivial	5 (16.7)	19 (27.1)	
Mild	7 (23.3)	23 (32.9)	
Moderate	7 (23.3)	18 (25.7)	

PTX3: Pentraxin-3; RV: Right ventricle; LAD: Left anterior descending; RCA: Right coronary artery; LCX: Left circumflex artery; LM: Left marginal; PCI: percutaneous coronary intervention

* P-values based on chi-square test except for pre-/post-dilation, thrombectomy and need to repeat PCI which were tested with Fisher's exact test

Discussion

Inflammatory mediators are related to a cascade of events leading to the beginning, progression, and rupture of atherosclerotic plaques. The results of our study were in agreement with those of Inoue et al.;[5] however, it seems necessary to conduct more studies on larger populations. Inoue et al. examined 52 patients with stable angina, averring that PTX3 does not have any association with coronary risk factors such as hypertension, diabetes mellitus, and hyperlipidemia. PTX3 levels in unstable angina were clearly higher than those in the stable angina.[5] Furthermore, they suggested that PTX3 levels in patients with arterial inflammation, especially unstable angina, were increased and originated from atherosclerotic plaques. Thus, this reflects the active atherosclerosis process, indicating PTX3 as a useful predicting factor for the unstable angina.[5] On the contrary, Salio et al. studied the rat model and reported that PTX3 plays a crucial role as a

regulator and cardio-protector and carries out this role by regulating the complement cascade.[10]

In our study, GRACE score was higher in the group with abnormal PTX3 levels. GRACE risk score is "a multinational registry covering all forms of ACS, including STEMI, non-ST elevated myocardial infarction (NSTEMI), and unstable angina which consists of clinical parameters concerning patients' mortality when at hospital and six months after discharge. GRACE scoring system includes parameters such as age, history of CHF, history of MI, heart rate during rest, systolic blood pressure at the time of admission to hospital, ST-segment depression, initial serum creatinine, and elevated cardiac enzyme level in the hospital.[11] Recently, Latini et al. reported that PTX3 as an "acute phase protein" is a 3-month mortality predictor after adjusting for major risk factors and other prognostic markers in the acute phase.[7]

In our study, the number of the involved vessels, MI type, stent length and lesion culprit, and the need to have PCI all had a significant relation with abnormal PTX3 levels, representing the severity of coronary artery disease in patients with abnormal levels of PTX3.

In the study by Namazi et al., increased levels of PTX3 were high differentiation indices for high SYNTAX score, and PTX3 levels higher than 0.29 ng/dl had high specificity for the detection of coronary stenosis complex.[12] In the study by Karakas et al. carried out on patients with chronic stable angina, PTX3 was related to complexity with hs-CRP and severity of coronary artery disease and was an independent predictor for higher SYNTAX score.[13]

In our study, the increased levels of PTX3 received higher Killip class, lower ejection fraction, and higher GRACE score. To evaluate the role of PTX3 in the pathology of CHF, more interventions in larger populations are required as multicenter trials. Thus far, several studies have suggested that plasma PTX3 levels increase in patients with heart failure and are independently associated with the increasing risk of cardiac events. Suzuki et al. showed that plasma PTX3 levels in patients with heart failure were significantly higher than those in the control group, and by improving New York Heart Association (NYHA) class, particularly in patients with severe heart failure, the functional classes of III and IV increase.[14]

In our study, the group with abnormal PTX3 had a significant difference in platelet counts and platelet cells in comparison with the group with the normal level of PTX3. By using Pearson correlation, a weak correlation ($r = 0.4$) was found between the level of PTX3 and TIMI frame count; moreover, a weak correlation ($r = 0.4$) was discovered between platelets and lymphocytes ratio and the level of PTX3. In both cases, the calculated correlation was significant ($P < 0.001$). Furthermore, previous studies have indicated that higher amounts of platelets and lymphocyte counts were less associated with adverse cardiovascular outcomes. Currently, platelet-lymphocyte ratio (PLR) has been proposed as a new negative predictor of cardiovascular consequences.[15] Azab et al. demonstrated that higher levels of PLR act as long-term mortality markers in patients with NSTEMI.[16] Moreover, Balta and Ozturk stated that PLR may be a useful inflammatory indicator in clinical practice.[17] A strong correlation has been found between acute phase reactants, pro-inflammatory proteins such as hs-CRP, tumor necrosis factor (TNF), interleukin-1 (IL-1), and IL-6, and increased platelet counts in non-specific inflammatory conditions.[18] Increased platelet count may reflect a basic inflammatory marker by which various inflammatory mediators stimulate the proliferation of megakaryocytes, thus leading to relative thrombocytosis. However, studies have shown that in patients with coronary atherosclerosis, the increased levels of platelets and monocytes accumulate in the peripheral blood, which is associated with plaques sustainability. Duygu et al. showed that the average size of plaques as an index of platelet activation is associated with the reduced coronary flow after the coronary intervention.[19] Higher platelet counts are markers of the pre-thrombotic situation. On the other hand, higher platelet counts may indicate a higher proportion of platelet-rich thrombi in atherosclerotic plaques, resulting in worse outcomes.[18]

There are some limitations to this study that should be acknowledged. Our study was conducted in one medical center. Our recommendation is to conduct a multi-central study so that it can be more comprehensive. The sample size was small and we could investigate a single marker. Future studies should have a bigger sample size and other markers should be measured in order to get a comprehensive result and conclusion.

Conclusion

Currently, the biomarkers are extremely important in the field of cardiovascular diseases. The diagnostic and prognostic importance of PTX3 as a new marker has been underscored in recent studies, and it can play a significant role to triage patients

with MI. Differentiating between high-risk patients with acute cardiac infarction and low-risk ones through their clinical signs has been difficult. In this study, we found that people with a higher PTX3 level are in greater urgency for hospitalization and treatment compared with normal PTX3 level.

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Conflict of Interests

Authors have no conflict of interests.

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Acute myocardial infarction in very young adults: A clinical presentation, risk factors, hospital outcome index, and their angiographic characteristics in North India-AMIYA Study

Santosh Kumar Sinha[1], Vinay Krishna[1], Ramesh Thakur[2], Ashutosh Kumar[3], Vikas Mishra[3], Mukesh Jitendra Jha[3], Karandeep Singh[3], Mohit Sachan[3], Rupesh Sinha[3], Mohammad Asif[3], Nasar Afdaali[3], Chandra Mohan Varma[2]

Original Article

Abstract

BACKGROUND: India is currently in the fourth stage of epidemiological transitions where cardiovascular disease is the leading cause of mortality and morbidity. Purpose of the present study was to assess the risk factors, clinical presentation, angiographic profile including severity, and in-hospital outcome of very young adults (aged ≤ 30 years) with first acute myocardial infarction (AMI).

METHODS: Total of 1,116 consecutive patients with ST-segment elevation acute myocardial infarction (STEMI) were studied between March 2013 and February 2015 at LPS Institute of Cardiology, Kanpur, Uttar Pradesh, India.

RESULTS: Mean age of the patients was 26.3 years. Risk factors were smoking (78.5%), family history of premature coronary artery disease (CAD) (46.8%), obesity (39.1%), physical inactivity (38.7%) and stressful life events (29.6%). The most common symptom and presentation was chest pain and anterior wall myocardial infarction (AWMI) in 94.8% and 58.8%, respectively. About 80.6% of patients had obstructive CAD with single vessel disease (57.6%), double-vessel disease (12.9%) and left main involvement (3.2%). Left anterior descending (LAD) was commonest culprit artery (58.1%) followed by right coronary artery in 28.2%. In-hospital mortality was 2.8%. Percutaneous coronary intervention was performed in 71.6% of patients. Median number and length of stent were 1.18 and 28 ± 16 mm, respectively.

