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ARYA Atherosclerosis

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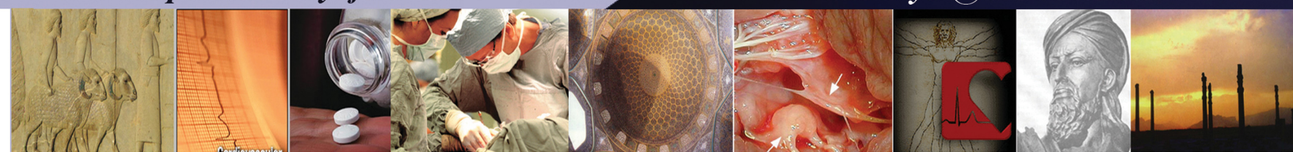

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3. Gaston M. The psychological care of patients following a myocardial infarction [Online]. 2003; Available from: URL: http://www.nursingtimes.net/the-psychologicalcare-of-patients-following-a-myocardialinfarction/199464.article/

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Staged inflation: An approach with achievement of optimal luminal gain and reduced rate of spontaneous coronary artery dissection

Mohammad Hashemi[(1)], Mohaddeseh Behjati[(2)]

Editorial

Date of submission: 16 June 2015, ***Date of acceptance:*** 09 Sep 2015

Introduction

Nowadays, interventional cardiology brought a great success to the treatment of many cardiovascular disorders. Despite these great beneficial effects, it has side effects related to the applied techniques. Among them, inflation pressure and pattern of inflation play fundamental role in this regard. By low and very high inflation pressures, the rate of stent thrombosis and in-stent restenosis becomes very high even with the use of anti-platelets agents.[1] Stent edge dissection, coronary rupture, and intima/media rupture are seen commonly by inflation at very high pressure or in distal side of long stents with diameter discrepancy between proximal and distal parts. These events could occur even by application of nominal pressure.[1,2] Currently, high pressure stent inflation is applied by many interventional cardiologists due to the more immediate luminal gain and decreased rate of sub-acute stent thrombosis.[2] However, application of high pressure brings greater rate of dissection and vessel trauma.[1]

By now, there is no standardized approach for optimal inflation pressure and pattern. Complete stent expansion is essential for achievement of adequate luminal gain and abolishment of neointimal hyperplasia. Indeed, by optimal pressure application, proper stent apposition will be achieved. Optimal inflation pressure and pattern could be defined as inflation with achievable optimal luminal gain without imposing the risk of edge dissection, stent thrombosis, and in-stent restenosis. Hereby, we describe staged inflation approach with very low risk of spontaneous coronary artery dissection. We currently use this approach for cases that undergo coronary intervention for de novo coronary lesions, regardless of lesion complexity or underlying diseases as diabetes mellitus. In this procedure, the first inflation will be set on 6 atm. Then, balloon will be inflated about 1atm every 5 seconds. At each stage, balloon should be observed simultaneously on fluoroscope scene for expansion and manometer for pressure decrease and occurrence of minimal spontaneous deflation. Inflation rate will be continued until achievement of nominal pressure. In the case of spontaneous minimal deflation, inflation should be continued. If the final diameter is not achieved by reaching nominal pressure, it will be inflated until achievement of optimal luminal diameter (compared with proximal part of the lesion). In lesions with the long segment and or lesions with the great discrepancy between proximal and distal size, the required inflation rate seems to be higher than nominal pressure, especially for drug-eluting stent deployment.

In this study, all applied instruments will be FDA (Food and Drug Administration) approved ones. We did not follow cases for long-term outcomes. We just aimed to assess the occurrence of spontaneous coronary artery dissection as a cause of in-stent thrombosis following vascular intervention. End point of this investigation was occurrence of dissection. Occurrence of flow reducing and no-flow reducing spontaneous coronary artery dissection, haziness, low flow and no-reflow phenomenon were determined by final injection.

Coronary artery dissection is amongst complications related to the mechanical trauma to vessel wall during angioplasty, which might have a poor prognosis with great influence on patient survival. By staged inflation approach, immediate luminal gain is achieved with reduced rate of spontaneous coronary artery dissection (less than 0.01% in more than 1000 cases). Current reports on spontaneous coronary artery dissection following

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coronary intervention procedures note an incidence of 0.10-0.28%.[3-5] The reduced rate of spontaneous coronary artery dissection with application of this procedure was seen for all lesions as small vessel lesions and bifurcation lesions. Staged inflation causes adjustment of muscles of medial compartment by increase in applied force due to balloon inflation. A sudden increase in diameter causes rupture in both intima and muscular layers. In this method, muscular layer becomes relaxed after application of minimal force. Indeed, the rate of local inflammation is decreased. Thus, better appointment of stent and intima would be achieved.

Staged inflation in interventional cardiology could be used for achievement of optimal luminal gain and reduced rate of spontaneous coronary artery dissection.

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Hereby, we acknowledge staffs of Sina Hospital Cath. lab.

Conflict of Interests

Authors have no conflict of interests.

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Synergistic effect of hypertension with diabetes mellitus and gender on severity of coronary atherosclerosis: Findings from Tehran Heart Center registry

Farzad Masoudkabir[(1)], Hamidreza Poorhosseini[(2)], Ali Vasheghani-Farahani[(2)], Elham Hakki[(3)], Pegah Roayaei[(4)], Seyed Ebrahim Kassaian[(2)]

Original Article

Abstract

BACKGROUND: We performed this study to evaluate the possible synergism between hypertension and other conventional risk factors of coronary artery disease (CAD) on an angiographic severity of coronary atherosclerosis.

METHODS: A cross-sectional study was conducted on 10502 consecutive patients who underwent coronary angiography in the cardiac catheterization laboratory of Tehran Heart Center Hospital (Tehran University of Medical Sciences, Iran), and their conventional risk factors including male gender, hypertension, diabetes mellitus (DM), dyslipidemia, smoking, and family history of premature CAD were recorded. The severity of coronary atherosclerosis evaluated by calculation of Gensini's score.

RESULTS: All aforementioned conventional risk factors of CAD were independently associated with severity of CAD. Multivariate linear regression analysis demonstrated that hypertension had synergistic effect with male gender [Excess Gensini's score: 5.93, 95% confidence interval (CI): 2.72-9.15, P < 0.001] and also with DM (Excess Gensini's score: 3.99, 95% CI: 0.30-7.69, P = 0.034) on severity of CAD. No interaction was observed between hypertension and smoking, dyslipidemia and also with a family history of CAD.

CONCLUSION: Hypertension has a synergistic effect with DM and male gender on the severity of CAD. These findings imply that more effective screening and treatment strategies should be considered for early diagnosis and tight control of hypertension in male and diabetic people for prevention of advanced CAD.

Keywords: Hypertension, Synergism, Atherosclerosis

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Introduction

Cardiovascular disease (CVD) has emerged as a global epidemic and is currently the major cause of death and disability worldwide.[1-3] About 83% of CVD mortality and 86.0% of CVD disability-adjusted life years took place in low-and middle-income countries.[3] In parallel with the escalating number of developing countries undergoing the epidemiologic transition (shifting from infectious diseases to chronic diseases) and demographic transition (aging of population),[2,4] the burden of CVD will undoubtedly continue to increase in coming years. Middle Eastern countries are of special concern in this context, because in the next two decades they will face the greatest increment in the absolute burden of CVD in the world.[5,6] Hence, determining the main risk factors of CVD in these countries might have pivotal role in more comprehensive and targeted planning for prevention of CVD.

Data from the reduction of atherothrombosis for continued health registry shows that hypertension is the most common risk factor of coronary artery disease (CAD) all over the world which is present in 80.3% of patients.[7] Besides, Isfahan cohort study, Iran, demonstrated that among conventional risk factors of CAD including diabetes mellitus (DM), smoking, dyslipidemia and hypertension; the presence of hypertension imposes the highest risk for developing CAD in developing countries.[8]

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There is evidence that some of conventional risk factors of CAD have the synergistic effect on the presence of CAD.[9,10] However, possible interaction between risk factors of CAD on its severity has received little attention. Identifying such potential interactions between risk factors of CAD might lead to more timely and effective preventive interventions in special populations, who have these risk factors concurrently. With this in mind, we performed this study to evaluate the possible interaction between hypertension and other conventional risk factors of CAD on the angiographic severity of coronary atherosclerosis.

Materials and Methods

This study was a cross-sectional study derived from the Tehran Heart Center hospital's cardiac catheterization registry, Iran. Tehran Heart Center is a tertiary care cardiovascular center affiliated to Tehran University of Medical Sciences. Daily prospective data collection is performed on all patients undergoing cardiac catheterization by trained research staff, and the validity of the entered data is checked by periodical rechecking of the 5% of computerized data with hard copies. This database contains about 200 variables pertaining to the demographic data, risk factors of ischemic heart disease, glucose and lipid profile, as well as findings of non-invasive studies and also coronary catheterization.

Between March 2010 and March 2012, 19128 consecutive patients (aged between 18 and 80 years) underwent elective diagnostic coronary angiography at cardiac catheterization laboratory of our center. After excluding patients with a history of previous percutaneous coronary intervention (PCI) (n = 889) or coronary artery bypass grafting (CABG) surgery (n = 434), and those with a history of previous myocardial infarction (n = 7303), a total of 10502 patients were retained for final analyses. The study protocol was approved by the Ethics Committees of Tehran University of Medical Sciences and Tehran Heart Center (Approval date: 2009/03/03- Approval number: 88-01-30-8399). Investigators guaranteed to use the medical documents of the study participants secretly. The analysis was performed on a dataset with unique patients' codes for each record without direct visibility of patients' identity.

Qualified trained staff measured waist circumference (WC) and blood pressure prior to coronary angiography. WC was measured at the minimum circumference between the iliac crest and the rib cage at minimal respiration.[11,12] For measuring the blood pressure, the subjects remained at rest for at least 15 minutes then the same staff measured blood pressure on the right arm at the sitting position.[12,13]

The family history of premature CAD was defined as a positive history of CAD including angina, angiographically determined CAD, CABG, PCI, myocardial infarction, and/or sudden cardiac death without obvious cause diagnosed at age less than 55 years for male first-degree relatives or less than 65 years for female first-degree relatives.[14]

Current smoking was defined as a regular or occasional use of tobacco in the last year.[14]

Dyslipidemia was defined as presence of any of the following:

- Total cholesterol (TC) level > 200 mg/dl,
- Low-density lipoprotein cholesterol (LDL-C) level > 130 mg/dl,
- High-density lipoprotein cholesterol (HDL-C) level < 40 mg/dl,
- Triglyceride (TG) level > 150 mg/dl,
- Patients receiving lipid-lowering agents because of diagnosis of dyslipidemia made by a physician.[14]

Hypertension was defined by any one of the following:

- History of hypertension diagnosed and treated with medication, diet and/or exercise
- Prior documentation of blood pressure greater than 140 mmHg systolic and/or 90 mmHg diastolic for patients without diabetes or chronic kidney disease, or prior documentation of blood pressure greater than 130 mmHg systolic and/or 80 mmHg diastolic on at least two occasions for patients with diabetes or chronic kidney disease
- Currently on pharmacologic therapy for treatment of hypertension systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or currently receiving antihypertensive treatments.[14]

DM was defined as fasting blood sugar (FBS) ≥ 126 mg/dl in two measurements, or a random blood sugar level ≥ 200 mg/dl and/or use of the antiglycemic agents.[14]

All pre-procedural blood biochemistry assays for patients scheduled for coronary catheterization in our center are performed in the Tehran Heart Center Laboratory with adherence to external quality control. Peripheral venous blood specimens are collected from an antecubital vein after 10-12 hours fasting of subjects.[15] FBS is measured by the

glucose oxidation method (Pars Azmoon, Tehran, Iran) and TC, TG, and LDL-C are determined by enzyme colorimetric assay (Pars Azmoon, Tehran, Iran) using a Hitachi Autoanalyzer (type 717, Hitachi medico, Tokyo, Japan). HDL-C is measured using precipitation based method.

Coronary angiography was performed using standard techniques and recorded in multiple projections for left and right coronary arteries. In this study, all the angiograms were assessed by a cardiologist, blinded to the patients' medical and anthropometric status. Obstructive CAD was defined as ≥ 50% luminal diameter stenosis in one or more major epicardial vessel.[16]

The Gensini's score was used for the assessment of the severity of CAD. This severity score has been described previously.[17] Briefly, the coronary arterial tree was divided into segments with multiplying factors according to the geographic functional importance of any given segment (5 for the left main stem to 0.5 for the most distal segments) as well as the percent reduction in the lumen diameter. The roentgenographic appearance of concentric lesions and eccentric plaques was assigned a score (0, 1, 2, 4, 8, 16, or 32 according to the degree of luminal stenosis). The sum of the segmental scores yielded the Gensini's score.[18]

The Kolmogorov-Smirnov test was applied to examine normal distribution. Logarithmic transformation was done for non-normal distributions. The continuous variables are expressed as mean ± standard deviation (SD), and they were compared using the Student t-test. The categorical variables were compared using a chi-square test or the Fisher exact test, as appropriate, and they are presented as absolute frequencies with percentages. The predictive values of the conventional CVD risk factors for the severity of CAD were assessed via linear regression analyses. First, univariate regression analysis was employed to assess the relationship between the presence of conventional risk factors and the severity of coronary atherosclerosis and thereafter independent predictive value of each risk factor was tested using multivariate regression analysis.[11] A categorical "interaction-term analysis" was performed to assess the possible synergistic effect of hypertension with other conventional risk factors of CAD including male sex, dyslipidemia, smoking, and DM.[19] The interaction terms and also the conventional risk factors of CAD were entered into a backward stepwise multiple linear regression models to assess the independent predictors of severity of CAD. For all analysis, the SPSS software (version 13, SPSS Inc., Chicago, IL, USA) was used. All P values were 2-tailed with significance defined as P ≤ 0.050.

Results

Of a total 10502 study subjects compatible with our selection criteria (mean age of 59.2 ± 10.9 years), 5611 (53.4%) were men, and 5247 (49.9%) patients were found to have obstructive CAD. The baseline clinical and laboratory characteristics of the study patients are presented in table 1.

Table 1. Baseline clinical and laboratory characteristics of study patients*

Clinical characteristics	CAD		P
	Present (n = 5247)	Absent (n = 5255)	
Age (year) (mean ± SD)	62.1 ± 10.0	56.4 ± 11.1	< 0.001
Male sex [n (%)]	2308 (44.0)	2938 (56.0)	< 0.001
Waist circumference (cm) (mean ± SD)	102.1 ± 10.5	103.4 ± 11.4	< 0.001
DM [n (%)]	1888 (36.0)	1115 (21.3)	< 0.001
Systemic hypertension [n (%)]	3278 (62.6)	2638 (50.4)	< 0.001
Dyslipidemia [n (%)]	3516 (67.9)	3018 (58.1)	< 0.001
Current smoking [n (%)]	1000 (19.1)	698 (13.3)	< 0.001
Family history of CAD [n (%)]	900 (17.2)	822 (15.8)	0.048
Waist circumference (cm) (mean ± SD)	102.1 ± 10.5	103.4 ± 11.4	< 0.001
Biochemical profile			
Ln (LDL-C) (mean ± SD)	4.69 ± 0.36	4.67 ± 0.35	0.007
Ln (HDL-C) (mean ± SD)	3.70 ± 0.26	3.76 ± 0.26	< 0.001
Ln (TC) (mean ± SD)	5.17 ± 0.26	5.16 ± 0.25	0.022
Ln (TG) (mean ± SD)	5.00 ± 0.50	4.90 ± 0.49	< 0.001
Fasting glucose (mg/dl) (mean ± SD)	124.4 ± 54.1	111.2 ± 40.6	< 0.001

*All plus-minus values are mean ± SD.