CONCLUSION: AMI in very young adult occurred most commonly in male. Smoking was the most common risk factor. AWMI owing to LAD artery involvement was the most common presentation. Mean time of presentation after symptom onset was 16.9 hours. In contrast to western population, it is characterised by earlier onset, delayed presentation, more severity, diffuse disease, and more morbidity but with favourable in-hospital mortality.

Keywords: Myocardial Infarction, Angiography, Percutaneous Coronary Intervention, Young Adults

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Introduction

Coronary artery disease (CAD) is the leading cause of mortality worldwide[1] and by 2020, will be the leading cause of disability.[2] India is going through an epidemiologic transition whereby burden of communicable diseases has been declining slowly, but that of non-communicable diseases (NCD) has been rising rapidly, thus facing a dual burden. Current estimates from various epidemiologic studies indicate the prevalence of coronary heart disease (CHD) to be 7%-13% in urban[3] and 2%-7% in rural[4] populations. Acute myocardial infarction (AMI) is one of the most common presentations of CAD.[5] Although individuals younger than 40 years of age account for only 3% of all patients with coronary artery disease,[6] they are not completely immune from CAD.[7] Additionally, AMI in very young patients aged ≤ 35 years has been poorly

1- Assistant Professor, Department of Cardiology, Laxmipat Singhania (LPS) Institute of Cardiology, Ganesh Shankar Vidyarthi Memorial (GSVM) Medical College, Kanpur, India
2- Professor, Department of Cardiology, Laxmipat Singhania (LPS) Institute of Cardiology, Ganesh Shankar Vidyarthi Memorial (GSVM) Medical College, Kanpur, India
3- Department of Cardiology, Laxmipat Singhania (LPS)Institute of Cardiology, Ganesh Shankar Vidyarthi Memorial (GSVM) Medical College, Kanpur, India
Correspondence to: Santosh Kumar Sinha, Email: fionasan@rediffmail.com

described but is estimated to be less than 2%.[8] Moreover, it carries significant morbidity, psychological impact, and financial burden for the patient and their family when it occurs at a young age as the productive age group is being affected. The prevalence of CAD as well as AMI has progressively increased in India in the last three decades from 1.1% to 7.5% in the urban and 2.1% to 3.7% in the rural population.[9] CAD among Indians occur at a younger age, with more extensive angiographic involvement contributed by genetic, metabolic, and conventional causes.[10] Hypertriglyceridemia, low levels of high-density lipoprotein cholesterol (HDL-C), metabolic syndrome, high lipoprotein-a, dietary habits, and unplanned modernization associated with sedentary but stressful lifestyle are suggested as additional risk factors for CAD. Apart from smoking, ST-segment elevation acute myocardial infarction (STEMI) in the very young (≤ 30 years) is likely related to drug abuse[11] or non-traditional risk factors, such as hyperhomocysteinemia.[12] The pattern of care and outcomes of very young with STEMI is therefore not well defined.[13] Coronary angiography (CAG) performed in young patients with AMI has identified a relatively high incidence of non-obstructive stenosis or single-vessel disease.[2] Very few studies have been conducted among North Indian patients regarding the risk factors, clinical features, coronary angiographic findings and in-hospital outcome in very young adults (< 30 years) with STEMI. So, this study was conducted to learn the details of such patients.

Materials and Methods

The present study was a prospective, single-center trial conducted among 1,116 patients. Inclusion criteria were based on diagnosis of STEMI defined by the European Society of Cardiology (ESC)/American College of Cardiology Foundation (ACCF) as (a) new ST elevation at the J point in ≥ 2 contiguous lead of ≥ 2 mm in men or ≥ 1.5 mm in women in leads V2–V3 and/or of 1 mm in other contiguous chest or the limb leads, and (b) new or presumably new left bundle branch block (LBBB) was considered STEMI equivalent. Exclusion criteria were: (a) patients with prior history of MI, coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI), (b) electrocardiogram (ECG) suggesting bundle branch block or left ventricular hypertrophy, (c) electrolyte abnormality, (d) certain conditions influencing ST-segment on ECG (e.g. suspected myocarditis, pericarditis, hypothermia, receiving amiodarone treatment etc.). Patients subsequently underwent coronary angiography and revascularization by either primary PCI or pharmaco-invasive PCI or CABG surgery after obtaining informed consent with study protocol approved by Institutional Ethics Committee compelling the principal of Helsinki.

All patients were clinically evaluated after detail history taking. Routine biochemistry [complete hemogram, urea, creatinine, viral markers such as hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) and human immunodeficiency virus (HIV), urine examination including routine and microscopy-active sediment], fasting lipid profile, antinuclear antibody (ANA), c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), plasma homocysteine level, ECG and echocardiography were performed. Smokers were defined as those who were either currently smoking (> 4 weeks) including bidi, cigarette and cigar or who had quit their smoking (< 1 year). Participants were classified as physically active if they reported moderate (walking, cycling) or strenuous exercise (jogging, football, vigorous swimming) for ≥ 4 hours/week.

Anthropometric and clinical examination including blood pressure (BP) measurement were carried out for each subject. Body weight and height were measured with participants standing without shoes in light clothes. Bodyweight was measured in kilograms to the nearest 0.1 kg using a digital scale, which was calibrated regularly. Height was measured to the nearest 5 mm using a height gauge. Body mass index (BMI), was also calculated using Quetlet's formula as weight in kg/square of the height in meters.[2] Overweight was defined as BMI > 25 kg/m^2. Blood pressure was recorded in left arm in supine position with an appropriately sized cuff using a sphygmomanometer. Hypertension was defined as systolic blood pressure ≥ 140 and/or diastolic ≥ 90 mmHg and/or on anti-hypertensive treatment. Diabetes mellitus (DM) was defined as patients having fasting plasma glucose (FPG) ≥ 126 mg/dl and/or post-prandial plasma glucose (PPPG) ≥ 200 mg/dl or a past history of DM and/or taking medication for diabetes. Hyperlipidemia was defined as serum cholesterol of ≥ 200 mg/dl, triglyceride (TG) >150 mg/dl, low-density lipoprotein > 130 mg/dl, HDL-C < 50 mg/dl for female and < 40 mg/dl for male, a total cholesterol/HDL-C value of ≥ 4.5, known cases of dyslipidemia and/or those on medication for dyslipidemia. Homocysteine was measured by

enzyme immunoassay (Axis-shield, Dundee, United Kingdom) according to the kit manual. Hyperhomocysteinemia was defined as plasma level ≥15 µmol/l. The risk factors which were studied were hypertension, diabetes mellitus, smoking habits, overweight, hyperlipidemia, hyperhomocysteinemia, physical inactivity, stressful life events (using Presumptive Stressful Life Events Scale i.e. PSLES) and a family history of premature CAD (in first degree relatives < 55 years in men and < 65 years in women). Obstructive CAD was defined as ≥ 70% lesion in major epicardial arteries or ≥ 50% lesion in left main coronary artery. Intermediate disease was defined as 50% to 69% stenosis of major epicardial arteries whereas minimal disease was defined as ≤ 50% lesion, and together they were combined and classified as having non-obstructive disease.[11] Culprit artery was diagnosed on the angiographic finding.

Statistical analyses were performed using the SPSS for windows (version 17.0, SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation whereas categorical variables were given as numbers (percentages). The comparison between groups was done by Mann-Whitney U test for continuous variables and by chi-square or Fisher`s exact test for categorical variables. P < 0.05 was considered statistically significant.