DM: Diabetes mellitus; CAD: Coronary artery disease; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; SD: Standard deviation

Table 2. Linear regression analysis for the predictive value of conventional risk factors of coronary artery disease for severity of coronary artery disease

Characteristics	Univariate			Multivariate*		
	Coefficient	95% CI	P	Coefficient	95% CI	P
Age (year)	0.81	0.74-0.88	< 0.001	0.79	0.72-0.87	< 0.001
Male sex	14.40	12.96-16.03	< 0.001	15.87	14.08-17.66	< 0.001
DM	14.08	12.38-15.78	< 0.001	12.98	11.18-14.79	< 0.001
Systemic hypertension	6.21	4.64-7.75	< 0.001	3.94	2.23-5.65	< 0.001
Dyslipidemia	5.90	4.29-7.51	< 0.001	5.34	3.63-7.05	< 0.001
Current smoking	7.92	5.80-10.03	< 0.001	5.10	2.87-7.33	< 0.001
Family history of CAD	1.50	−0.60-3.59	0.162	6.22	4.09-8.35	< 0.001

*Adjusted for age, sex, hypertension, diabetes mellitus, dyslipidemia, smoking and family history of CAD.
DM: Diabetes mellitus; CI: Confidence interval; CAD: Coronary artery disease

Table 3. Multivariate linear regression analysis for independent predictors of severity of coronary artery disease (CAD) measured by Gensini's score

Characteristics	Coefficient	95% CI	P
Age (year)	0.80	0.72-0.87	< 0.001
Male sex	20.00	17.46-22.51	< 0.001
DM	15.66	12.63-18.69	< 0.001
Systemic hypertension	7.45	4.85-10.05	< 0.001
Dyslipidemia	4.84	3.16-6.52	< 0.001
Current smoking	5.55	3.34-7.75	< 0.001
Hypertension and male gender	5.93	2.72-9.15	< 0.001
Hypertension and DM	3.99	0.30-7.69	0.034

DM: Diabetes mellitus; CI: Confidence interval

Linear regression analysis demonstrated that all conventional risk factors of CAD including age, male sex, DM, hypertension, dyslipidemia, and positive family history of premature CAD were positively associated with severity of CAD measured as the Gensini's score even after adjustment for potential confounders (Table 2). Among conventional risk factors of CAD male gender ($\beta = 15.87$, $P < 0.001$) and DM ($\beta = 15.87$, $P < 0.001$) were the two most powerful independent predictors of the severity of CAD while systemic hypertension solely had the weakest independent association with the severity of CAD ($\beta = 3.94$, $P < 0.001$).

As mentioned before, we used regression-term analysis for assessment of the possible synergistic effect of hypertension with other conventional risk factors of CAD on severity of CAD. As shown in table 3 hypertension had the synergistic effect with male gender on the severity of CAD. In fact presence of hypertension in men (rather than women) results into an average 5.93 [95% confidence interval (CI): 2.72-9.15] excess Gensini's score over the expected sum of scores from both of these risk factors. Similarly, concurrent presence of hypertension and DM in a patient results into 3.99 Gensini's score (on average) over the value resulting from simply summing the adjusted scores of both of them (coefficient: 3.99, 95% CI: 0.30-7.69).

Discussion

In this study, we evaluated the independent effect of conventional risk factors of CVD on the severity of CAD. Meanwhile, we assessed the synergistic effect of hypertension with other conventional risk factors of CAD on the severity of CAD. The main findings of our study were that all conventional risk factors of CVD including age, male sex, DM, hypertension, dyslipidemia, smoking, and family history of CAD were independently associated with severity of coronary atherosclerosis. Moreover, we observed that hypertension has synergistic interaction with male gender and DM on severity of CAD which means that coexistence of hypertension with these risk factors results in excess atherosclerosis beyond that predicted by the additive effect of the individual risk factors.

Our findings are consistent with previous studies showing that clustering of multiple cardiovascular risk factors is associated with increased risk for CVD.[9,10,20] Our study demonstrated that hypertension has a more deleterious effect on coronary atherosclerosis in men than women. On the other hand, we performed an analysis in current dataset and in agreement with previous reports[8,16,21] we observed that 89.9% of our male patients were hypertensive while hypertension was found in 43.7% of female patients. These findings might be

translated into recommendation of starting the screening for hypertension at lower ages and more frequently in men than women and also to more tight control of hypertension in men.

In this study, we demonstrated a synergistic effect between hypertension and DM. In agreement with our findings, Tomiyama et al.[22] observed that raised blood pressure and raised blood glucose, even those below defining hypertension and diabetes, synergistically lead to progression of arteriosclerotic arterial damage in Japanese men. In a recent study published by Mitsutake et al.[23] it was found that gender and diabetes history were the best predictors of CAD for the patients with hypertension. The results of a recent study suggested that the coexistence of DM and hypertension augmented the production of advanced glycation end products.[24] Additional studies are proposed to clarify the underlying mechanisms of the synergistic effects of the 2 abnormalities, even in their early stage, on the accelerated progression of structural arterial stiffening.

This study has potential limitations that should be mentioned. In this study, we used Gensini's scoring system as a widespread and familiar scoring system for quantification of severity of CAD. However, at present, there are more updated and accurate scoring systems for this purpose like "Syntax score"[25] that did not administered in this study and should be acknowledged as a limitation of our study.

In conclusion, hypertension has the synergistic effect with DM and male gender on the severity of CAD. These findings imply that more effective screening and treatment strategies should be considered for early diagnosis and tight control of hypertension in male and diabetic people for prevention of CVD.

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Conflict of Interests

Authors have no conflict of interests.

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Dairy consumption, cardiovascular risk factors and inflammation in elderly subjects

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Original Article

Abstract

BACKGROUND: Previous epidemiological studies of dairy product consumption and health outcomes have reported mixed findings. Despite increasing in life expectancy, scarce data are available in this field in elderly individuals. We tested the hypothesis that greater dairy intake is associated with lower high sensitive C-reactive protein (hs-CRP) level and better lipid profile and glycemic control.

METHODS: This cross-sectional study was undertaken on 107 elderly individuals who aged 60-78 years. Usual dietary intakes were assessed by means of a validated food frequency questionnaire (FFQ). Anthropometric measures and biochemical markers were determined using standard protocols.

RESULTS: The reported mean ± standard deviation (SD) of daily intake of dairy products and age were 588.02 ± 418.88 g/d and 63.22 ± 6.92 years, respectively. After control for demographic characteristics and dietary intakes, dairy consumption was not significantly related to the increased risk of insulin resistance [Odds ratio (OR): 2.19, 95% confidence interval (CI): 0.54, 8.86; P = 0.520] and elevated hs-CRP (OR: 1.54, 95% CI: 0.37, 6.35; P = 0.550). Participants in the top tertile of dairy had greater, but statistically not a significant risk of elevated triglyceride (TG), total cholesterol and low-density lipoprotein cholesterol (LDL-C). No significant relations were seen for hs-CRP, insulin resistance and lipid profile across tertiles of dairy products.

CONCLUSION: In this elderly population, total dairy consumption was not associated with inflammatory biomarkers levels and other cardiometabolic risk factors.

Keywords: Dairy Products, Elderly, Cardiovascular, Inflammation, Insulin Resistance

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Introduction

Aging is accompanied by the chronic inflammatory state which increases the risk of insulin resistance, metabolic syndrome and cardiovascular diseases (CVDs).[1] Sarcopenia is a common phenomenon by aging. In addition, older people are at risk for obesity. Both of these physiological states are associated with greater adipose tissue that is known as the main source of inflammatory markers and induces higher insulin resistance. Therefore, elevated inflammatory markers and insulin levels by aging and consequently chronic diseases and metabolic syndrome are expected.[1] It seems that lifestyle factors such as dietary intakes and physical activity could modulate inflammation state and insulin resistance by affecting fat mass.

Higher diet quality is associated with lower levels of inflammatory markers,[2,3] fat mass and body mass index (BMI).[4,5] A healthy diet (e.g., dash diet) is considered as a diet rich in vegetable, fruit, whole grains and low-fat dairy products which have a protective role against CVDs.[6] Although the relations between individual food groups and chronic diseases have been investigated in several researches,[7,8] there is

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still debate regarding the effects of dairy products.[9-18] While some clinical trials and epidemiological studies have reported beneficial effects for dairies,[10,14] others failed to find significant associations,[9,15,16,18] and even some dietary guidelines recommend restriction of dairy intake.[19]

One explanation for this inconsistency is related to the different components of dairy products. Dairy is a complex food, and it is difficult to define its metabolic outcomes based on its individual components. Indeed, due to the high content of saturated fatty acids (SFA) in dairy products, lower consumption of dairy products has frequently been suggested.[12] On the other side, dairies are the important source of calcium that induces anti-inflammatory effects, enhances insulin sensitivity, lowers weight gain and consequently reduces cardiovascular risks.[14]

Although dairy consumption is important in all age groups, due to differences in body composition and metabolic profiles, elderly might be more or even differently affected by dairy products. In addition, due to lactase deficiency, elderly individuals are more likely to reduce dairy intake which causes calcium insufficiency. To the best of our knowledge, there is no report regarding dairy consumption among Iranian elderly subjects. Furthermore, there is little evidence to make a clear conclusion about health outcomes of dairy consumption, especially in elderly. Therefore, in the present study, we evaluated the associations of dairy consumption with dyslipidemia, insulin resistance, and inflammation in the elderly population.

Materials and Methods

This cross-sectional study was conducted in 2013 among a sample of Isfahan, Iran, elderly subjects. Participants were recruited from retired employee of Isfahan Steel Company, who aged > 60 years.[20] In total, 120 elderly subjects were selected using simple random sampling method. Subjects were enrolled into the study if they aged 60-85 years and they had no inflammatory diseases that would affect serum inflammatory cytokines levels. We excluded participants if they were on a specific diet, or suffered from inflammatory diseases. We also excluded individuals who were receiving lowering blood sugar or lipid profile agents. Enough sample size was determined based on C-reactive protein (CRP) as the main dependent variables.[21] The protocol of the study was approved by Regional Bioethics Committee of Isfahan University of Medical Sciences. All participants expressed their willingness to participate in the current study by written informed consent.

Dietary intake was assessed using a 168-item semiquantitative validated food frequency questionnaire (FFQ).[11] Each food item was along with usual portion size. All FFQs were obtained through face-to-face interviews by a trained nutritionist. Household measures were used to convert the portion sizes of consumed foods to grams. Dairy products included all types of milk, yogurt, doogh (a traditional drink made of yogurt), cheese, and ice cream. Mean of energy and nutrient intakes from the FFQs were computed by an adopted version of NUTRITIONIST IV software for Iranian foods (version 7.0; N-Squared Computing, Salem, OR, USA).

Biochemical assessment

All biochemical tests were done on 12-hour overnight fast venous blood samples. Fasting blood sugar (FBS) was measured on the day of blood sampling. Serum concentrations of FBS, total cholesterol, low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) were quantified using commercially available enzymatic reagents (Pars Azmoon, Tehran, Iran) adapted to an auto-analyzer system (Selectra E, Vitalab, Holliston, the Netherlands). Serum insulin levels were measured by enzyme-linked immunosorbent assay (ELISA) method (ELISA; Diagnostic Biochem Canada, Inc., Montreal, Canada). Insulin resistance was assessed by both homeostasis model assessment-insulin resistance (HOMA-IR)[22] and quantitative insulin sensitivity check index (QUICKI).[23] methods using fasting insulin and glucose levels. High sensitive CRP (High sensitive CRP) was measured in serum by using an ultrasensitive latex-enhanced immunoturbidimetric assay (Randox Laboratory Ltd., Belfast, UK). To determine the plasma concentration of fibrinogen, we used Clauss method which records the rate of fibrinogen conversion to fibrin by adding thrombin.

Anthropometric assessment

A trained dietitian measured body weight, waist circumference, and height. Body weight was estimated using calibrated digital scales while participants were minimally clothed and recorded to the nearest 100 g. Height was measured while shoulders were in normal position using an upstretched tape measure and registered to the nearest 0.5 cm. Waist circumference was measured at the narrowest level between the lowest rib and iliac crest over light clothing to the nearest 0.5 cm. BMI was calculated as body weight in kg divided by height in m^2.

Assessment of other variables

To measure blood pressure, participants were asked to rest for 10 minutes. Blood pressure was measured two times with at least a 30 seconds interval using a standard mercury sphygmomanometer. Final blood pressure was considered as the average of two measurements. Socio-economic status was evaluated using a valid Persian version questionnaire containing some questions regarding 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.[24] Thereafter, participants were categorized in three groups based on the tertiles of socioeconomic scores: weak (score < 33%), moderate (33 < score < 66%), and strong (score > 66). Other demographic variables (like smoking) were assessed by using a demographic questionnaire.

Statistical analysis was done on 107 elderly subjects. Normal distribution of variables was checked by Kolmogorov-Smirnov test and histogram. General characteristics of participants were compared across the tertiles of dairy intakes by using descriptive statistics. Analysis of variance was performed to find significant differences in continues variables, and Pearson's chi-square test was used to compare categorical variables across the tertiles of dairy intakes. Dietary intakes were adjusted for daily energy intake as a covariate and were compared using analysis of covariance.

To determine the association of dairy consumption and cardiometabolic risk factors, we used multiple logistic regressions in crude and various adjusted models. First, we controlled the confounding effect of sex, smoking, and socioeconomic status. Model II was further controlled for dietary variables including energy, fat, fruit, vegetables, fiber and red meat. Model III was additionally adjusted for BMI. In all statistical analysis, we considered low median of biochemical markers as reference and assessed the risk of being in high median in comparison with low median across the tertiles of dairy. For high-density lipoprotein cholesterol (HDL-C), high median was considered as reference. All statistical analyses were done by SPSS software (version 18, SPSS Inc., Chicago, IL, USA). $P < 0.050$ was considered significant.

Results

Mean ± standard deviation (SD) dairy intake in the study population was 588.02 ± 418.88 g/d. General characteristics of participants are indicated in table 1. Participants in the highest tertile were taller than others ($P = 0.026$). Despite small differences in the means of age, BMI, systolic blood pressure (SBP) and diastolic blood pressure (DBP), they were not significantly different across the tertiles of dairy.