Results

Baseline Characteristics: The mean age of the patients was 26 ± 3.9 years, with a maximum number of patients (60.2%) being within the age of 25–30 years and the rest in the age group of 20-25 years. The youngest patient was 20.1 years old. Men comprised 95.1% (n = 1061) of the patients (Table 1). AMI in very young patients was highly prevalent in urban population (63.9%). Smoking was the most common risk factor (77.4%), hyperlipidemia being the second common risk factor (78.5%), whereas 46.8% of the patients had a family history of premature CAD. Hypertension was seen in 229 patients (20.5%) while 191 patients had diabetes (17.2%). Hyperhomocysteinemia was present in 214 (19.2%) patients. Physical inactivity was present in 432 (38.7%) patients and obesity in 437 (39.1%) patients. Substance abuse was rare, 52 patients reported using cannabis (4.6%). Oral contraceptive drugs were used by 34 women (35.7%) while 27 (28.5%) were either tobacco chewer or smoker. Out of 95 five women (4.1%) were unmarried.

Mode of clinical presentation: The most common symptom was chest pain in 1057 (94.8%) patients with radiation of pain (49.7%), followed by sweating 1002 (89.8%), nausea/vomiting 370 (33.2%), breathlessness 98 (8.8%), and palpitations 46 (4.2%). Fifty patients (4.5%) had atypical symptoms. One hundred ninety-nine patients (17.8%) experienced prodromal symptoms (Table 2).

Table 1. Baseline characteristics of the patients (n = 1116)

Variables	n (%)
Age (year)	26.0 ± 3.9
Sex (male/female)	1061/95 (95.1/4.9)
Background (urban/rural)	714/452 (63.9/36.1)
Smoking	877 (78.5)
Hypertension	229 (20.5)
Diabetes	191 (17.2)
Family history of premature CAD	522 (46.8)
Obesity	437 (39.1)
Hyperhomocysteinemia	214 (19.2)
Physical inactivity	432 (38.7)
Substance abuse (cannabis)	52 (4.6)
Stressful life events	330 (29.6)
Dyslipidemia	236 (21.2)
Total cholesterol (mg/dl)	193.7 ± 36.4
LDL-C (mg/dl)	123.2 ± 26.1
TG (mg/dl)	177.1 ± 57.4
HDL-C (mg/dl)	33.2 ± 7.3
Non-HDL-C (mg/dl)	158.0 ± 14.9

CAD: Coronary artery disease; LDL-C: Low-density lipoprotein cholesterol; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol

The mean time of presentation after the onset of the symptoms was 16.9 hours.

Table 2. Clinical characteristics of the patients (n = 1116)

Variables	n (%)
Clinical presentation	
Chest pain	1057 (94.8)
Breathlessness	98 (8.8)
Nausea/vomiting	370 (33.2)
Sweating	1002 (89.8)
Palpitation	46 (4.2)
Diarrhea	123 (11.1)
Violent urge to defecate	35 (3.2)
Syncope	26 (2.3)
Atypical presentation	50 (4.5)
Prodromal symptoms	199 (17.4)
Pattern of AMI	
AWMI	656 (59.0)
IWMI without RVMI	370 (33.0)
IWMI with RVMI	48 (2.5)
LWMI	14 (1.2)

AMI: Acute myocardial infarction; AWMI: Anterior wall myocardial infarction; IWMI: Inferior wall myocardial infarction; RVMI: Right ventricular myocardial infarction; LWMI: Lateral wall myocardial infarction

Anterior wall myocardial infarction (AWMI) was found in 58.8% of the patients, 33.2% had inferior wall MI (IWMI) without right ventricular MI (RVMI), 4.3% had IWMI with RVMI, 2.5% had posteroinferior MI while 1.2% had lateral wall MI (Table 2). All patients were preloaded with 325 mg chewable aspirin and high-dose statin. One hundred seventy patients (15.3%) underwent primary Percutaneous transluminal coronary angioplasty (PTCA) within 12 hours of culprit artery and they received either clopidogrel, prasugrel or ticagrelor. About 310 patients (27.8%) presented late (> 12 hour) and they were managed medically as per guideline. Remaining 620 patients (55.6%) received thrombolysis with streptokinase, reteplase or tenecteplase (Table 3). Eight patients (1.3%) developed intracranial hemorrhage after thrombolysis of whom 4 died (50%). Thirty-one patients (2.7%) were in cardiogenic shock and they were managed with inotropes and Intra-aortic balloon pump (IABP) (Table 3). The remaining 25 patients refused the procedure. The rest of the patients were subjected to coronary angiography with intent to ad hoc PTCA (Figure 1).

Coronary angiographic characteristic and PCI: Angiography was done by either radial or femoral route after Allen's test (TIG Cath-Teumo Inc., USA; JL/JR Medtronic, USA) in 1061 patients. About 855 (80.5%) patients had obstructive CAD, 55 (5.2%) had normal angiogram while 21 (0.02%) had spontaneous dissection. Single vessel disease (SVD) was observed in 611 (71.5%), double vessel disease (DVD) in 137 (16.1%), triple vessel disease (TVD) in 56 (6.6%), left main in 28 (3.2%) and anomalous coronaries in 23 (2.3%) patients.

Table 3. Medications used during hospital stay (n = 1116)

Variables	n (%)
Aspirin	1116 (100)
Clopidogrel	817 (73.3)
Prasugrel	221 (19.8)
Ticagrelor	78 (6.9)
Tenecteplase (TNK)	266 (43.0)
Reteplase	85 (17.0)
Streptokinase (STK)	269 (44.0)
Statin	1116 (100)
Beta-blocker	794 (71.2)
ACEI/ARBs	721 (64.5)
Diuretics	299 (26.8)
Aldosterone antagonist	126 (11.3)
Amiodarone	24 (2.3)
Lignocaine (i.v)	26 (12.4)
Inotropes (i.v)	59 (5.3)
Magnesium (i.v)	19 (1.7)
Atropine	85 (7.6)
Heparin (UFH)	494 (44.3)
Enoxaparine	959 (85.9)
Abciximab	101 (9.1)
Temporary pacing	36 (3.2)
IABP	31 (2.7)
Stents [total number/number of patients (%)]	945/799 (71.6)
BMS	43 (5.3)
DES	902 (94.7)
i. Everolimus eluting stent	378 (41.4)
ii. Zotarolimus eluting stent	397 (44.4)
iii. Sirolimus eluting stent	109 (12.3)
BRS	18 (1.9)
Median stents/patient	1.18
LV function (EF)	43.0 ± 6.7
Median length of stent (mm)	28.0 ± 16.0

ACEI/ARBs: Angiotensin converting enzyme inhibitors/angiotensin receptor blockers; IABP: Intra-aortic balloon pump; LV: Left ventricle; BMS: Bare metal stent; DES: Drug-eluting stent; BRS: Bioresorbable scaffold