Table 2 shows dietary intakes of participants across the tertiles of dairy products. Participants in the top tertile consumed lower amounts of protein, fat, SFA, and cholesterol. Conversely, most of key micronutrients, including potassium, calcium, zinc, acid folic, vitamin C and A, were consumed in greater amounts by those. Although individuals in the top tertile consumed more carbohydrate, their dietary fiber intake was also higher in comparison with those in the lowest.

Table 3 presents the mean and SD of biochemical markers. Serum concentrations of FBS, hs-CRP, fibrinogen TG, total cholesterol, LDL-C, and HOMA-IR were not significantly different across the tertiles of dairy.

Table 1. General characteristics of participants across the tertiles of dairy intake

Variables	Dairy tertile			P*
	1 (< 334.06)	2 (334.06-689.12)	3 (> 689.12)	
Age (year) (mean ± SD)	61.54 ± 1.24	64.83 ± 1.19	63.28 ± 1.03	0.132
Male (%)	78.0	86.0	89.0	0.391
Married (%)	88.9	97.3	94.4	0.223
Smoker (%)	13.9	16.2	8.4	0.636
Family history (%)	38.5	40.9	38.9	0.986
Height (cm) (mean ± SD)	168.45 ± 1.44	164.91 ± 1.30	169.94 ± 1.27	0.026
BMI (kg/m^2) (mean ± SD)	26.00 ± 0.75	26.04 ± 0.61	25.91 ± 0.60	0.991
SBP (mmHg) (mean ± SD)	12.64 ± 0.26	12.47 ± 0.26	12.84 ± 0.30	0.995
DBP (mmHg) (mean ± SD)	7.91 ± 0.16	7.64 ± 0.14	7.93 ± 0.16	0.303

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; SD: Standard deviation
*By using one-way analysis of variance (ANOVA)

Table 2. Energy-adjusted of dietary intakes across the tertiles of dairy intakes

Variables	Dairy tertile			P*
	1 (< 334.06) (mean ± SE)	2 (334.06-689.12) (mean ± SE)	3(> 689.12) (mean ± SE)	
Protein (g/d)	230.86 ± 17.92	174.24 ± 17.59	122.68 ± 18.04	< 0.001
Carbohydrate (g/d)	253.33 ± 17.40	312.42 ± 17.07	396.13 ± 17.52	< 0.001
Fat (g/d)	77.60 ± 2.69	72.80 ± 2.64	61.90 ± 2.71	< 0.001
Cholesterol (mg/d)	587.32 ± 41.90	440.68 ± 41.17	227.20 ± 42.30	< 0.001
SFA (g/d)	20.21 ± 0.95	20.04 ± 0.93	17.00 ± 0.96	0.038
Potassium (mg/d)	3886.95 ± 125.13	4473.20 ± 126.00	5473.16 ± 126.00	< 0.001
Iron (mg/d)	36.66 ± 12.38	15.65 ± 12.15	14.40 ± 12.46	0.365
Calcium (mg/d)	798.14 ± 81.80	1258.56 ± 80.31	2339.10 ± 23.01	< 0.001
Magnesium (mg/d)	398.30 ± 23.44	379.10 ± 23.01	417.94 ± 23.60	0.520
Phosphorus (mg/d)	2285.48 ± 96.10	2277.64 ± 95.21	2569.55 ± 97.65	0.061
Zinc (mg/d)	10.49 ± 0.48	10.50 ± 0.47	13.41 ± 0.48	0.006
Selenium (µg/d)	5.76 ± 3.34	0.50 ± 3.28	0.23 ± 3.36	0.392
Vitamin A (RAE/d)	1104.61 ± 99.30	1409.18 ± 97.50	1510.08 ± 99.10	0.014
Vitamin E (mg/d)	10.14 ± 0.57	9.65 ± 0.56	7.26 ± 0.58	0.001
Folic acid (µg/d)	283.85 ± 19.70	378.07 ± 19.35	476.13 ± 19.80	0.001
Vitamin C (mg/d)	159.11 ± 15.80	208.21 ± 15.50	254.90 ± 15.92	< 0.001
Total dietary fiber (g/d)	14.01 ± 0.99	18.14 ± 0.97	21.28 ± 0.10	< 0.001

SFA: Saturated fatty acids; RAE: Retinol activity equivalents; SE: Standard error
*By using analysis of covariance (ANCOVA)

Table 3. Mean and standard error of biochemical markers across the tertiles of dairy

Variables	Dairy tertile			P*
	1 (< 334.06) (mean ± SE)	2 (334.06-689.12) (mean ± SE)	3 (> 689.12) (mean ± SE)	
HOMA-IR	89.64 ± 22.93	56.0 ± 12.85	73.62 ± 16.64	0.409
QUICKI	0.33 ± 0.008	0.35 ± 0.007	0.35 ± 0.007	0.485
Insulin (UIU/ml)	15.12 ± 3.24	10.91 ± 12.68	14.01 ± 2.51	0.503
FBS (mg/d)	123.94 ± 12.18	110.69 ± 5.42	104.46 ± 5.60	0.245
TG (mg/dl)	157.57 ± 13.07	156.53 ± 11.87	189.29 ± 33.63	0.486
Total cholesterol (mg/dl)	191.66 ± 8.95	194.39 ± 6.77	195.63 ± 4.21	0.927
LDL-C (mg/dl)	95.86 ± 4.74	100.83 ± 4.24	97.66 ± 4.02	0.713
HDL-C (mg/dl)	47.60 ± 1.86	51.25 ± 1.81	49.57 ± 1.27	0.305
hs-CRP (µg/ml)	5.80 ± 2.55	3.05 ± 0.87	2.59 ± 0.56	0.290
Fibrinogen (mg/dl)	278.28 ± 11.38	280.39 ± 6.84	271.59 ± 9.67	0.782

*Resulted from ANOVA
HOMA-IR: Homeostasis model assessment-insulin resistance; QUICKI: Quantitative insulin sensitivity check index; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; hs-CRP: High sensitive C-reactive protein; FBS: Fasting blood sugar; TG: Triglyceride; SE: Standard error

Crude and multiple-adjusted odds ratio (OR) and 95% confidence intervals (CI) for being in the high median of biochemical markers are provided in table 4. Higher dairy consumption was not significantly associated with increased risk of insulin resistance (P = 0.990), elevated serum levels of insulin (P = 0.470), hs-CRP (P = 0.460), LDL-C (P = 0.220), HDL-C (P = 0.900), TG (P = 0.140), total cholesterol (P = 0.330) and FBS (P = 0.550) in crude model. After adjustment for potential confounders these associations changed slightly but remained non-significant. Despite a marginal significant inverse association between dairy and elevated fibrinogen concentrations in crude model (P = 0.080), this association was eliminated in adjusted models.

Discussion

This cross-sectional study could not reveal any significant association between dairy consumption and various cardiometabolic risk factors including inflammation, insulin resistance and lipid profile among elderly individuals.

In a national report of Iran, ischemic heart disease is the second cause of death after injuries, and dietary risks are the most important risk factor to which deaths were attributable among adults.[25]

Table 4. Multiple-adjusted odds ratio (OR) and 95% confidence intervals (CI) for being in the high median of all biochemical markers and low median of high-density lipoprotein cholesterol

Variables	Dairy tertile			P*
	1 (< 334.06)	2 (334.06-689.12)	3 (> 689.12)	
HOMA-IR (> 38.88)				
Model I	1 (Ref)	0.84 (0.33, 2.17)	1.00 (0.38, 2.58)	0.990
Model II	1 (Ref)	0.85 (0.32, 2.25)	0.92 (0.32, 2.49)	0.950
Model III	1 (Ref)	0.98 (0.34, 2.81)	1.42 (0.39, 5.08)	0.800
Model IV	1 (Ref)	1.21 (0.39, 3.75)	2.19 (0.54, 8.86)	0.520
QUICKI (> 0.3399)				
Model I	1 (Ref)	0.84 (0.33, 2.17)	1.00 (0.38, 2.58)	0.990
Model II	1 (Ref)	1.17 (0.44, 3.10)	1.09 (0.40, 2.93)	0.950
Model III	1 (Ref)	1.02 (0.36, 2.93)	0.71 (0.20, 2.53)	0.800
Model IV	1 (Ref)	0.83 (0.27, 2.56)	0.46 (0.11, 1.84)	0.520
Insulin (> 8.85 UIU/ml)				
Model I	1 (Ref)	0.85 (0.33, 2.19)	1.42 (0.545, 3.70)	0.470
Model II	1 (Ref)	0.86 (0.33, 2.29)	1.33 (0.49, 3.62)	0.660
Model III	1 (Ref)	1.02 (0.35, 2.91)	2.45 (0.67, 8.94)	0.280
Model IV	1 (Ref)	1.16 (0.37, 3.61)	2.60 (0.66, 10.35)	0.340
FBS (> 96 mg/dl)				
Model I	1 (Ref)	1.60 (0.60, 4.10)	1.00 (0.39, 2.65)	0.550
Model II	1 (Ref)	1.34 (0.49, 3.72)	0.71 (0.25, 1.97)	0.450
Model III	1 (Ref)	1.43 (0.46, 4.42)	1.38 (0.38, 5.02)	0.810
Model IV	1 (Ref)	2.01 (0.61, 6.61)	2.26 (0.54, 9.50)	0.440
TG (> 139.4 mg/dl)				
Model I	1 (Ref)	1.60 (0.60, 4.30)	2.01 (0.80, 5.60)	0.140
Model II	1 (Ref)	1.63 (0.62, 4.28)	1.90 (0.70, 5.13)	0.420
Model III	1 (Ref)	1.82 (0.62, 5.31)	1.33 (0.38, 4.66)	0.540
Model IV	1 (Ref)	2.35 (0.75, 7.32)	1.66 (0.44, 6.27)	0.330
Total cholesterol (> 193 mg/dl)				
Model I	1 (Ref)	1.10 (0.40, 2.10)	1.62 (0.60, 4.30)	0.330
Model II	1 (Ref)	1.19 (0.45, 3.10)	1.45 (0.54, 3.88)	0.760
Model III	1 (Ref)	1.00 (0.33, 2.99)	1.17 (0.33, 4.17)	0.960
Model IV	1 (Ref)	0.97 (0.31, 3.01)	1.34 (0.35, 5.17)	0.860
LDL-C (> 99.5 mg/dl)				
Model I	1 (Ref)	1.83 (0.70, 4.80)	1.85 (0.70, 4.10)	0.220
Model II	1 (Ref)	1.83 (0.70, 4.80)	1.66 (0.62, 4.46)	0.430
Model III	1 (Ref)	1.10 (0.68, 5.70)	1.84 (0.54, 6.27)	0.430
Model IV	1 (Ref)	2.03 (0.67, 6.12)	2.18 (0.59, 8.00)	0.390
HDL-C (mg/dl) (< 49.5 mg/dl)				
Model I	1 (Ref)	0.69 (0.25, 1.93)	0.59 (0.21, 1.63)	0.900
Model II	1 (Ref)	0.69 (0.24, 2.00)	0.62 (0.21, 1.83)	0.670
Model III	1 (Ref)	0.71 (0.23, 2.20)	0.53 (0.15, 1.90)	0.620
Model IV	1 (Ref)	0.75 (0.24, 2.41)	0.46 (0.12, 1.76)	0.510
hs-CRP (> 2 µg/ml)				
Model I	1 (Ref)	1.61 (0.62, 4.20)	1.45 (0.55, 3.82)	0.460
Model II	1 (Ref)	1.67 (0.62, 4.46)	1.70 (0.62, 4.65)	0.500
Model III	1 (Ref)	1.65 (0.58, 4.71)	1.48 (0.43, 5.11)	0.640
Model IV	1 (Ref)	1.95 (0.58, 6.54)	1.54 (0.37, 6.35)	0.550
Fibrinogen (> 285 mg/dl)				
Model I	1 (Ref)	0.41 (0.15, 1.01)	0.40 (0.15, 1.10)	0.080
Model II	1 (Ref)	0.43 (0.15, 1.23)	0.38 (0.12, 1.15)	0.180
Model III	1 (Ref)	0.36 (0.11, 1.15)	0.36 (0.09, 1.34)	0.180
Model IV	1 (Ref)	0.38 (0.12, 1.23)	0.36 (0.09, 1.46)	0.230

HOMA-IR: Homeostasis model assessment; QUICKI: Quantitative insulin sensitivity check index; hs-CRP: High sensitive C-reactive protein; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; TG: Triglyceride
Model I: Crude; Model II: Adjusted for gender, smoking, socioeconomic; Model III: Additional adjustment for fat, energy intake, fruit, vegetable, dietary fiber and red meat; Model IV: More control for BMI (Body mass index).
*From Mantel-Haenszel extension chi-square test.

In addition, in spite of increased life expectancy, few researches have been conducted among elderly people particularly in the context of diet. To our knowledge, there is no study examining dairy consumption in relation to cardiometabolic risk factors among Iranian elderly. It seems that association between diet and disease is something different among young adults in comparison with elderly that might be attributable to differences in fat mass, fat distribution and the grade of systematic inflammation.[1] Most of available information regarding diet-disease association among Iranian elderly is related to dietary patterns and cancer risks. Although dietary patterns could provide more holistic evaluation of diet-diseases association, assessing health outcomes of individual food groups has its important public health implications. Moreover, epidemiological studies may better reflect the roles of dietary intakes on health status and be more generalizable than clinical trials. Indeed, findings from epidemiologic studies indicate habitual dietary intakes, whereas clinical trials indicate the impact of changes in dietary intakes only for a short term and may be difficult to adhere in long-term.

Dairies contain some beneficial components such as calcium, magnesium, vitamin D and whey protein, which may ameliorate metabolic abnormalities by reducing fat mass and consequently insulin resistance.[26] However, dairy products are one of the main sources of SFA that may override favorable outcomes of dairy. In the present study, we could not assess the associations for various dairy products considering their fat content. It seems that eating high-fat products is more common among Iranian populations. Therefore, SFA content of dairy products might be a concern in this population. However, findings from dietary intakes of the study participants showed that SFA intake was lower in the top tertile of dairy that might be because of less consumption of red meats, as another main source of SFA.