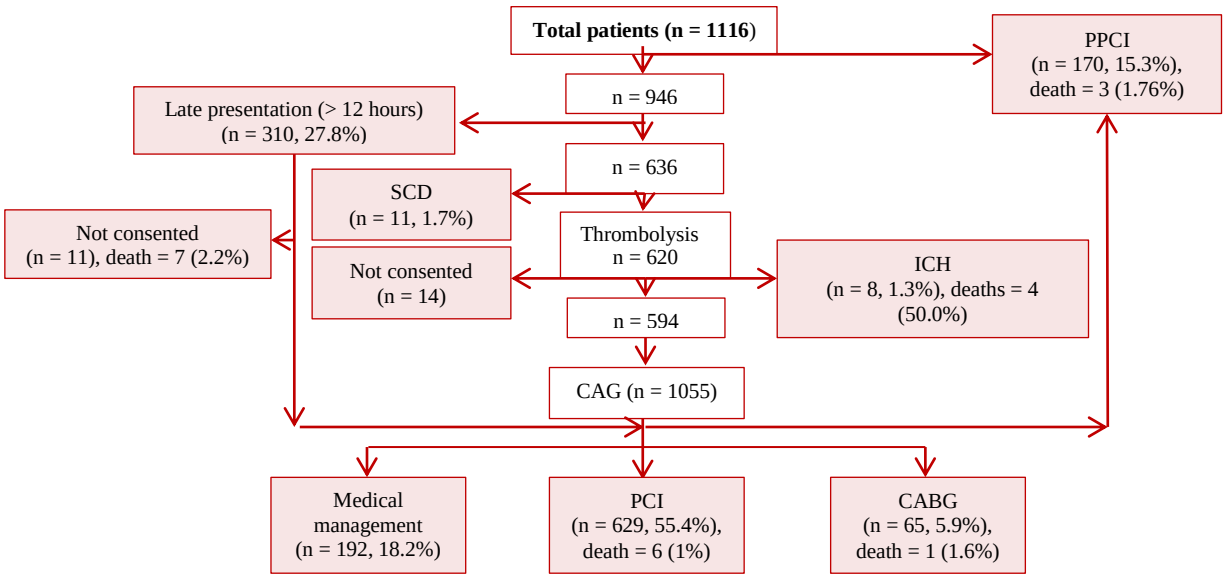

Figure 1. Flow chart of management of patients including their outcome
PPCI: Primary percutaneous coronary intervention; SCD: Sudden cardiac death; CAG: Coronary angiography; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft; ICH: Intracranial hemorrhage

Left anterior descending (LAD) artery was infarct related artery (IRA) in 58.1%, right coronary artery (RCA) in 28.2% and the left circumflex coronary artery (LCX) in 13.7% patients (Table 4).

Table 4. Coronary angiographic characteristics of the patients (n = 1061)

Variables	n (%)
Obstructive CAD	855 (80.6)
Single vessel disease	611 (71.5)
a. LAD	381 (58.1)
b. RCA	185 (28.2)
c. LCX	89 (13.7)
Double Vessel Disease	137 (16.1)
a. LAD and RCA	68 (6.4)
b. LAD and LCX	50 (4.8)
c. RCA and LCX	19 (1.8)
Triple vessel disease	56 (6.6)
Left Main disease	28 (3.2)
a. Isolated involvement	3 (0.3)
b. With SVD	19 (1.8)
c. With DVD/TVD	6 (0.5)
Anomalous coronaries	23 (2.8)
a. Split RCA	3 (13.0)
b. ACAOS	16 (69.6)
c. Single origin giving all three coronary arterie	4 (17.4)
Non-obstructive CAD	130 (12.2)
Spontaneous dissection	21 (0.02)
Normal coronaries	55 (5.2)
Lesion characteristics (length wise)	
a. Type A	34.1
b. Type B	18.4
c. Type C	47.5

CAD: Coronary artery disease; ACAOS: Anomalous coronary artery from opposite sinus; DVD: Double vessel disease; LAD: Left anterior descending artery; LCX: Left circumflex artery; RCA: Right coronary artery; SVD: Single vessel disease; TVD: Triple vessel disease

SVD was present in 58 (61.1%) of female patients whereas 542 (51.1%) of male patients had SVD (P < 0.002). DVD was present in 8 (8.4%) female patients in comparison to 129 (12.2%) male patients (P = 0.350). In DVD, LAD and RCA involvement in 68 (6.4%) were the most affected arteris followed by LAD and LCX involvement in 50 (64.8%), and the least common was LCX and RCA involvement in 19 (1.8%) patients. TVD was seen in 2 (2.1%) female patients but in 54 (5.1%) male patients. left main coronary artery (LMCA) disease was seen only in male patients whereas none was seen in female patients (P = 0.001). Non-obstructive CAD was seen in 7 (7.3%) female patients whereas 123 (11.5%) of male patients (P = 0.300). Spontaneous dissection was seen in 13 (13.7%) female patients compared to 8 (8.4%) male patients (P < 0.030). Normal coronaries were seen in 4 (4.3%) female patients and 51 (4.8%) of male patients (P = 0.430). Patients with diabetes had trend toward double vessel, multi-vessel and left main involvement in comparison to nondiabetic patients. DVD was seen in 41 (21.4%) of patients with diabetes and in 96 (10.4%) of patients without diabetes. TVD was present in 15 (7.8%) and 41 (4.5%) patients with and without diabetes, respectively (P = 0.040). LMCA was present in 7 (3.7%) and in 21 (2.3%) patients with and without diabetes, respectively (P < 0.050). In 799 (71.6%) patients who underwent PTCA, 945 stents were placed (43 bare metal stent in 40 patients and 902 drug eluting stents among 759 patients) with median of 1.18 stent per patient. Most of them had received everolimus-eluting stent (n = 378, 41.4%) followed by zotarolimus-eluting stent (n = 397, 44.4%), sirolimus-eluting stent (n = 109, 12.3%) and bioresorbable scaffold (n = 18, 1.9%). Lesion characteristics were type A (n = 336, 42%), type B (n = 175, 22%), and type C (n = 288, 36%). Median length of stented lesion was 28 ± 16 mm (Table 3).

Complication of acute coronary syndrome: About 166 (14.9%) patients developed complications during the acute MI phase (Table 5) including persistent chest pain in 26 (2.3%), pericarditis in 28 (2.5%), and heart failure in 114 (10.2%) patients.

Table 5. In-hospital outcome of the patients (n = 1116)

Variables	n (%)
Persistent chest pain	26 (2.3)
Pericarditis	28 (2.5)
Heart failure	114 (10.2)
Atrioventricular (AV) block	50 (4.5)
Arrhythmia	59 (5.2)
Mitral regurgitation	148 (13.2)
Mild to moderate	143 (96.7)
Severe	5 (3.3)
Ventricular septal rupture	4 (0.3)
Rupture of ventricular free wall	2 (0.17)
Cardiogenic shock	55 (4.9)
Pulmonary Edema	26 (2.3)
Intracranial bleed	08 (1.3)
Reinfarction	19 (1.7)
Retro peritoneal bleed	1 (0.1)
Survivor of cardiac arrest	33 (2.9)
Mortality	32 (2.9)

Heart failure was classified according to Killip-Kimball classification. Killip I was found in 21 (1.8%), Killip II in 29 (2.6%), Killip III in 39 (3.5%) and Killip IV in 26 (2.3%) patients. Pulmonary edema occurred in 26 (2.3%) patients of which 4

(4.2%) were female and 22 (95.8%) were male. Fifty-nine (5.3%) patients had severe rhythm disturbances: atrial fibrillation 13 (1.1%), junctional rhythm 16 (1.4%), idioventricular rhythm 7 (0.7%), ventricular tachycardia 19 (1.7%) or ventricular fibrillation 4 (0.3%). Fifty-five (4.9%) patients were in cardiogenic shock of which 5 (5.2%) were female and 50 (5.4%) were male. ventricular septal rupture (VSR) was seen in 4 (0.3%) patients and all were male. Two (0.17%) patients had free wall rupture, one male and one female. Nineteen (1.7%) patients suffered reinfarction of which one had sub-acute stent thrombosis, four of them were previously thrombolysed with streptokinase and the rest of them were those who had presented late. Atrioventricular (AV) block was seen in 50 (4.5%) patients of which 33 (2.9%) were I° AV block, 12 (1.1%) were II° AV block, and 5 (0.5%) patients had complete heart block which recovered completely. Echo based mitral regurgitation (MR) was noted in 148 (13.2%) patients of which 143 (12.3%) patients had mild to moderate MR whereas 5 (0.5%) had severe MR. Of severe MR, two were female and three were male. Intracranial bleeding were reported in 8 patients (1.3%) who had been thrombolysed.