To date, many studies were conducted to examine the associations of dairies and cardiometabolic risk factors, but the evidence is not conclusive. Although some studies have reported beneficial effects for dairies, other studies suggested no association.[15,27] In a meta-analysis of clinical trials, Benatar et al.[15] indicated that low and whole fat dairy foods increased body weight, but did not significantly changed waist circumference, HOMA-IR, fasting blood glucose, LDL-C, HDL-C, systolic and DBP and CRP. Moreover, analysis of 3 cohorts of US adults showed that only yogurt reduced the risk of diabetes type 2 while total dairy and other dairy foods were not significantly related to the risk of diabetes.[27]

The associations of dairy products consumption and inflammatory biomarkers are inconsistent either in clinical trails[28,29] or in observational studies.[30,31] A recent systematic review on clinical trials indicated that dairy products consumption could not significantly influence low-grade systematic inflammation.[32] Findings from a cross-sectional study suggested inverse association between dairy consumption and systematic inflammation,[30] but another one failed to find significant relation for total dairy consumption in a representative sample of Iranian female.[31]

However, in this study, after subgroup analysis based on fat content of dairy products, low-fat and high-fat products were differently correlated with inflammatory biomarkers. We were not able to do such subgroup analysis because of small sample size, and larger studies are required to indicate if low-and high-fat dairy products are differently related to inflammatory biomarkers. Similar discrepancy is also observed for the effects of dairies on insulin sensitivity, as the main component of metabolic syndrome. A systematic review on short-and long-term interventions indicated that only one study has found negative association between dairy and insulin sensitivity, whilst others have reported no significant or positive relation.[33]

The lack of significant difference across the tertiles of dairy for various metabolic disorders might be attributable to low content of vitamin D in our dairy products. On the other hand, because of non-fortification of dairy products with vitamin D, vitamin D deficiency is now known as a public health concern among Iranian populations. However, consuming greater dairy products could not compensate vitamin D deficiency, and thereby could not exert their beneficial effects. There are more reasons for our non-significant findings. First, fat content of dairy products may modify their associations with metabolic profile. Second, various dairy products, including, milk, yogurt, cheese, fermented or non-fermented dairy products may influence their physiological impacts. For example, in a cross-sectional study among elderly women, only yogurt was inversely associated with common carotid artery intima-media thickness,[34] while in another cross-sectional study among adolescents, negative correlation was observed between cardiometabolic risk

factors and milk, but not yogurt, total dairy products, and cheese.[35] Moreover, body weight and composition may also affect the health benefits of dairy products.[36] More studies specifically designed to examine various types of dairy products in different BMI categories and age groups particularly elderly are warranted.

Despite neutral association between dairy product consumption and metabolic abnormalities in this population, consuming higher amounts of dairy may still be useful. Our findings suggest that individuals in higher tertile of dairy had better micronutrients intakes than those in the lowest. These findings are supported by previous research,[37] and could be relevant findings in elderly individuals to provide adequate nutrients intake.

Several limitations need to be taken into account in the interpretation of our findings. The major concern of the present study is the cross-sectional design that could not reveal causal-inference associations. It is possible that individuals with abnormal metabolic profile modify their dietary intakes and have healthier food choices. Second, using FFQ to assess dietary intakes is another limitation of our study. Since FFQ is a retrospective to assess dietary intakes, recall of dietary intakes might have been biased and consequently lead to misclassification. Although we tried to control known confounding factors, controlling all residual confounders in our study, as in all observational studies, is inevitable.

Given the aforementioned limitations, we found a neutral association between dairy products and different cardiometabolic risk factors. However, since dairy products are essential contributors of micronutrients and protein, they should be consumed in recommended amounts by dietary guidance. Clinical trials are needed to prove the exact effects of dairy products on health outcomes particularly in elderly who may limit their dairy consumption.

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Conflict of Interests

Authors have no conflict of interests.

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Prognostic factors of 28 days survival rate in patients with a first acute myocardial infarction based on gender in Isfahan, Iran (2000-2009)

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Original Article

Abstract

BACKGROUND: Determinant prognostic factors of 28 days survival rate in patients with a first acute myocardial infarction (AMI) based on gender in teen year's period in Isfahan, Iran, was the aim of this study.

METHODS: This study is a prospective hospital-based study that consisted, all patients with AMI admitted to all hospitals (private and universal hospitals) in Isfahan and Najafabad (Iran) during 2000-2009. To determinant the prognostic factors of 28 days survival rate in patients based on gender, analysis conducted separately for male and female. In analysis, we use of t-test, log Rank tests, Kaplan–Meier method, and univariate and multivariate Cox regression model.

RESULTS: Short-term (28 days) survival rate was 92.5% in male and 86.7% in female ($P < 0.001$). The adjusted hazard ratio (HR) of death for age group 80 years and older was 12.7 [95% confidence interval (CI): 5.14-31.3] in male and 8.78 (95% CI: 1.2-63.1) in female. HR for acute transmural MI of the unspecified site in male was 8.9 (95% CI: 4.68-16.97) and in female 9.33 (95% CI: 4.42-19.7). HR for receive of streptokinase in male was 1.11 (95% CI: 0.94-1.31) and in female was 0.69 (95% CI: 0.56-0.84).

CONCLUSION: Short-term survival rate in male was a higher than female. In male age, anatomic location of MI and hospital status and in female streptokinase use and anatomic location of MI was the most important prognostic factors of survival in-patient with AMI in Isfahan.

Keywords: Myocardial Infarction, Survival Rate, Gender, Isfahan (Iran)

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Introduction

Cardiovascular disease is one of the first causes of death in the world and Iran.[1] These diseases have increasing trends particularly in low-and moderate-income countries.[2] According to international reports, mortality from acute myocardial infarction (AMI) have rising trend,[3] and coronary artery disease (CAD) will remain among the three main causes of the global burden of disease to 2030.[4] According to the first national burden of disease study in Iran, CAD was the third factors of disability-adjusted life years in all ages and two genders (16% of total burden of disease). That led to 1 billion years of life lost resulted of premature mortality and 500

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thousand years lived with disability.[5] Despite a significant reduction in the amount of prevalence of coronary heart disease (CHD) in many countries[6] and advances in the treatment of patients,[7] case fatality rate (CFR) the following the incidence of AMI in both genders has remained high.[8] On the other hand, death from cardiovascular disease is the primarily cause of mortality in Iran.[1,9]

Accordingly, identifying predictive factors of mortality in patients could be an important role in reducing deaths from the disease, partially in countries such Iran that scattered reports have about the factors affecting the survival of patients with AMI. In studies that conducted in different parts of the world, factors such as diabetes mellitus, smoking, age, sex, hyperlipidemia, hypertension, previous MI introduced as the predictor of survival from AMI.[10,11]

In this study, in addition the demographic variables, we assess the role of type of AMI base on International Classification of Diseases version-10 (ICD-10), cardiac enzymes, symptoms, type of hospital, the first referral center for health services and streptokinase use as predictor of survival after first AMI, which less attention has paid to them in other studies. Thus, the aims of this study are determination of prognostic factors of 28 days (short-term) survival rate in patients with the first AMI based on gender in 10-year period in Isfahan, Iran.

Materials and Methods

This study is a prospective hospital-based study that consisted all patients with first AMI during 2000-2009 in the Isfahan and Najafabad (Iran). At the time, the study was performed about 13 hospitals were admitting and managing CHD patients in Isfahan.

In this registry, all possible CHD events were registered with ignoring MONICA age limitation. The MONICA MI diagnostic criteria were applied.[12] Diagnostic criteria are based on a collection of standardized information including past history of MI or ischemic heart disease, symptoms at onset, maximum levels of serum enzymes in admitted 1st day in the hospital, and relevant electrocardiograms (coded according to the Minnesota codes).[13] The World Health Organization (WHO) MONICA Project is concerned with events, not persons. Events are classified as first or recurrent.[12] In this study, only first events are included.

Hospital intensive care unit (ICU), coronary care unit (CCU), and cardiology ward admission and discharge lists were used for case finding. Records of patients hospitalized in cardiology wards, CCUs or in other wards but under complete or partial supervision of cardiologists were evaluated for possible signs and symptoms of CHD events. This evaluation was done by three experienced registered nurses trained in this regard before the study. They summarized proper records in special checklists containing information in age, sex, event date and hospitalization date, symptoms, history of previous MI, enzymes, admission electrocardiogram, whether the event was iatrogenic, survival status in discharge and after 28 days follow-up, and whether thrombolytic were used during hospitalization. The filled records were checked by an expert nurse with special training for the MONICA registration system. Moreover, 10% of the checklists was randomly chosen and refilled by the expert nurse from the original hospital records and compared with ones registered nurses had filled to see if any mistakes occurred. The patients investigated after admission to hospitals and patients with AMI related to different event locations assigned a specific code according to ICD-10, these codes were I21.0 (acute transmural MI of anterior wall), I21.1 (acute transmural MI of inferior wall), I21.2 (acute transmural MI of other sites), I21.3 (acute transmural MI of unspecified site), I21.4 (acute subendocardial MI) and I21.9 (AMI, unspecified), considering categorized AMI.[14]

MONICA and the WHO protocol defined AMI as a 28 days repeated attack, not considered as separate attacks but in fact related to the first AMI; however, following the first night of the 27th day after the attack it is considered as a new attack. Patients who died during the first 28 days are considered as death due to first AMI.[15] After collecting basic information about patients, their survival or death during the 28 days after the AMI were evaluated. For discharged patients, follow-up was the first executed by telephone but when their survival rates were not determined after three telephone calls, we went to the patients' homes. When previous efforts in terms of getting information about survival rate failed, using the national organization for civil registration and Isfahan cemetery, we tried to find out if the patient had died; we found the cause of death and exact date and location of the burial.[16] A detailed description of the methods used in this project was provided in previous reports.[16-24]

Overall, 14450 patients (10334 men and 4116 women) with first AMI, that inhabitants in Isfahan

and Najafabad entered in the study, 886 patients (564 men and 322 women) were excluded because their AMI type was not determined according to the ICD-10. In addition, 118 patients (82 men and 36 women) exclude from the study, because died during the 28 days after the first attack without mention of any cardiovascular disease due to accident, suicide, homicide, chronic obstructive pulmonary disease (COPD), cancer, liver cirrhosis, rheumatic heart disease, vascular disease, or atherosclerosis. In addition, 418 patients (292 men and 126 women) were excluded because outcome was unknown, and 128 patients (89 men and 39 women) was excluded from the study, Because the exact date of the occurrence or death from the disease was not specified and the 28 days duration after the attack could not be calculated in these cases,[15] also 85 patient (47 men and 38 women) were excluded because symptom or cardiac enzymes was not recorded. Therefore, 12815 patients, 9307 (72.6%) men and 3508 (27.4%) women, remained in the study (Tables 1 and 2).

Table 1. Clinical survival predictive factors in male with acute myocardial infarction

Variables	Total patients	Alive patients	Deaths patients	*Survival rates	**Adjusted HR (95% CI)	P
Age in male (year)						
39 year and lower	399	394	5	98.75	R	-
40-49	1629	1587	42	97.42	2.24 (0.88-5.66)	0.091
50-59	2525	2423	102	95.96	3.48 (1.41-8.55)	0.007
60-69	2343	2150	193	91.76	7.00 (2.87-17.00)	< 0.001
70-79	1886	1629	257	86.37	10.54 (4.34-25.60)	< 0.001
80 year and older	525	427	98	81.33	12.7 (5.14-31.30)	< 0.001
Streptokinase						
Receiving	5181	4864	317	93.88	R	-
Not receiving	4126	3746	380	90.79	1.11 (0.94-1.31)	0.340
ICD-10						
Acute subendocardial MI	752	736	16	97.87	R	-
Acute transmural MI of other sites	232	225	7	96.98	1.42 (0.58-3.47)	0.299
Acute transmural MI of inferior wall	2759	2650	109	96.05	1.74 (1.02-3.00)	0.035
Acute transmural MI of anterior wall	3187	2974	213	93.32	3.02 (1.78-5.11)	< 0.001
Acute MI, unspecified	2266	1938	328	85.53	5.90 (3.54-9.86)	< 0.001
Acute transmural MI of unspecified site	106	82	24	77.36	8.92 (4.68-16.97)	< 0.001
The first center was referred						
Non-specialized hospitals	638	573	65	89.81	2.11 (1.23-3.75)	0.011
Specialized hospital	8137	7547	590	92.75	1.50 (0.89-2.51)	0.200
Unknown	235	208	27	88.51	2.17 (1.11-4.00)	0.027
Health network or clinic	297	282	15	94.95	R	-
Symptoms						
Typical	7773	7250	523	93.27	R	-
A typical	1085	993	92	91.52	1.06 (0.85-1.36)	0.391
Others	414	339	75	81.88	1.67 (1.29-2.63)	< 0.001
Miss	6	5	1	83.33	1.87 (0.87-4.00)	0.094
***Cardiac enzymes						
A typical	1087	1026	61	94.39	R	-
Typical	7080	6597	483	93.18	1.27 (0.97-1.67)	0.078
Others	825	780	45	94.55	0.96 (0.65-1.40)	0.880
Not clear	315	207	108	65.71	4.81 (3.46-6.67)	< 0.001
Hospital						
Privative hospitals	763	716	47	93.84	R	-
Academic hospitals	8544	7894	650	92.39	1.45 (1.12-1.96)	0.018

*Survival rates at 28 days after the occurrence of the disease (percent). **Every variable adjusted for other variables. ***LDH (lactate dehydrogenase), CPK (creatine phosphokinase) and troponin.
HR: Hazard ratio; ICD: International classification of disease-10; CI: Confidence interval; MI: Myocardial infarction

Table 2. Clinical survival predictive factors in female with acute myocardial infarction

Variables	Total patients	Alive patients	Deaths patients	*Survival rates	**Adjusted HR (95% CI)	P
Age in female (year)						
39 year and lower	41	40	1	97.56	R	-
40-49	234	224	10	95.73	1.86 (0.23-14.11)	0.553
50-59	611	569	42	93.13	2.55 (0.35-18.63)	0.318
60-69	1038	920	118	88.63	4.39 (0.61-31.50)	0.123
70-79	1152	962	190	83.51	6.01 (0.84-43.00)	0.060
80 year and older	432	327	105	75.69	8.78 (1.20-63.10)	0.025
Streptokinase						
Receiving	1483	1260	223	84.96	R	-
Not receiving	2025	1782	243	88.00	0.69 (0.56-0.84)	< 0.001
ICD-10						
Acute subendocardial MI	438	426	12	97.26	R	-
Acute transmural MI of other sites	87	78	9	89.66	2.46 (1.02-5.90)	0.043
Acute transmural MI of inferior wall	901	819	82	90.90	2.27 (1.22-4.12)	0.009
Acute transmural MI of anterior wall	1069	945	124	88.40	3.09 (1.68-5.67)	< 0.001
Acute MI, unspecified	969	749	220	77.30	6.36 (3.53-11.45)	< 0.001
Acute transmural MI of unspecified site	44	25	19	56.82	13.12 (6.28-27.39)	< 0.001
The first center was referred						
Non-specialized hospitals	238	185	53	77.73	1.65 (0.94-2.90)	0.136
specialized hospital	3080	2697	383	87.56	0.83 (0.50-1.38)	0.344
Unknown	80	66	14	82.50	1.25 (0.60-2.61)	0.621
Health network or clinic	110	94	16	85.45	R	-
Symptoms						
Typical	2855	2489	366	87.18	R	-
A typical	408	367	41	89.95	0.83 (0.60-1.16)	0.250
Others	226	171	55	75.66	1.52 (1.12-2.03)	0.021
Miss	19	15	4	78.95	1.35 (0.52-3.63)	0.736
***Cardiac enzymes						
A typical	546	491	55	89.93	R	-
Typical	2464	2175	289	88.27	1.05 (0.77-1.40)	0.447
Others	318	281	37	88.36	1.37 (0.90-2.08)	0.186
Not clear	180	95	85	52.78	4.58 (3.24-6.54)	< 0.001
Hospital						
Privative hospitals	278	246	32	88.49	R	-
Academic hospitals	3230	2796	434	86.56	1.23 (0.85-1.77)	0.229

*Survival rates at 28 days after the occurrence of the disease (percent). **Every variable adjusted for other variables. ***LDH (lactate dehydrogenase), CPK (creatine phosphokinase) and troponin.
HR: Hazard ratio; ICD: International classification of disease-10; CI: Confidence interval; MI: Myocardial infarction

Variables that considered in the study include, age that divide in six sub-group (39 years and lower, 40-49, 50-59, 60-69, 70-79, and 80 and older), streptokinase use (receiving or not receiving), type of AMI based ICD-10, that include six categories (acute subendocardial MI, acute transmural MI of other sites, acute transmural MI of inferior wall, acute transmural MI of anterior wall, AMI, unspecified, acute transmural MI of unspecified site), the first center that patient referred forget medical care (non-specialized hospitals, specialized hospital, unknown, health network or clinic), symptoms (typical, A typical, others, not clear), cardiac enzymes (A typical, typical, others, not clear) and hospital status (privative hospitals and academic hospitals).

In this study, continuous variables are presented as mean ± standard deviation (SD). To compare average age in two genders, we use of the independent t-test. Time-dependent event (survival) rates were estimated by Kaplan-Meier method and P values were determined by use of log-rank statistics. The assumption of proportional hazards assessed by graphing the log-minus-log. Furthermore, to calculate the hazard ratio (HR) of death in 28 days of onset AMI, multivariate Cox regression analyses were used for calculation adjusted HR and category that have the lowest mortality, considered as reference group. In

calculate of adjusted HR every variable adjusted for other variables. Statistical significance was assumed if P < 0.050. All reported P values are two-sided. Statistical analyses were performed using SPSS software (version 15, SPSS Inc., Chicago, IL, USA).

Results

In this study, the average age of the patient in the time of disease occurrence was (12815 patients) 61.8 ± 12.6, in male (9307 patients) 60.0 ± 12.5 and in female (3508 patients) 66.7 ± 11.3, that this different was statically significant (P < 0.001). Sex ratio (male/female) was 2.65. Short-term (28 days) survival rate in study period was 90.9%, in male 92.5% and in female 86.7% (P < 0.001).

In male, the HR of death in the first 28 days after the occurrence of MI increased, so in 50-59 years age group HR was 3.48 [95% confidence interval (CI): 1.41-8.55, (P < 0.001)], in 60-69 years age group was 7 [95% CI: 2.87-17.00, (P < 0.001)], in 70-79 years age group was 10.54 [95% CI: 4.34-25.60, (P < 0.001)], and in 80 years and older was 12.7 [95% CI: 5.14-31.30, (P < 0.001)]. HR of death for other variables is presented in table 1.

HR for patients that referred to non-specialized hospitals as the first center for getting medical care was, 2.11 [95% CI: 1.23-3.75, (P = 0.011)], for unknown status was 2.17 [95% CI: 4.68-16.97, (P < 0.001)]. For patients with symptom other than typical, and A typical was 1.67 [95% CI: 1.29-2.63, (P < 0.001)]. In patients with cardiac enzymes [creatine phosphokinase (CPK) and lactic dehydrogenase] unclear was 4.81 [95% CI: 3.46-6.67, (P < 0.001)] and for patents in Academic hospitals was 1.45 [95% CI: 1.12-1.96, (P = 0.018)]. HR of death within 28 days after the occurrence of MI for other variable and sub variables in male was not statistical significant (Table 1).

In Female, HR of death in the first 28 days after the occurrence of MI were statistical significantly, only in 80 years and older age group that was 8.78 [95% CI: 1.20-63.10, (P = 0.025)]. HR of death for other variables is presented in table 2.

For patients with symptom other than typical, and A typical was 1.52 [95% CI: 1.12-2.03, (P = 0.021)]. In patients with cardiac enzymes (CPK and lactate dehydrogenase (LDH)] unclear was 4.58 [95% CI: 3.24-6.54, (P < 0.001)]. HR of death within 28 days after the occurrence of MI for other variable and sub-variables in female was not statistically significant (Table 2).

Discussion

In overall, from 12815 patients with AMI that included in the study, 9307 (72.6%) were males, and sex ratio was 2.65, a higher proportion of men than women in the disease has been observed in other studies.[25-28] The mean age at the time of occurrence of the disease in female, in average was 6.64 ± 3.04 years higher than male. In other studies observed, that the average age in time of occurrence of the disease is higher in female than male.[11,29,30] Short-term (28 day) survival rate in the entire study period is 90.9%, for males 92.5% and for females 86.7%. Perhaps higher mortality during the first 28 days after the occurrence of MI in female resulting from to higher age, higher prevalence of diabetes, higher ratio of female with poor prognosis who survived to the hospital and due to the fact that aging is reduced pain perception and response to pain.[20,29,31-37] Also, in recent years improvement in health care and the use of new technology and treatment can improve the survival rate. Of course, in Isfahan the Isfahan Healthy Heart Program (IHHP) in survival rates over time can be efficient.[38]

As expected, in both sexes with increasing age-adjusted HR of mortality is increased compared to baseline group, in a study that conducted by Stevenson et al. age was one of important determent factors in six-month survival rate in patients with AMI.[39] However, The risk of death increased with rising age has been observed in other studies.[40,41]

According to the ICD-10, MI divided into six categories. In this study, for the determent HR of mortality from AMI, considered group of patients who had the higher survival rate, as base group (acute subendocardial MI) and HR other groups, determined compared to this group. In two genders, acute, acute transmural MI of unspecified site have the highest HR compare basic group and after AMI, unspecified.

In both sexes, acute transmural MI of anterior wall has higher HR compare acute transmural MI of inferior wall. Thus, in this study the anatomic location of MI was a significant predictor of survival. In a number of studies, prognosis of MI based location was different, So that the anterior surface infarction has a worse prognosis compared to inferior level.[11,40,42] However, according to the method of data analysis in this study, difference in adjusted HR between various MI cannot caused by a variety of factors such as: gender, age, type of hospital, receive or did not receive streptokinase and type the first center to receive medical care. On

the other hand, because correct data about the differences among the mean interval between the occurrence of MI and go to health centers was not available, cannot image that this variable was ineffective, in the difference between the HRs among different types of MI.

Streptokinase is the first fibrinolytic drug, which widely used in the word. This drug is derived from the group A streptococcus. Patients may have or produce antibodies against it microorganism or drug, respectively. If a patient has antibody agent this, antibody led to increased incidence of allergic reactions (severe type of anaphylaxis). In addition, the presence of antibodies against the drug can lead to streptokinase thrombolytic effectiveness reduced. In England, overall 82.0% of hospitals used streptokinase for treatment of patients that for the first time suffering from AMI and have medical conditions of receiving this drug.[43] In this study not receiving streptokinase therapy in male, is not led to higher HR for death in the first 28 days after the occurrence of the disease, compared to the group receiving streptokinase (Table 1), but in female patients who received treatment (streptokinase therapy), compared to the group not receiving the drug has a lower HR (HR = 69%, 95% CI: 56-84), that is statistically significant.

In the present study, the HR of occurrence of death in both sexes in public hospitals is higher than private hospitals. Nevertheless, it should be note that the HR was statistically significant only in males. In a study that conducted with Chen et al.[44] in American with name, "Do 'America's best hospitals' perform better for AMI?" That conducted on 149, 177 patients with MI, the odds ratio (OR) for hospital mortality for the hospital with high rank was [relative risk (RR) = 76%, 95% CI: 69-84] against other hospitals. Survival was higher in patients admitted in this hospitals after entering variables such as disease severity and demographic characteristics of the patients, but after entering treatment quality indicators, adjusted OR was weaker and in terms of statistical not significant, so that its OR was equals (RR = 92%, 95% CI: 82-1.04) which is not significant, in actually shows that higher use of drugs such as beta blockers and aspirin in high-rank hospitals in American, lead to lower mortality.[44]

In calculation of the adjusted HR in this study, variables such as age, type of MI, receiving and not receiving the streptokinase, etc., that can be confounding role, considered. So cannot postulate that difference in survival rates due to differences in this variable, but we have not correct information about the differences between patients for receiving aspirin therapy. This article extracted from research project with code 84130 in 2011 in Isfahan Cardiovascular Research Institute.

Limitations

A difficulty of this study is a lack of complete, community-based case ascertainment, which contains through procedures for finding community fatal and nonfatal MI cases who are not admitted to the hospitals. Most important is the lack of data about out of hospital fatal cases, such as MI cases that managed at homes or in health centers. This figure might be unimportant since MI event is considering an emergency in Iran health care organization and total hospitals should admit such patients regardless of their insurance status. In Danish MONICA population, this number was measured to be not as much of as 0.1% of total MI cases in a year.[45] Therefore, the missing these patients would not lead to sham decline in MI CFR. However, in this study due to lack of data about confounding variables such as diabetes, hypertension, smoking higher ratio of female with poor prognosis who survived to the hospital and due to the fact that aging is reduced pain perception and response to pain, are not included in the statistical model. Probably, perhaps higher mortality during the first 28 days after the occurrence of MI in female resulting from to higher age, a higher prevalence of diabetes, higher ratio of female with poor prognosis who survived to the hospital and due to the fact that aging is reduced pain perception and response to pain.[20,29,31-37] Furthermore, in recent years improvement in health care and the use of new technology and treatment can improve the survival rate. Of course, in Isfahan the IHHP in survival rates over time can be efficient.[38]

Conclusion

The short-term survival rate in male was higher than female. In male age, anatomic location of MI and hospital status and in female streptokinase use and anatomic location of MI was the most important prognostic factors of survival in-patient with AMI in Iran.

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Conflict of Interests

Authors have no conflict of interests.

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The effect of positive thinking training on the level of spiritual well-being among the patients with coronary artery diseases referred to Imam Reza specialty and subspecialty clinic in Shiraz, Iran: A randomized controlled clinical trial

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Original Article

Abstract

BACKGROUND: Positive thinking which is derived from an optimistic view toward the universe and plays an important role in the incidence of better and a more targeted behavior among human beings. It can improve spiritual health in the individuals through increased communication with God and thanksgiving and accelerate the healing process. Accordingly, we aimed to evaluate the effect of positive thinking on the level of spiritual health in the patients with coronary artery disease (CAD) referred to Imam Reza specialty and subspecialty clinic in Shiraz, Iran.

METHODS: In this study randomized controlled clinical trial, we enrolled 90 patients with confirmed CAD referred to Imam Reza clinic, Shiraz, during April to July 2013. A blocking randomization method was used to randomize the final 90 participants into intervention (n = 45) and control groups (n = 45). After obtaining written informed consent, the participants were asked to complete two questionnaires. Data were collected using Ellison and Paloutzian's spiritual well-being scale (SWBS) and a demographic questionnaire. The patients in the intervention group participated in 7 training sessions on positive thinking in which several topics were discussed. The SWBS questionnaire was completed two more times by the participants; once immediately after, and once 1 month after the intervention. 16 patients were excluded from the study due to different reasons, and finally the analysis was performed on 74 patients.

RESULTS: The mean ± standard deviation (SD) of spiritual well-being (SWB) increased from 88.71 ± 12.5 to 96.63 ± 12.58 in the intervention group; while, it decreased from 93.19 ± 17.55 to 94.45 ± 16.01 in the control group in the interval of before and 1 month after the intervention. We observed a statistically significant difference between the two groups regarding both variables of time and group ($P < 0.001$).

CONCLUSION: SWB is an important factor which should be considered in the treatment process, and nurses could maintain and improve such dimension of health in the patients through their intervention including drawing the patients' attention to optimism and positive thinking.

Keywords: Spiritual, Coronary Artery Disease, Thinking, Training

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Introduction

Coronary artery disease (CAD) is one of the most important diseases which involve one of the most vital organs in the body. CAD is considered as a leading cause of mortality worldwide which accounts for 20.0% of global deaths and 28.5% of deaths in developing countries. Likewise, it causes 30-35% of deaths in Iran as 150000 Iranian people die annually from such disease.[1,2]

The methods of treatment include diagnosis, treatment of underlying diseases, reducing the risk factors of the disease, pharmaceutical and non-pharmaceutical methods and coronary artery bypass grafting as a final solution.[3] The incidence of

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the disease not only can lead to severe crisis in the individual's health,[4] but it also can cause depression, anxiety and arrhythmia in patients.[1,5] Currently, various pharmaceutical and non-pharmaceutical methods such as exercise, suitable diet and nutrition, rest, relaxation techniques and music are applied to reduce sympathetic reactions.[6]

Usually, these patients are suffering from anxiety, depression, hopelessness and feeling of emptiness because of the complication of their treatment especially aggressive treatment, which can reduce the speed of recovery process and even reverse it.[1,4,5]

Previous studies have found that depression and spiritual health or hope and positive thinking are associated with each other. For example if positive thinking improves, the level of spiritual health enhances and enhancing the level of spiritual health can reduce the level of depression.[7-10]

Therefore in addition to current therapy a complementary treatment such as cognitive therapy can be useful and improve spiritual health.

Cognitive therapy is another technique which can also help to treat psychiatric disorders. It is basically a scientific method based on a simple theory indicating that they are people's thought and attitudes toward their environment which shape their mood.[11] Positive thinking is a branch of cognitive therapy which can be defined as the use of all promising, joyous and positive mental capacities in life for not giving up to mind-made negative factors and despairing feelings resulted from difficulty of communication with people and confrontation with nature.[12] It is derived from an optimistic view toward the universe and plays an important role in the incidence of better and more targeted behaviors among human beings and provides them with success.[13] Moreover, it can improve spiritual health in the individuals through increased communication with God and thanksgiving and accelerate healing process.[14,15]

Spiritual well-being (SWB) is a feeling or power which can make coordination between physical, psychological and social dimensions. The concept of SWB can be described in two vertical dimensions (including a relationship with a divine source) and a horizontal dimension (including communication with other people and nature).[16] It is also characterized by stability in life, peace, balance and harmony, and a sense of close relationship with self, God, society, and environment. Moreover, it can specify the integrity of individuals[17] and makes them seek the meaning and goal of their life at the time of disease.[4] If such dimension of health is seriously compromised, the individual may be afflicted by psychological disorders and feelings such as loneliness, depression loss of meaning in life.[17] It can also improve quality of life.