Mortality data: Among 1116 patients, 32 (2.9%) patients died during index hospitalization (5.0 ± 2.1 days) (Table 5 and Figure 1). Mortality was more in 25-30 years age group compared with 20-25 years age group (P = 0.350). Mortality was more in male patients (30 out of 1021, 2.9%) compared to female patients (2 out of 95, 2.1%) with P < 0.01 with similar mean age. In-hospital mortality was more in the group of patients with diabetes (7 out of 191, 3.7%) compared to the group of patients without diabetes (25 out of 925, 2.7%, P = 0.040). There were three deaths (1.76%) in primary PCI group (two had ostial LAD lesion and one had DVD with proximal LAD lesion) of which one had no reflow, one had acute, and another had subacute stent thrombosis. All of them had extensive AWMI with severe left ventricle dysfunction and one was in cardiogenic shock. Sudden cardiac death was noted among 11 patients (1.7%) because of ventricular tachycardia or fibrillation which were though cardioverted but could not be revived. There were seven deaths (2.2%) in those who had presented late (n = 320, 27.8%) of which free wall rupture (n = 2), ventricular septal rupture (n = 4), and sudden death (n = 1) were the reasons. Among eight patients (1.3%) who developed intracranial bleeding, four deaths were observed in thrombolytic group (n = 620). Three had received streptokinase, three had tenecteplase, and two were thrombolysed with reteplase. There were six deaths in pharmaco-invasive PCI group (n = 629, 1%) of which retroperitoneal bleeding (n = 1), stent thrombosis (n = 2), progressive pump failure (n = 1), sepsis (n = 1) and intracranial hemorrhage (n = 1) were the reasons. One who had intracranial hemorrhage had received prasugrel after PCI. One death after CABG surgery was attributed to multi-organ failure.

Discussion

With rising prevalence of CAD in India, World Health Organization (WHO) estimates that by the end of 2020, India will be the cardio-diabetic capital of the globe. CVD tends to be more aggressive and starts manifesting at a younger age[14] which was also noted in our study. One of the most consistently demonstrated risk factors for CAD is male sex. The skewed gender distribution among males (95.1%) vs females (4.9%) of the study population is attributed to the protective effects of estrogens in preventing atherosclerosis and prevalence of smoking which was much more common amongst male that has been clearly demonstrated in various epidemiological studies.[15] It manifests decades earlier than western population as in GUSTO trial in which mean age was 62 ± 5 years as conducted by Hochman et al.[16] Atypical presentation which is also common amongst female has also got a role to play; a feature noted in INTERHEART study (overall male, 76%) and its South Asian cohort (85%).[17]

MI without prodromal symptoms is more common in younger patients with CAD[18] as seen in our study. Histopathological studies have shown that these plaques contain more lipid with relative lack of cellular scar tissue and are present for a shorter period of time or develop more quickly than plaques seen in older patients. These vulnerable plaques are prone to rupture that attributes for more STEMI at younger age than chronic stable angina.[19] High prevalence of stressful life events (29.6%) may have accounted for the instability of the plaque leading to its rupture culminating into STEMI. The relatively high prevalence of DVD (21.4%) and TVD (7.8%) in patients with diabetes when compared with those free of diabetes (10.4% and 4.5%, respectively) confirms the role of diabetes as a risk factor in CAD.[19]

Hypertension is another conventional risk factor for CAD. In our study, 20.5% of the patients had

hypertension which was lower than South Asian cohort of INTERHEART study (31.1%) as population subgroup were different.[17]

Following age, cigarette smoking is the most important and consistent risk factor for CAD with contribution ranging from 62% to 90%[20,21] in various studies. Like previous studies, smokers comprised 78.5% of the population.[22] It adversely affects all phases of atherosclerosis by hastening thrombotic process, endothelial dysfunction, and coronary vasoconstriction, induces proinflammatory effects and ultimately creats a thrombotic milieu. Smoking cessation should be started as primordial prevention. There should be a strong legislation as well to prevent its uptake as it will cut down the major risk.

Obesity was the infrequent cause in all the earlier studies with incidence of 3.3%–20%.[20] Physical inactivity was present in 53.5% patients. The prevalence of obesity was 39.1% in our study which was similar to South Asian cohort of INTERHEART study (44.2%).[17] Lakka et al. in have reported that abdominal obesity is an independent risk factor for acute coronary syndrome in middle-aged men and in combination with smoking, the risk of coronary events increases by 5.5 times.[22] Central obesity, an important component of metabolic syndrome is more frequent in persons of Indian origin.

In our study, hyperhomocysteinemia was seen in 58.5% of the patients with MI which was consistent with the study by Masoomi et al.[23] reporting a prevalence of 49.4%. These observations are important for primary prevention in India. The mechanisms include its effect on the vascular endothelium, platelets and its role in increasing the risk of thrombosis.[24]

In our study TG was directly and HDL-C was inversely related with relative risk of MI, a finding similarly shown by Hughes et al. among Asian Indians in contrast with western world where increased low-density lipoprotein (LDL) is more responsible for CAD.[25] Another finding which emerged from our study was that non-HDL-C may also be an implicating factor.

AWMI was the most common STEMI in our study which was similar to earlier studies among those ≤ 35 years.[16] Angiographic data in very young patients of STEMI is sparse as only a very small percentage of young patients undergo angiography. Regarding the extent of coronary lesions, our study revealed a preponderance of SVD followed by DVD and TVD among both sexes, which had also been reported by another study.[26] Among various studies among patients < 35 years of age, significant CAD was seen in 73.3% to 78% of the patients following the first MI[18,27] and TVD in 42% which is similar to our study although incidence of TVD in our study was much lower. Our finding is consistent with the other studies carried among Indian population but angiography was carried in a smaller fraction of patients than ours.[3,16,19] Also, the rate of total occlusion was quite high as acute thrombosis of a single lesion as a cause of infarction in patients with SVD and otherwise normal coronary arteries.[20] This was also our finding as 15.3% of patients underwent primary PCI and 55.4% of patients underwent PCI after thrombolysis meaning that all these lesions were amenable for PCI. Only a small fraction of patients received primary PCI as it was more expensive. Also, cath-lab is nonoperational at night and many patients were admitted during night-time and therefore the majority received pharmaco-invasive treatments. Similarly, in the daytime, when expected door to balloon time was ≥ 90 min, thrombolysis was offered and subsequently PCI was performed. The extent of disease was also advanced as two third had either type B or C lesion. Left main involvement was higher (3.2%) than previous studies which implies different atherosclerotic behavior and burden than western population. Another interesting finding in our study was anomalous origin of coronary arteries from opposite sinus (2.8%) and single origin of all three coronary arteries in 4 cases which in itself is exceedingly rare. Incidence of angiographically normal coronary arteries in patient < 35 years in various studies were 9% to 17% which appears little higher than ours (5.2%)[20,28] but most of these studies are from the western world. Causes could be coronary spasm, spontaneous recanalization or thrombosis with reperfusion.[29] Rupture of an insignificant plaque promoting thrombosis may have caused infarction and subsequent lysis may then leave lumen intact. Without intravascular ultrasound, possibility of Glagov phenomenon cannot be ruled out. High prevalence of complex lesions (25.9%) observed in our study suggests that premature CAD is associated with rapid disease progression rather than a gradually evolving process.[30] Left main disease were significantly higher in view of diabetes. Unstable left main and those with mechanical complication were urgently referred for CABG surgery and those who were not amenable for PCI were referred for staged CABG surgery. Spontaneous dissection as cause of STEMI was significantly higher in women.

Complications as VSR, cardiogenic shock, free wall rupture and pulmonary edema were more common in women and in patients with diabetes as explained by other studies.[31] Late presentation, atypical presentation and underlying TVD or left main involvement were the reasons. Increased awareness and education will be of great importance to cut down these complications. Local site complication was slightly higher in femoral route. In-hospital mortality was also significantly higher among patients with diabetes and multivessel disease in our study but the overall outcome was fair.