Asaroudi et al.[18] conducted a study to investigate the relationship between SWB and quality of life in nurses and observed a positive and significant correlation between the higher levels of SWB and various dimensions of quality of life. However, no one can ever deny the importance of spiritual needs, present health care system only concerns about people' physical health care.[19]

Nevertheless, in recent years, researchers has investigated and trained the methods of taking correct attitudes toward life, positive thinking and its good effects on human spirit as well as achieving success in life. They concluded that there is a significant correlation between optimism, hope and health.[8] Investigating the effect of positive thinking on the level of SWB in the patients with CAD could be helpful in the treatment of spiritual and psychological disorders in such patients since no study has addressed such issue yet. It is worth mentioning that the area of spiritual care is the one that has been frequently ignored or delegated to a religious leader in some countries; however, addressing spiritual needs is an essential part of holistic care in nursing. Therefore, nurses should recognize the importance of considering social, emotional, psychological, physical and moral aspects of the patients.[19]

Since the nurses could play an important role in the prevention and controlling CAD, they should effort to improve the level of expectancy and SWB among the patients. Therefore, they should initially learn positive thinking and apply it in their own interventions and second or third level of prevention depending on the patient's condition.

Accordingly, we aimed to evaluate the effect of positive thinking on the level of spiritual health in the patients with CAD referred to Imam Reza specialty and subspecialty clinic in Shiraz.

Materials and Methods

This study was a randomized controlled clinical trial with before, after and 1 month follow-up. Our study was approved by the Ethics Committee of Shiraz University of Medical Sciences (Ethics Committee Approval Number: 92-6607). We enrolled 90 patients aged 42-79 with confirmed CAD referred to Imam Reza specialty and subspecialty clinic, Shiraz, during April to July 2013.

To carry out the study, the researcher was

introduced to the authorities of Imam Reza clinic (cardiac clinic) in coordination with the authorities of Fatima Faculty of Nursing and Midwifery. After obtaining permission from the authorities of the clinic, the researcher selected the samples in collaboration with a research assistant and a cardiovascular specialist in a period of 2 months, 3 days a week. The patients were selected using a simple sampling method.

Inclusion criteria included confirmed diagnosis of CAD, lack of blindness and deafness, ability to read, write, understand and communicate in Persian language, residence in the city in which the study was done. However, exclusion criteria included being absent of more than two sessions, participating in similar training courses and unwillingness to continue participation in the study.

The sample size was calculated as 45 in each group (by considering loss rate of 20%) based on the data of similar studies using following formula and MedCalc software bvba (Acacialaan 22 8400 Ostend Belgium) [power: 80%, α: 0.05, mean difference: 3.01 and standard deviation (SD): 4.75 (intervention group) and 4.43 (control group)]. A blocking randomization (block size = 4) method was used to randomize the participants, who had inclusion criteria, into intervention (n = 45) and control groups (n = 45).

After obtaining written informed consent, the researcher explains the aims and method of the research to the patients and then the participants were asked to complete two questionnaires. Data were collected using Ellison and Paloutzian's spiritual well-being scale (SWBS) and demographic questionnaire enquired about age, sex, educational level, employment status, and marital status, monthly income.

The patients in the intervention group participated in training sessions on positive thinking consisted of one 75-minute session per week for 7 consecutive weeks. The topics included the importance of anthropology and self-analysis, cognitive errors, definition and the role of positive thinking in life, overcoming the disease, the importance of prayers, communication with God and thanksgiving, training relaxation techniques, visualization and positive imagery and considering relaxation factors (prayer, patience, forgiveness, and trust in God) as well as the causes of fear of death.

16 patients were excluded from the study due to different reasons (In the intervention group, 7 patients were excluded due to the absence of more than two sessions and 9 of them in the control group refused to continue participating in the study) and finally the analysis was performed on 74 patients.

The SWBS questionnaire was completed immediately after and 1 month after the intervention by the participants, again (Figure 1).

SWBS is a 20-item questionnaire consists of two 10-item sections. It measures two dimensions of SWB including religious well-being (RWB) and existential well-being (EWB). Participants responded to the items using a 6-point Likert scale ranging from 1 "Strongly disagree" to 6 "Strongly agree". The total score ranged from 20 to 120. But, inverse scoring was used for 9 questions. Finally, SWB score was classified into three levels of low (20-40), moderate (41-99) and high (100-120). Its reliability and validity were assessed in some studies and were also estimated and confirmed in Iran by Baljani et al.,[8] after being translated into Persian. Cronbach's alpha was calculated as 0.88.

The collected data were analyzed using SPSS software (version 16, SPSS Inc., Chicago, IL, USA). To analyze qualitative data (Sex, education, marital status, income and job), chi-square method was used and to analyze quantitative data independent t-test (for age and spiritual health) and analysis of variance of repeated measures (just for spiritual health) were used. The significance level was set at < 0.05. Kolmogorov-Smirnov test was used to examine the normality of quantitative variables and the results confirmed that the variables had a normal distribution.

Results

We finally enrolled 74 patients with CAD of which 38 were in the intervention, and 36 were in the control group. The age range of the patients was 42-79 years. The mean ± SD age of the patients were (60.24 ± 6.88) and (58.08 ± 9.05) in the intervention and control groups respectively. There was not any significant difference between the intervention and control groups with respect to their age (P = 0.251).

The results showed that the two groups had no statistically significant difference in terms of marital status (P = 0.463), educational level (P = 0.535), employment status (P = 0.298) and sex (P = 0.363) (Table 1).

According to the results of independent t-test, no significant difference was observed between the two groups regarding the total scores of SWB (P = 0.089), EWB (P = 0.205) and RWB (P = 0.086) before the intervention.

The mean ± SD total score of EWB was

38.34 ± 7.15 and 40.97 ± 10.31 and the mean ± SD total score of RWB was 50.36 ± 7.49 and 53.47 ± 7.85 in the intervention and control groups, respectively, before the intervention.

According to table 2, the mean ± SD total scores of SWB in the intervention group were 88.71 ± 12.50, 95.28 ± 11.02 and 96.63 ± 12.58 before, immediately after and 1 month after the intervention respectively indicating that SWB scores enhanced over the time in this group. However, in the control group, the mean ± SD total scores of SWB were 94.45 ± 16.01, 92.70 ± 16.26, and 93.19 ± 17.55 before, immediately after and 1 month after the intervention, respectively, reflecting a reduce in SWB scores after the intervention.

The analysis of variance of repeated measures was used to compare the intervention and control groups at 3-time points without considering the variable of group. The results reported a significant difference between the groups in this regards (P = 0.014) indicating that time was an important factor and due to the effects of two variables of time and group, the changes were significant (P < 0.001).

76.31% of the patients in the intervention and 58.33% of those in the control group reported an intermediate level of SWB. 23.68% of the participants in the intervention and 41.66% of those in the control groups reported a high level of SWB. However, no patient maintained a low level of SWB (Figure 2).

Table 1. Frequency distribution of participants' demographic characteristics

Variable	Intervention group (n = 38)	Control group (n = 36)	*P
Sex [n (%)]			
Female	23 (60.5)	18 (50.0)	0.363
Male	15 (39.5)	18 (50.0)	
Marital status [n (%)]			
Married	33 (86.6)	29 (80.6)	0.463
Widow	5 (13.2)	7 (19.4)	
Educational status [n (%)]			
Under graduate	27 (71.1)	26 (72.2)	0.535
Graduate	11 (28.9)	10 (27.8)	
Occupational status [n (%)]			
Clerk	5 (13.2)	5 (13.9)	0.298
Retired	14 (36.8)	10 (27.8)	
Self-employed [n (%)]	2 (5.3)	7 (19.4)	
Housewife [n (%)]	17 (44.7)	14 (38.9)	
Monthly income (Rials) [n (%)]			
< 6 million	12 (34.2)	10 (27.8)	0.754
6-10 million	18 (47.4)	18 (50.0)	
> 10 million	7 (18.4)	8 (22.2)	

*chi-square test

Table 2. Comparison of spiritual well-being total score and its dimensions before and after intervention as well as 1 month after the intervention in the intervention and control groups

SWB mean score	Group	Time			*P (time)	*P (group)	*P (group/ time)
		Before intervention (mean ± SD)	After intervention (mean ± SD)	1 month follow-up (mean ± SD)			
EWB	Intervention	38.34 ± 7.15	42.47 ± 7.10	43.47 ± 7.31	< 0.001	0.863	0.002
	Control	40.97 ± 10.31	40.72 ± 10.50	41.58 ± 10.96			
RWB	Intervention	50.36 ± 7.49	52.81 ± 5.72	53.15 ± 7.06	0.706	0.890	0.001
	Control	53.47 ± 7.58	51.97 ± 7.58	51.52 ± 7.81			
Total SWB score	Intervention	88.71 ± 12.50	95.28 ± 11.02	96.63 ± 12.58	0.014	0.975	< 0.001
	Control	94.45 ± 16.01	92.70 ± 16.26	93.19 ± 17.55			

*Analysis of variance of repeated measures test.
SWB: Spiritual well-being; EWB: Existential well-being; RWB: Religious well-being; SD: Standard deviation

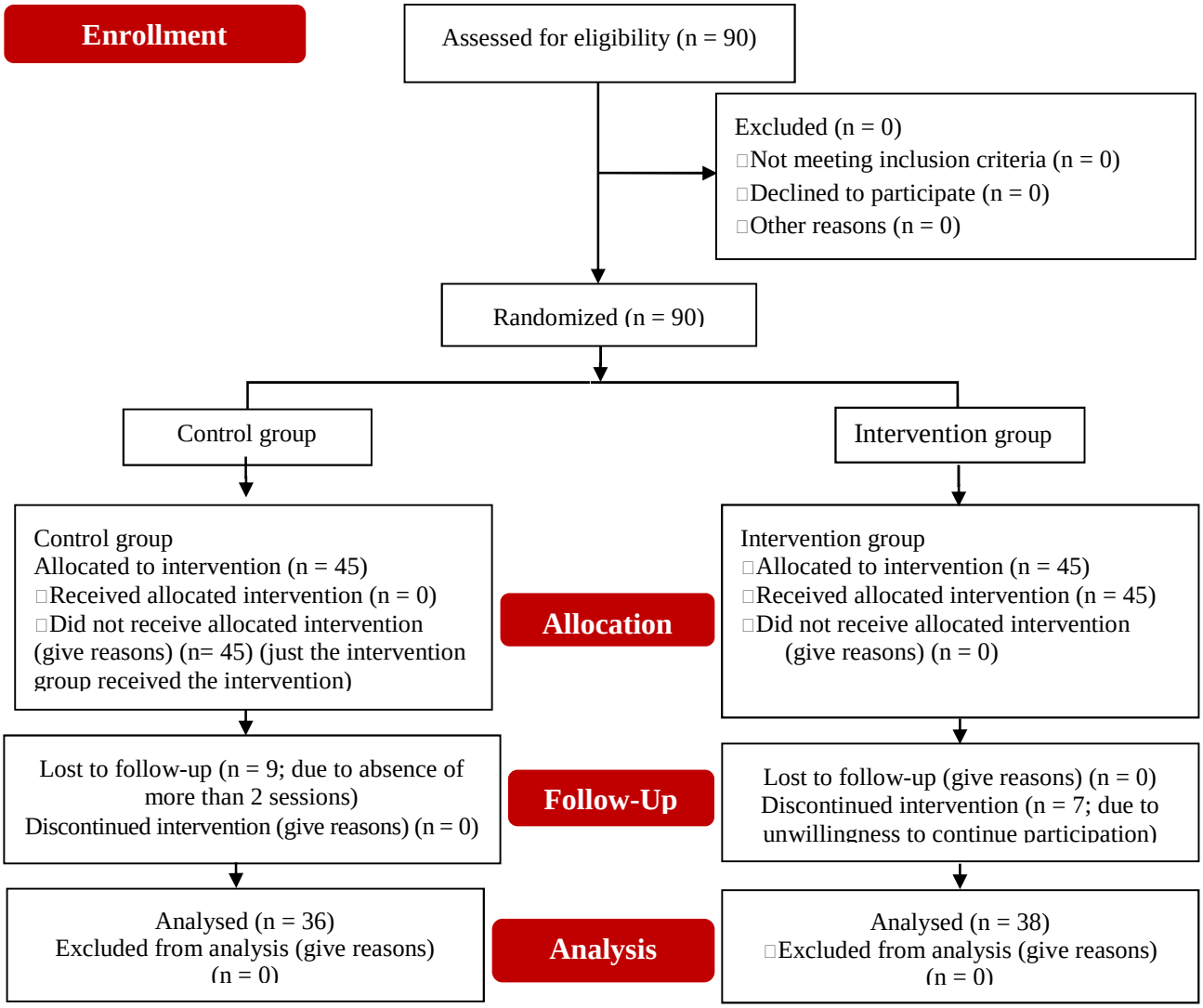

Figure 1. The process of study on spiritual well-being in patients with coronary artery disease (CAD)

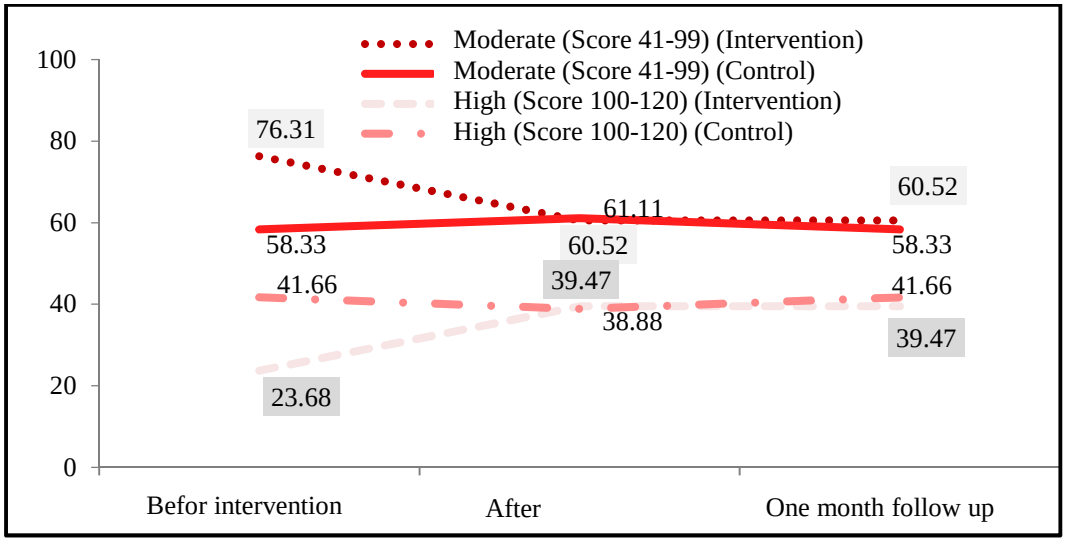

Figure 2. Comparison of spiritual well-being (SWB) levels (total score) before and after intervention and 1 month follow-up in the intervention and control groups

*No patients reported a low level of SWB

Discussion

In general, we found that positive thinking training to the patients with CAD could improve their SWB effectively as its effect also could last for at least 1 month. Despite the limited number of the studies which address the effect of positive thinking on SWB, the results of similar studies such as those of Bekelman et al.[10] Asgari et al.[20] and Smith et al.[21] were consistent with ours. Nevertheless, more studies are required to assess the effect of such intervention in longer time intervals.

We found that majority of our participants reported moderate levels of SWB. Such finding was consistent with those of Asaroudi et al.[18] and Allahbakhshian et al.[22] While, we observed no difference between the two groups with respect to the total score of SWB; Jadidi et al.,[16] in a recent study, investigated the relationship between SWB and quality of life among elderly people and found that majority of the participants maintained a high level of SWB which can be attributed to their age. The correlation between age and SWB has also been confirmed in the studies by Rezaei et al.[4] and Seyed Fatemi et al.[17]

It should also be mentioned that after the intervention, 60.52% of patients in the intervention and 61.11% of those in the control group reported an intermediate level of SWB; while, 39.47 and 38.88% of the patients reported a high level of SWB in the intervention and control group respectively. While the mean score of SWB did not change significantly in the control group with high level of SWB in the after intervention phase compared with before-intervention; it reached from 23.68 (before-intervention phase) to 39.47 (after intervention phase) in the intervention group and did not changed after 1 month.

This study indicates that the positive thinking training can improve existential dimension (EWB) and religious dimension (RWB) of SWB in such a patient. Our results demonstrated that the mean score of RWB was higher than EWB in both groups. It was consistent with the findings of Rezaei et al.,[4] Asaroudi et al.[18] and Jadidi et al.[16] and in contrast with that of Allahbakhshian et al.[22] The fact that the mean score of EWB and RWB were higher in most of the mentioned studies may be due to the religious beliefs of Iranian people. Secondly, it may also be derived from the fact that RWB measures the level of communication with God. Besides, EWB seems a little more difficult to be achieved since it evaluates the feelings of individuals about their life's goal and satisfaction and it is associated with human's existential philosophy. Moreover, another reason could be the difference which exists between the aforementioned studies regarding the type of recruited participants. The studies were done on the patients with cancer, nurses, elderly people and the patients suffering from multiple sclerosis respectively.

In our study, analysis of chi-square and independent t-test showed no significant difference between the intervention and control groups with respect to demographic variables (including sex, age, marital status, educational level and occupational status) and it was also similar to the findings of Allahbakhshian et al.,[22] Jadidi et al.,[16] and Büssing et al.[23]

Rezaei et al.[4] conducted a cross-sectional study on 360 patients with cancer to examine the relationship between praying and SWB. However, there was no significant correlation between SWB and sex; they found that it was correlated with the three factors of age, marital status and educational level as older, widowed and divorced people maintained higher levels of SWB. We found no correlation between SWB and demographic variables due to our small sample size. Therefore, studies with larger sample size are required to examine such correlation.

Optimism is an effective factor in human's well-being especially SWB. Despite, the advances in the skills and knowledge of physician and medical staff, non-material needs of human being still calls for attention. The importance of considering SWB in the treatment of patients is emphasized in the studies by Abolghasemi Mahani,[19] Jadidi et al.,[16] Allahbakhshian et al.,[22] Mazaheri et al.,[24] and Lin and Bauer-Wu.[25] However, more studies in this filed are still required.

Conclusion

We can conclude that positive thinking training could improve SWB in the patients with CAD. Positive thinking could increase the patients' SWB through reminding them of their positive aspects of their life, improving their communication with God as a divine source and teaching those strategies such as thanksgiving.

In general, optimism and positive thinking training are important measures in the treatment of the patients suffering from CAD and should be considered in nursing interventions and educations.

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Conflict of Interests

Authors have no conflict of interests.

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Advanced method used for hypertension's risk factors stratification: support vector machines and gravitational search algorithm

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Original Article

Abstract

BACKGROUND: The aim of this study is to present an objective method based on support vector machines (SVMs) and gravitational search algorithm (GSA) which is initially utilized for recognition the pattern among risk factors and hypertension (HTN) to stratify and analysis HTN's risk factors in an Iranian urban population.

METHODS: This community-based and cross-sectional research has been designed based on the probabilistic sample of residents of Isfahan, Iran, aged 19 years or over from 2001 to 2007. One of the household members was randomly selected from different age groups. Selected individuals were invited to a predefined health center to be educated on how to collect 24-hour urine sample as well as learning about topographic parameters and blood pressure measurement. The data from both the estimated and measured blood pressure [for both systolic blood pressure (SBP) and diastolic blood pressure (DBP)] demonstrated that optimized SVMs have a highest estimation potential.

RESULTS: This result was particularly more evident when SVMs performance is evaluated with regression and generalized linear modeling (GLM) as common methods. Blood pressure risk factors impact analysis shows that age has the highest impact level on SBP while it falls second on the impact level ranking on DBP. The results also showed that body mass index (BMI) falls first on the impact level ranking on DBP while have a lower impact on SBP.

CONCLUSION: Our analysis suggests that salt intake could efficiently influence both DBP and SBP with greater impact level on SBP. Therefore, controlling salt intake may lead to not only control of HTN but also its prevention.

Keywords: Support Vector Machines, Gravitational Search Algorithm, High Blood Pressure

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Introduction

Hypertension (HTN) is one the most prevalent risk factors of cardiovascular disease (CVD) in Iran.[1] Worldwide, approximately 12.8% of total deaths are estimated to be due to HTN.[2] It is well-documented that some risk factors such as age, sex, obesity, and dietary habits strongly affect the occurrence of HTN.[3] HTN is demonstrated to be a multifactorial disease. Therefore, numerous lifestyle changes could decrease and control high blood pressure by modifying the risk factors.[4] Many studies have shown different factors such as aging, genetics, obesity, non-healthy diet, and bad lifestyle all correlates with high blood pressure.[5] Therefore, both genetics and environmental factors could affect the increase in blood pressure.[6] The impact degree of genetic factors on high blood pressure reported to be between 0.5 and 0.6, while the environmental parameters include bad lifestyle, unhealthy diet, obesity, and aging impact reported

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approximated between 0.4 and 0.5.[7] Genetic factors are complicated and impossible for us to modify. Therefore, we should focus on modifiable risk factors to select a good strategy in HTN control.[8] Lifestyle is one of the modifiable factors that if changed to a healthy lifestyle could prevent or reduce the incidence of high blood pressure.[9]

Novel soft computing methods are utilized in realizing tractability, robustness, and to present a solution with an acceptance of vagueness, uncertainty, partial truth, and approximation.[10] Support vector machine (SVMs) are a novel machine learning technique formerly used for pattern recognition problem based on structural risk minimization.[11] Essentially, SVMs have a theoretical relation with artificial neural network (ANN). An SVM model using sigmoid kernel function is equal to a two-layer perceptron neural network. Using a kernel function, the SVMs are different training techniques for polynomial, radial basis function, and multilayer perceptron classifiers in which the weights of the network are set up by answering a quadratic programing problem with linear constraints, rather than by solving a non-convex, unconstrained minimization problem as in standard ANN training.[11] Finding optimal values for parameters of SVMs is a significant step in the SVMs analysis which has a great influence on its modeling ability and on its accuracy. Using metaheuristics can be helpful in determining the suitable value of SVM parameters for the best estimation and approximation performance.[12] Gravitational search algorithm (GSA) is one of the recognized metaheuristics that can find out a high-quality solution to an optimization problem.[13,14] In comparison with some other research techniques, GSA has established higher performance in handling various non-linear functions.

We investigated the potential use of the optimized SVMs for analyzing the impact levels of risk factors on developing high blood pressure. Showing some examples, we evaluated the capabilities of optimized SVMs and compare it with two common statistical methods, generalized linear modeling (GLM) and multiple linear regression (MLR), to model the associations between age, urinary volume, serum creatinine, waist circumference (WC), salt intake, body mass index (BMI), and systolic blood pressure (SBP) and diastolic blood pressure (DBP). The proposed approach is evaluated and used to stratify the impact level of the above risk factors on SBP and DBP in the Iranian urban population.

Materials and Methods

The salt intake study is a cross-sectional study which has been developed based on a probabilistic sample of Isfahan, Iran, residents aged 19 years or more from 2001 to 2007. Sampling strategy, survey, data entry, and analysis have been previously described.[13] Study subjects were selected through stratified random sampling based on age and sex. Inclusion and exclusion criteria of study participants explained elsewhere.[14] One of the household members was randomly selected to train on the purpose of the research and invited to participate in the study. An oral consent was obtained from each participant. The project received approval from the Research and Ethics Committees of Isfahan University of Medical Sciences.

Primary evaluation and the baseline data collection were carried out by a trained nurse and through phone interviews. A questionnaire was used to collect demographic and anthropometric information. The subjects were invited to an information session to be briefed on urine sample collection and blood pressure measurement. We used 24-hour urinary sodium excretion as an indicator of sodium intake for the accuracy. The participants instructed to collect urine samples for 24-hour (7 AM to 7 AM of the following day). The Sodium (mmol/l) was measured by commercial kits using flame spectrophotome. The blood pressure was measured by a trained nurse using a bench-mounted mercury column sphygmomanometer. The blood pressure was measured with the individual seated and rested for a minimum of 5 minutes after emptying the bladder.

Descriptive statistics of the investigational data include mean, minimum, maximum, standard deviation (SD), and skewness were all calculated by SPSS software (version 18, SPSS Inc., Chicago, IL, USA). Scatterplot matrices, demonstrating associations between the data (i.e., age, urinary volume, serum creatinine, WC, salt intake, BMI, SBP, and DBP), were acquired by VisuLab (ETH University, Zurich, Switzerland). The subsequent equation used to normalize every input data to a range of 0.1-0.9:

$$x_i = 0.8 \times \left[\frac{(x - x_{\min})}{(x_{\max} - x_{\min})} \right] + 0.1$$

Furthermore, the data set was separated into three subsets for training, testing, and verification. The training subset was randomly selected from 60% of the main data set. The remaining data set (40% of the data) were utilized uniformly and separated into two parts as the testing and validation subsets.

Optimized SVM

The SVM implemented the principle of structural risk minimization by constructing an optimal separating hyperplane for more mathematical details; please refer to Vapnik.[15] The parameters of SVM have a most important impact to the model's correctness, learning effectiveness, and generalization capability.[12] Since using classical optimization techniques for parameters optimization is time-consuming and needs human knowledge, in this paper, the GSA is utilized to optimize the parameters above for SVM model. It uses the law of gravity and mass interactions and has been applied in different areas.[16,17]

Results

Table 1 demonstrates the small variation of observed data (variables utilized in the study). It also shows a normal distribution of the data. The scatterplot matrices show correlations between the input variables (i.e., BMI, WC, Salt intake, age, urinary volume, and serum creatinine) and model outputs, SBP, and DBP. The results show although the associations between input variables and the model outputs exist. However, the trends and patterns appear to be comparatively complex. While based on clinical studies mentioned variables influence both SBP and DBP, it is not understood how this process occur and also there is no study about stratifying their impact levels on blood pressure. It seems that the studied variables possibly either directly or indirectly influence SBP and DBP in the Iranian urban population. Therefore, the proposed approach is useful when looking for a correlation of such data to estimations SBP and DBP. Table 2 shows some fitting values of different models. To calculate the performance of recommended techniques, the measured and estimated values that were utilized are as follows; mean square error (MSE), model efficiency factor (MEF), correlation coefficient (r), and error percentage (ERROR %). The MSE, MEF, and ERROR % statistics are described as follow:

$$\mathrm{MSE} = \frac{1}{n}\sum_{k=1}^{n}[y_k - \hat{y}_k]^2$$

$$\mathrm{MSF} = 1 - \frac{\sum_{k=1}^{n}(y_k - \hat{y}_k)^2}{\sum_{k=1}^{n}[y_k - \overline{y_k}]^2}$$

$$\mathrm{ERRORE\%} = \frac{\sum_{k=1}^{n}|y_k - \hat{y}_k|}{\sum_{k=1}^{n} y_k} \times 100$$

Where y_k denotes the estimated value, y_k is the measured value, $\overline{y_k}$is the mean of measured values, and n is the total number of observations.

The MLR model had lowest estimation effectiveness compared to the optimized SVM. Using MLR with input data resulted in the lower correlation coefficient between the measured and estimated SBP and DBP values (Figure 1). The MSE value for the developed MLR model for SBP was 0.00774 (Table 2), while the MEF and ERROR % values were 0.298 and 14.14, respectively. The MSE, MEF, and ERROR % values for the developed MLR model using DBP data set were 0.0073, 0.2006, and 13.83, respectively (Table 2). In accordance with the evaluation results, it seems that regression model was to some level poor in estimating SBP and DBP in this study.

The MSE, MEF, and ERROR % values for the developed GLM model using SBP data set were 0.0056, 0.4843, and 12.123, respectively (Table 2). Furthermore, the coefficient of correlation between the measured and estimated DBP values for the constructed GLM model was 0.65802. MSE, MEF, and ERROR % value for DBP were 0.0057, 0.3728, and 12.25, respectively (Table 2). These consequences propose a better performance of GLM method for predicting DBP and SBP in comparison to MLR technique. Nevertheless, it seems that this method also fails to be reliable for estimating SBP and DBP.

The acquired evaluation criteria and correlation coefficient values among the estimated and measured values for both SBP and DBP demonstrated that optimized SVM has the highest estimation potential (Figure 2), particularly, when its performance is evaluated with regression and GLM methods. The MSE, MEF, and ERROR % values for the developed optimized SVMs model using SBP as a target were 0.0004194, 0.962003012, and 3.135, respectively while for the DBP were 0.0006281625, 0.931873605, and 4.0151, respectively (Table 2).

Evaluating the acquired consequences from MLR, GLM, and optimized SVMs models showed that optimized SVMs method yields better results compared with GLM and MLR methods. This may be caused by the ability of optimized SVMs in recognizing complex correlations because of their distributed and parallel computing nature. The cause of the estimators on the SBP and DBP may not be linear in nature, and this might be a reason the linear models may not be reliable for estimation of DBP and SBP in the Iranian urban population. The optimized SVMs model could result in more

acceptable estimation of blood pressure parameters due to the flexibility and ability to model nonlinear correlations. Furthermore, the better performances of the developed soft computing models were probably because of their higher degree of robustness tolerance than the classical statistical models. Therefore, it seems that in the case of estimating blood pressure and risk factors stratification which MLR and GLM fail to be reliable, optimized SVMs might be chosen as a preferred option. After choosing a superior model based on performance evaluation procedure, we used sensitivity analysis and reported its output as an impact level (Figure 3).