Conclusion

AWMI owing to LAD occlusion is the most common presentation of STEMI among the Indian population < 30 years which manifests decades earlier compared to Western population. Smoking, family history of premature CAD, hyperhomocysteinemia and obesity were the most common risk factors. Multivessel disease and complication were more in diabetic population but had favorable in-hospital outcome overall. Primordial prevention about smoking cessation and life style modification in cutting down obesity will be important epidemiological tool. Awareness on this topic, importance of golden hour and early diagnosis and treatment will have huge economic impact as sizeable number of patients present late.

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None.

Conflict of Interests

Authors have no conflict of interests.

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Two cases of parachute tricuspid valve confirmed by three-dimensional echocardiography

Hedieh Alimi[(1)], Afsoon Fazlinezhad[(2)]

Case Report

Abstract

BACKGROUND: Parachute tricuspid valve is a rare congenital malformations explained in the literature. In most cases, this malformation coexists with other congenital defects. The importance of this condition depends on its functional consequences.

CASE REPORT: First case was a 52-year-old female patient presented with palpitation. She had a history of paroxysmal supraventricular tachycardia. Transthoracic echocardiography revealed large secundum type atrial septal defect and all the tricuspid valve leaflets appeared to be connected to a single calcified papillary muscle in right ventricle suggestive of parachute tricuspid valve. Echocardiography showed severe right ventricle and right atrial enlargement, and moderate to severe tricuspid regurgitation without significant tricuspid stenosis. Another case was a 30-year-old female patient referred for echocardiography prior to her breast cancer chemotherapy. Transthoracic echocardiography revealed a right ventricle with an unusual fusion of papillary muscles resulting in a single calcified head for the attachment of all tricuspid leaflets. These findings were suggestive of a parachute-like tricuspid valve. Other data were mild to moderate tricuspid regurgitation without any stenosis, and normal right ventricle size and function. In both cases, parachute tricuspid valve was confirmed by three dimensional echocardiograph.

CONCLUSION: In our first case, parachute tricuspid valve was associated with atrial septal defect, although in the second case, no associated anomaly was detected, a condition not previously reported in the literature. In both cases, parachute tricuspid valve was not associated with tricuspid stenosis. Based on other published cases, parachute involvement of the tricuspid valve is less often reported than cases involving the mitral valve. Additionally, the associated consequences in tricuspid valve position such as tricuspid stenosis seem to be less significant than cases involving mitral valve. It is recommended that in patients with tricuspid valve involvement, parachute anomaly should be considered as a possible rare cause.

Keywords: Tricuspid Valve, Congenital Abnormalities, Atrial Septal Defect, Echocardiography

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Introduction

Isolated congenital malformations of the tricuspid valve are relatively rare. In most cases, these malformations coexist with other associated defects. The importance of this condition and related symptoms depends on functional consequences such as tricuspid regurgitation and/or stenosis and presence of other associated lesions.

A parachute deformity is one of these congenital malformations. It occurs when the chordae tendineae arise from a single papillary muscle or muscle group.[1] This type of deformity may involve one or both atrioventricular valves.

The first case involving parachute deformity of tricuspid valve was confirmed in 1972 via necropsy and was published in the literature.

Our current report includes two new cases of parachute tricuspid valve that were identified and documented in the past three years in Quaem hospital in Mashhad, Iran.

Case Report

First case involves a 52-year-old female patient with chief complaint of palpitation at the time of admission to the cardiology department.

Cardiovascular examination revealed a grade

1- Assistant Professor, Cardiovascular Research Center AND Department of Cardiology, School of Medicine, Quaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran
2- Professor, Cardiovascular Research Center AND Department of Cardiology, School of Medicine, Quaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran
Correspondence to: Afsoon Fazlinezhad, Email: fazlinejada@mums.ac.ir

III/VI pansystolic murmur at the right lower sternal border and fixed splitting of second heart sound.

Electrocardiogram showed non-specific ST segment and T wave (ST-T) changes.

Patient's past medical history included paroxysmal supraventricular tachycardia which was recorded in her previous palpitation attack electrocardiography.

Transthoracic echocardiography revealed large (26 mm) secundum type atrial septal defect with left to right shunt and all the tricuspid valve leaflets appeared to be connected to a single calcified papillary muscle in right ventricle suggestive of parachute tricuspid valve (Figure 1). Other findings were severe right ventricle and right atrial enlargement and moderate to severe tricuspid regurgitation without significant tricuspid stenosis. Measured systolic pulmonary pressure gradient was 47 mmHg.

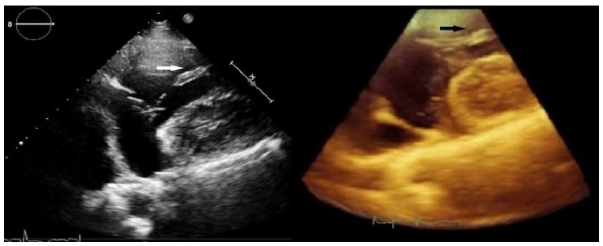

Figure 1. Transthoracic two-dimensional (left image) and three-dimensional (right image) echocardiograms in case 1, in mid-systolic time and right ventricle inflow view showing the attachment of the anterior and the septal leaflets of the tricuspid valve to a single papillary muscle (arrows)

Three-dimensional transesophageal assessment of right ventricle was also performed and parachute tricuspid valve with single papillary muscle was confirmed (Figure 2).

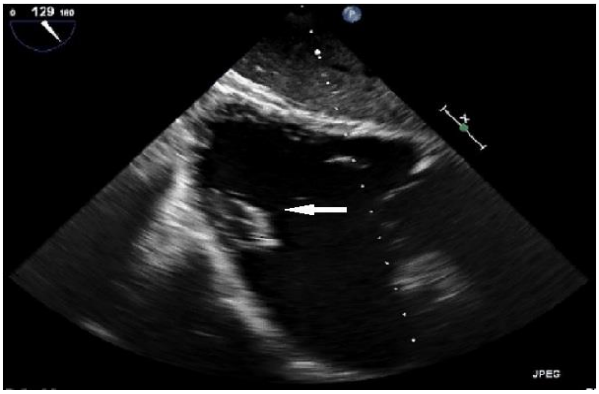

Figure 2. Two-dimensional transesophageal echocardiogram in case 1, in transgastric right ventricle view showing only single papillary muscle (white arrow)

The patient underwent atrial septal defect device closure. Transthoracic echocardiography follow-up two months later showed mild right ventricular enlargement with mild to moderate tricuspid regurgitation, without tricuspid stenosis and residual shunt.

Second case was a 30-year-old female patient referred to the cardiology department for echocardiography prior to her breast cancer chemotherapy.

Cardiovascular examination revealed a grade II/VI pansystolic murmur at the lower right sternal border.

Electrocardiogram was normal.

Transthoracic echocardiography revealed a right ventricle with unusual fusion of papillary muscles resulting a single calcified head for attachment of all tricuspid valve leaflets. These findings were suggestive of a parachute-like tricuspid valve. Other data were mild to moderate tricuspid regurgitation without any stenosis, normal right ventricle size and function without any associated anomaly (Figure 3). Parachute-like tricuspid valve was confirmed by three dimensional echocardiography (Figure 4).

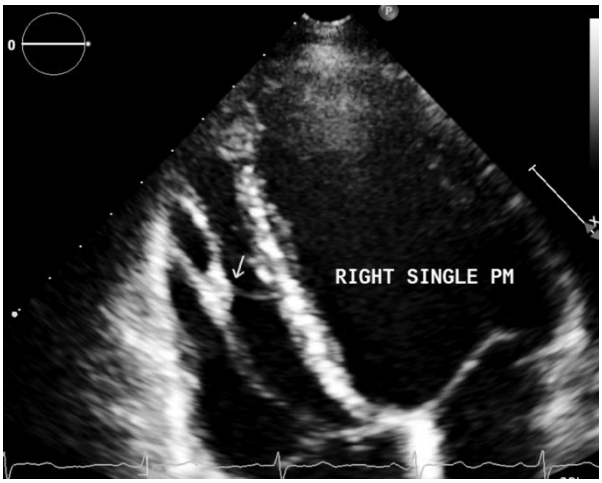

Figure 3. Transthoracic echocardiogram in case 2, in mid-systolic time and four chamber view of the right heart showing the unusual fusion of right ventricle papillary muscles (PM) resulting in a single calcified head for attachment of all tricuspid leaflets (white arrow)

We recommended follow-up echocardiography.

Discussion

Until late 2015, only six patients with parachute tricuspid valve abnormality were reported and almost all of them had other associated malformations.

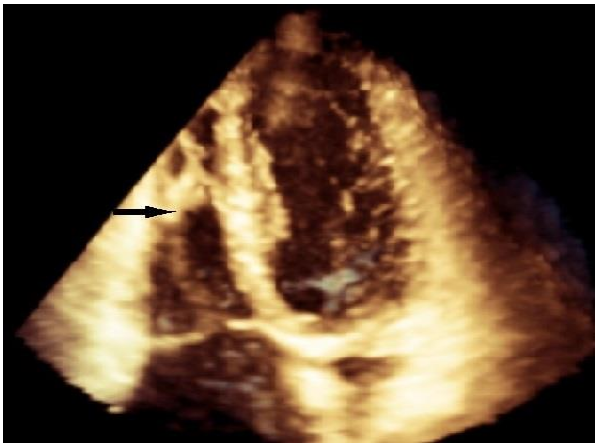

Figure 4. Three-dimensional transthoracic echocardiogram in case 1, in mid-systolic time and four chamber view of the right heart showing a single calcified papillary muscle for attachment of all tricuspid leaflets (black arrow)

First case of parachute tricuspid valve was reported in 1979 by Milo et al. whose findings included associated anomalies of double-chamber right ventricle and straddling of mitral valve in 10-week-old child.[1] In 1980 Ariza et al. described presence of parachute tricuspid valve in association with tetralogy of Fallot resulting in tricuspid stenosis.[2] Two additional cases of parachute tricuspid valve described by Marwah et al.[3] and Mohan et al.[4] were associated with atrial septal defect with or without ventricular septal defect. Neither of these two cases had tricuspid stenosis. Kurtul et al.[5] and Mohan et al.[6] reported two cases of parachute both in mitral and tricuspid valves. Mild mitral valve stenosis and normal functioning tricuspid valve at former case and moderately severe regurgitation at latter case were also noted.

In our first case, we demonstrated parachute tricuspid valve with associated anomaly (atrial septal defect) as Marwah et al.[3] and Mohan et al.[4] had reported. In our second case we did not find any associated anomalies which to our knowledge, has not been previously reported in the literature. In the first case there was no tricuspid stenosis and atrial septal defect device closure eliminated severity of tricuspid valve regurgitation. We proposed that this was due to reduction of tricuspid annular size and reduction of right ventricular volume overload. In the latter case, parachute tricuspid valve was not associated with consequences of tricuspid stenosis and significant regurgitation.

Based on published cases, parachute involvement of tricuspid valve is less common and its consequences such as tricuspid stenosis are less significant than involvement in mitral valve position.

We believe that the larger size of tricuspid valve annulus was a crucial factor in explanation of having less significant tricuspid stenosis in this position.

It is recommended that in patients with tricuspid valve involvement, parachute anomaly should be considered as a possible rare cause.

Acknowledgments

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Conflict of Interests

Authors have no conflict of interests.

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Right ventricular thrombosis as a manifestation of Behçet's syndrome

Payam Ebrahimifar[1], Javad Shahabi[2]

Case Report

Abstract

BACKGROUND: Behçet's disease (BD) is a rare condition with a classic triad of oral and genital ulceration and eye disease. Cardiovascular complication is a rare finding in BD.

CASE REPORT: In this report, we present a seventeen years old patient with a history of fever for 20 days, who developed a clot in right ventricle (RV). Cardiac magnetic resonance imaging (MRI) and echocardiography demonstrated a thrombosis in RV and a thoracic multi detector computed tomographic image showed pulmonary thromboembolism (PTE) in patient. The patient was administered with methylprednisolone, cyclophosphamide and anticoagulant. A regular follow-up was carried out. Two months later, the RV clot had disappeared on transthoracic echocardiography (TTE).

CONCLUSION: In BD, early cardiac MRI and echocardiography should be performed for the detection of cardiac involvement, and medical treatment is the first choice of treatment.

Keywords: Behçet's Disease, Cardiac Complication, Thrombosis, Magnetic Resonance Imaging

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Introduction

Behçet's disease (BD) is a rare condition with a classic triad of oral and genital ulceration and eye disease. The other manifestations of BD are rare and include cardiovascular, gastrointestinal, musculoskeletal and central nervous systems.[1] Intracardiac thrombosis is a rare and serious complication that can occur in half of the BD cases although cardiac involvement is not common.[2] The management of this complication is difficult due to recurrence even after surgical resection of the thrombus. Intracardiac thrombosis is a rare complication of BD which has not been established much in the literature. We report here a case of BD who had thrombosis in right ventricle (RV) due to BD.

Case Report

In March 2015, a 17-year-old man was referred to our hospital by infectious disease specialists for the evaluation of fever for over 20 days. He was treated for viral infection at first by infectious disease specialists. Then antibiotic therapy was conducted due to painful oral and skin lesions on scrotum. Patient suffered from bilateral vision loss and photophobia initiated 3 days before admission to hospital. His body temperature was 38.8 °C, systolic/diastolic blood pressure was 115/70 mmHg and heart rate was 96 bpm when physically examined.

The heart sounds were normal without any murmurs and the lung fields were clear to auscultation. The electrocardiogram showed normal sinus rhythm. The chest X ray was normal. We noted an inflammatory syndrome in the laboratory results (white blood cell count: 113,000 mm^3, neutrophil: 60%, C-reactive protein: 62 mg/l, erythrocyte sedimentation rate: 71 mm/hour). Therefore, antibiotics were started due to endocarditis. Blood cultures and serology tests for fever, Legionella, Bartonella, Tropheryma whipplei, Chlamydia, Mycoplasma, and Brucella were negative. The transthoracic echocardiography (TTE) showed a left ventricle ejection fraction of about 65% and a mobile mass seen in RV apex which was hyperechoic and well circumscribed (Figure 1).

A thoracic multi detector computed tomography (MDCT) confirmed the diagnosis of bilateral segmental pulmonary thromboembolism (PTE) and infarction. A transesophageal echocardiogram (TEE) did not show the nature of RV mass. Three differential diagnosis were introduced for RV mass including fever including infection, malignancy and clot. Thus, cardiac magnetic resonance imaging (MRI) was performed and showed that the nature of mass was clot in RV trabeculae (Figure 2).

1- Cardiologist, Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
2- Assistant Professor, Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
Correspondence to: Payam Ebrahimifar, Email: payame1383@yahoo.com

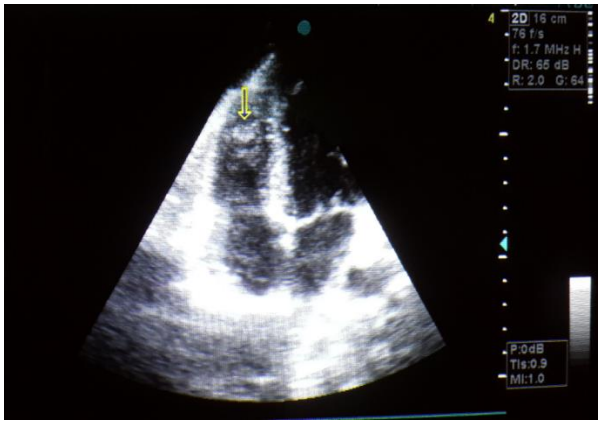

Figure 1. Transthoracic echocardiography (parasternal short-axis view) shows a cardiac mass in the right ventricle (RV)

Oral ulcers had a nonspecific pathology with a variable infiltrate of lymphocytes, macrophages, and neutrophils at the base of the ulcer that showed autoimmune disorder in histopathologic examination. We started treatment with anticoagulant since the patient was at risk of PTE and RV clot caused by leukocytoclastic and lymphocytic vasculitis which may also be seen in severe inflammation. The thrombophilia study did not show any abnormalities, and antinuclear antibody, anti-DNA antibody, anti-extractable nuclear antigen (anti-ENA) antibody, and anti-neutrophil cytoplasmic antibody tests and tumor markers were all negative. We noted a positive HLA-B51 and HLA-B5 serologic typing. Taking these findings together, the patient was diagnosed with BD.

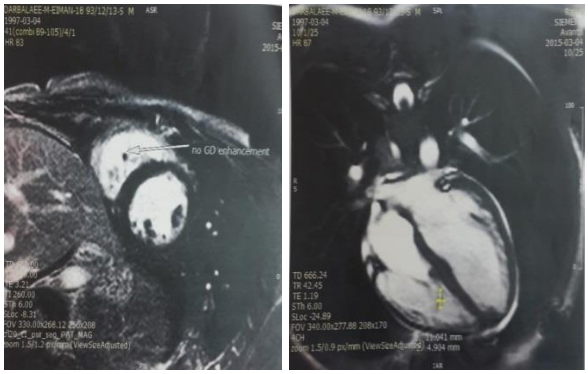

Figure 2. Cardiac magnetic resonance imaging (MRI) shows a clot in the right ventricle (RV)

Corticosteroid (methylprednisolone 1 g per day for 3 days and followed by oral prednisone 1 mg/kg) with cyclophosphamide (1 gram monthly) treatment was started. In addition, warfarin was administered to maintain the international normalized ratio (INR) at 2.5 or above. Two months later, the RV clot had disappeared on TTE.

Discussion

Behçet's syndrome has been known since Hulusi Behçet, a Turkish dermatologist, described the triple symptom-complex including orogenital ulcerations and iritis with hypopyon.[3] Although, the prevalence of vascular involvement in BD varies from 7.7% to 43%, vascular involvement is very important in BD due to serious complications and death.[4] The underlying pathological mechanism of thrombosis among BD patients is not well known. Several causal factors have been established including endothelial cell disruption, antiphospholipid antibodies,[5-7] deficiencies of protein S, protein C, and antithrombin,[8] increase in von Willebrand factor antigen levels,[9] and fibrinolysis abnormalites[10] which increase the risk of thrombosis in BD patients. Arachidonic acid metabolism plays an important role in the process of hemostasis and thrombosis. Stimulation of endothelium and platelets results in formation of eicosanoid derivatives including thromboxane B2 (TXB2) and 6-keto-prostaglandin Fl alpha (PGFla).[11]

Thrombosis in veins and arteries is one of the most frequent complications in BD which is associated with ocular involvement.[12] Cardiac involvement can be find in 1 to 5 percent of clinical series.[13]

Only 50 cases had been reported with intracardiac thrombi which is a very rare complication.[14,15] This condition is often associated with deep vein and vena cava thrombosis (50% and 22% of cases, respectively),[5] and pulmonary complications including pulmonary artery aneurysm or pulmonary embolism were also found.[16-18] Intracardiac thrombosis usually involves the right side of the heart in 78% of cases,[19-22] however some studies[23,24] have reported left ventricle involvement. In our patient, the thrombus was found in the right ventricle, like most of the studies.

Transesophageal and transthoracic echocardiography are appropriate methods for the diagnosis of cardiac thrombosis which show a mass, heterogeneous and echogenic[25] that could also be seen in intracardiac tumors such as a myxoma or endomyocardial fibrosis.[16] Imaging tests such as chest computer tomography (CT) and MRI could be helpful in the assessment of thoracic manifestations of BD including thrombus of the systemic veins, heart and pulmonary arteries.

In the present observation, the diagnosis of the

thrombus was obvious on cardiac MRI. Lack of pathognomonic symptoms and diagnostic laboratory tests makes BD difficult to diagnosis. In addition to performing lab tests and imaging, epidemiologic data should also be evaluated such as residing in Mediterranean area, young age and male sex, which increase the risk of BD. The aim of intracardiac thrombosis treatment is to control the underlying disease and resolve the thrombus. Anticoagulant and antithrombotic agents are the first line of therapy.[7] Surgery might become necessary in cases of massive or recurrent cardiac thrombosis.[2] In the case presented here, we found that Behçet's syndrome was controlled by immunosuppressive drugs and corticosteroids in our patient.

As a conclusion, one of the possible complications of BD is the thrombosis of the right heart cavities that can lead to pulmonary embolism. Early cardiac MRI and echocardiography should be performed to detect cardiac involvement, and medical treatment is the first choice of treatment.

Acknowledgments

None.

Conflict of Interests

Authors have no conflict of interests.

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Some facts about the Metabolic Syndrome in Iran

Abdollah Mohammadian-Hafshejani[(1)], Nizal Sarrafzadegan[(2)], Masoumeh Sadeghi[(3)]

Letter to Editor

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Dear Editor

Metabolic syndrome (MetS) is a group of abnormalities characterized by central obesity, high triglycerides, hypertension or high normal blood pressure, low high-density lipoprotein (HDL) cholesterol, and diabetes or high fasting glucose. Subjects with this condition are at increased risk for developing diabetes mellitus and cardiovascular disease as well as increased mortality from other causes.[1] The prevalence of MetS in the Iran, according to Isfahan Healthy Heart Program (IHHP), was 20.7% (men: 14.2%, women: 27.1%; $P < 0.01$), that in compassion of other Asian countries such as Turkey with 28.8% (men: 23.1%, women: 33.5%; $P < 0.01$),[2] China with 13.8 % (men: 09.8%, women: 17.8%; $P < 0.01$),[3] and India with 31.6% (men: 22.9%, women: 39.9%; $P < 0.01$),[4] the prevalence of MetS in Iran is in moderate level.[5-7] However, should bear in mind that the prevalence of MetS have an increasing trend, age increased in both gender.[5] In Iran, According to the Iranian national census, elderly people have an increasing trend, so in 2006 in Iran, 7.26% of population were in age group of 60 years and older, and in 2011, elderly people included 8.19% of the population. However, with passage of time and increased life expectancy among Iranian population, we expect that observe increase in the prevalence of the MetS. According to IHHP in the center of Iran, the prevalence of MetS in people in age group of 60 years and older was 43.8 % (men: 31.5%, women: 56.5%; $P < 0.01$); and in under-60-years age group, the prevalence was 17.2% (men: 11.5%, women: 22.8%; $P < 0.01$). Based on this result, if Iranian policymakers of healthcare system do not take effective preliminary and primary prevention programs, the prevalence of the MetS in the next few decades will be very high in Iran. In Isfahan (one of industrial provinces of Iran), one community-based intervention (IHHP) launched form 2000 with the aim of lifestyle modification such as increasing physical activity, weight loss, improved diet, and quitting smoking; it seems that IHHP and similar intervention programs could improve people's lifestyle and be successful in halting or decreasing the slope of incidence of MetS.[8]

Conflict of Interests

Authors have no conflict of interests.

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1- PhD Candidate, Department of Epidemiology and Biostatistics, School of Public Health, Isfahan University of Medical Sciences, Isfahan AND Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
2- Professor, Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
3- Professor, Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
Correspondence to: Masoumeh Sadeghi, Email: sadeghimasoumeh@gmail.com

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