Table 1. Summary statistics of variables employed in developing prediction models

Parameter	Descriptive statistics			
	Mean ± SD	Minimum	Maximum	Skewness
SBP (mmHg)	104.00 ± 11.88	80.00	145.00	0.819
DBP (mmHg)	69.18 ± 8.81	50.00	97.50	0.346
BMI (m^2/kg)	25.47 ± 4.39	15.76	45.64	0.512
WC (cm)	82.59 ± 12.07	54.50	172.00	0.698
Salt intake	139.07 ± 3.18	132.00	147.00	0.079
Age (year)	37.29 ± 12.59	19.00	81.00	0.725
Urinary volume (ml)	1094.09 ± 437.63	200.00	2875.00	1.006
Serum creatinine (mg/dl)	0.98 ± 0.21	0.60	2.40	1.490

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; WC: Waist circumference; SD: Standard deviation

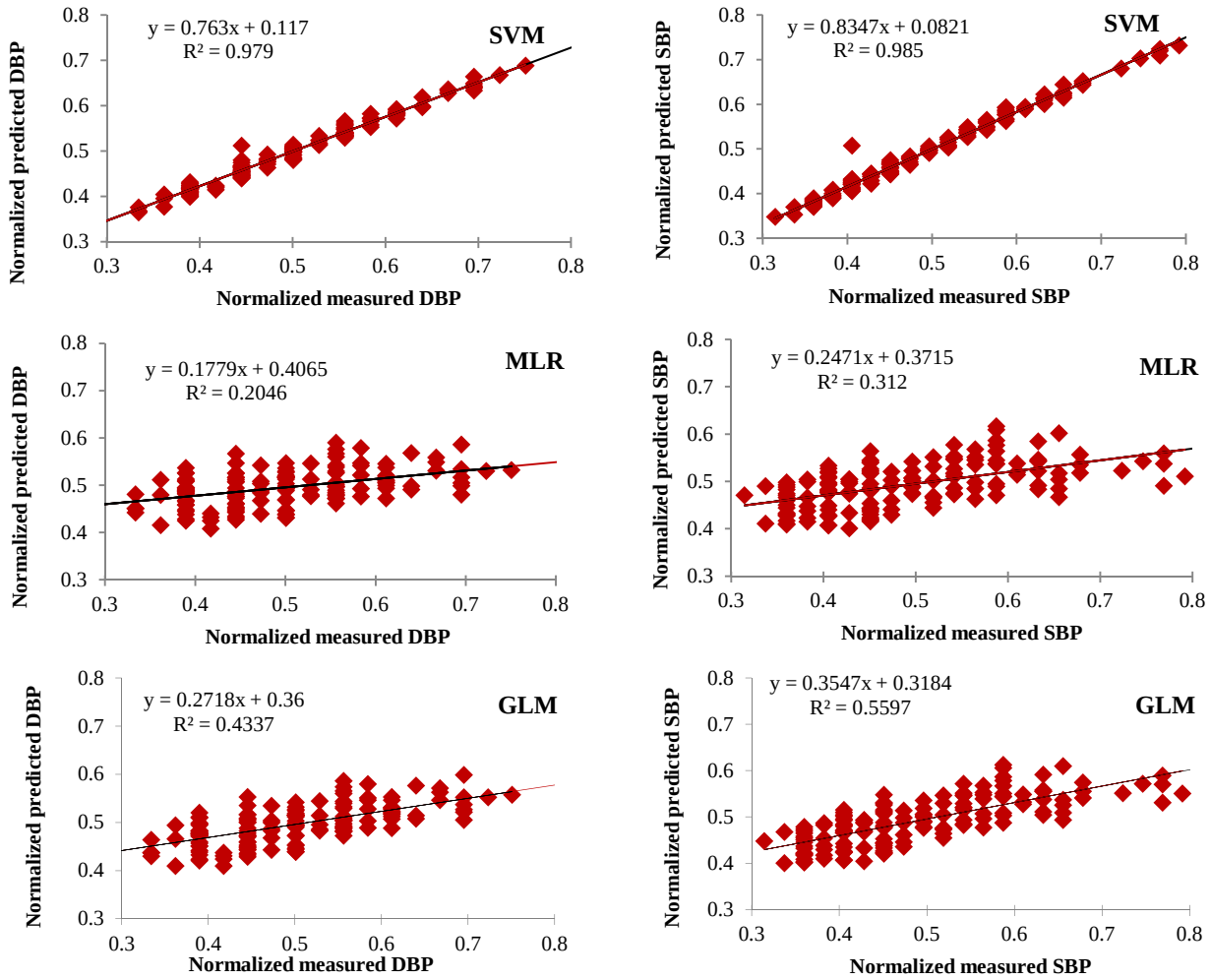

Figure 1. Relationships between the normalized predicted and measured systolic blood pressure (SBP) and diastolic blood pressure (DBP) values for the test sample sets of constructed multiple linear regression (MLR) and support vector machine (SVM) models
GLM: Generalized linear modeling

Table 2. Goodness-of-fit of proposed multiple linear regression model model, generalized linear modeling, and support vector machine model models for the prediction of systolic blood pressure and diastolic blood pressure

Blood pressure type	Model type	Evaluation criterion			
		MEF	MSE	r	ERROR (%)
SBP	MLR	0.298080	0.007748	0.559	14.1445
SBP	SVM-GSA	0.962003	0.000419	0.992	3.1356
SBP	GLM	0.484303	0.005692	0.748	12.1238
DBP	MLR	0.200616	0.007370	0.452	13.8368
DBP	SVM-GSA	0.931873	0.000628	0.989	4.0151
DBP	GLM	0.372892	0.005782	0.658	12.2555

MLR: Multiple linear regression model; SVM: Support vector machine model; GSA: Gravitational search algorithm; MEF: Model efficiency factor; MSE: Mean square error; GLM: Generalized linear modeling; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

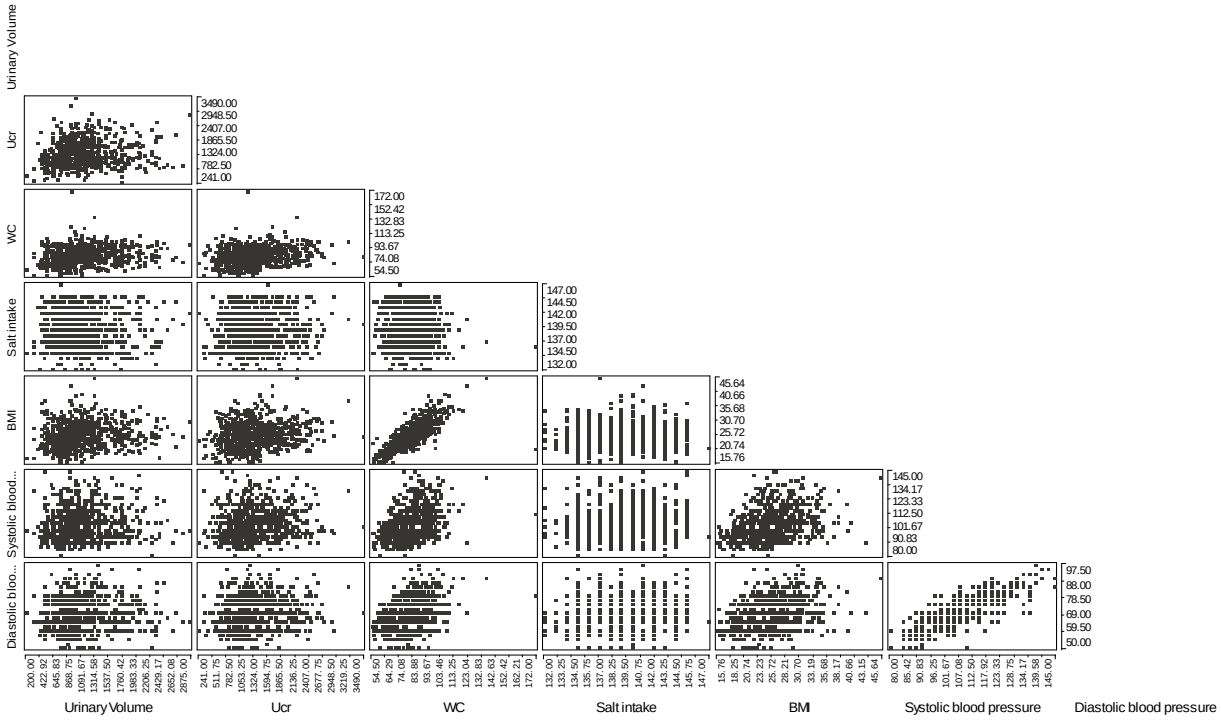

Figure 2. Scatterplot matrices displaying the relationships between the analyzed variables, age, urinary volume, serum creatinine, waist circumference, salt intake, body mass index, systolic blood pressure and diastolic blood pressure

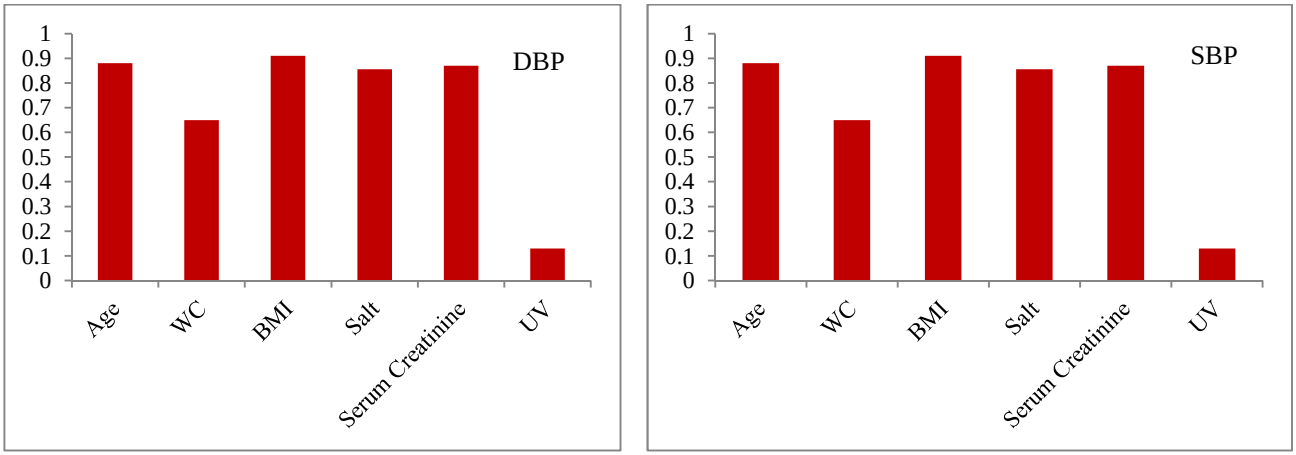

Figure 3. Impact level identification for systolic blood pressure and diastolic blood pressure
WC: Waist circumference; BMI: Body mass index; UV: Urinary volume

Discussion

In this study, the novel method for exploratory risk factor stratification was performed to determine the impact level of each risk factor on DBP and SBP. Based on our findings, the first important risk factor is age. It has the highest impact level on SBP while falls second on the impact level ranking on DBP (Figure 3). This is in agreement with intersalt study result that showed an increase in SBP with age.[18,19] Another study by Janus et al. showed an increase in SBP with age in 7730 individuals randomly chosen in Hong Kong.[20]

The results also showed that basal metabolic rate (BMR) falls first on the impact level ranking on DBP while have a lower impact on SBP, While the evaluation of WC indicated that it falls on the second and fifth impact level ranking on SBP and DBP, respectively. In previous studies, BMI and waist-to-hip ratio used to be frequently employed as indicators of overweight and obesity as well as body fat distribution pattern. In some researches from Western countries, BMI has been constantly shown to be associated with high blood pressure. Some cross-sectional reports documented such an association among overweight and hypertensive.[21-23]

Some hypothesis proposed that overweight is related with elevated cardiac output, increased blood volume, and increased peripheral vascular resistance.[24] Weight circumference demonstrated to be a superior indicator of abdominal fat compared to waist-to-hip ratio. The use of WC when evaluating abdominal fat is newly suggested by the National Institutes of Health Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity. In our population, WC is recognized as a risk factor with a more impact on SBP compared to BMI itself. As shown in scatterplot matrices, the association between BMI and WC is very significant. The body fat distribution is an important contributor to the association of obesity and high SBP. This result is in agreement with the results obtained from the Olivetti Heart study.[25] Our results also demonstrate the association between WC and high blood pressure among Iranian urban population.

This present study is the first community-based research on salt intake impact level stratification in the urban region of Iran. We attempted to achieve a population-view to choose proper management strategy and reducing the high blood pressure. We estimated blood pressure and salt intake in Iranians based on the new formulation presented by Tanaka et al., for determining daily sodium intake from urinary sodium secretion (estimated 24-hour sodium intake (mEq/day) = 21.98 × Na0.392).[24,25] Derived from intersalt results[26] association between blood pressure and salt intake was weak in some countries. Even within a single country, the results from studies on the correlation between salt intake and blood pressure could vary.[27] Our analysis suggests that salt intake could efficiently influence both DBP and SBP with greater impact level on SBP. Therefore, controlling salt intake may lead to not only control of HTN but also its prevention. Our results also in agreement with the Dietary Approaches to Stop Hypertension (DASH) study.[28] Which demonstrated that SBP considerably decreased both in the control-diet group and DASH-diet group when the sodium intake level decreased (from high to intermediate and then to low level).[29]

Based on our results, serum creatinine has a higher degree of impact level on DBP than salt while it has fifth impact level on SBP. This study also considered the potential relation between blood pressure and renal function which is demonstrated by serum creatinine in the Iranian urban population. Creatinine clearance has been frequently employed as a factor to show renal function in health. Since this process needs 24-hour urine gathering, which is not easy to achieve from individuals involved in large population-based researches, increasing in serum creatinine level has commonly been utilized as a measure of renal morbidity. Our analyzes advise that serum creatinine could powerfully influences both DBP and SBP with superior impact level on SBP which is in agreement with results from the Bogalusa Heart Study on white community.[30-33]

Acknowledgments

None.

Conflict of Interests

Authors have no conflict of interests.

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Systematic review of zinc biochemical indicators and risk of coronary heart disease

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Review Article

Abstract

BACKGROUND: Poor zinc nutritional status is suspected as a risk factor for coronary heart disease (CHD). Since zinc absorption may be influenced by some nutritional and physiologic factors, it would be better to investigate zinc status through biochemical measurements. The objective of the present study was to review recent studies investigating the association of zinc biomarkers with CHD, systematically.

METHODS: The MEDLINE database was used for relevant studies published from January 2009 to December 2013 with appropriate keywords. Articles were included in this study if they were human studies, original articles, and published in English.

RESULTS: Six case-control studies and two prospective cohort studies that measured zinc biomarkers were included in the study. Almost all case-control studies suggest that decreased plasma zinc was associated with increased CHD risk. Cohort studies did not support this relationship.

CONCLUSION: The majority of the evidence for this theory is extracted from case-control studies, which might have bias. Prospective studies and randomized clinical trials are needed to investigate whether poor zinc status is associated with increased CHD risk. Consequently, a protective role of zinc in CHD could not be still established.

Keywords: Zinc, Coronary Heart Disease, Minerals, Systematic Review, Cardiovascular, Myocardial Infarction

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Introduction

Cardiovascular disorders are the most common cause of mortality in the world.[1] Mortality due to cardiovascular diseases has increased from 31.9% in 1990 to 46.8% in 2010, in Iran.[2] There are several risk factors have been considered to be effective in the pathogenesis of cardiovascular disorders. Among them, nutrition has an important role.[3,4] High intake of calorie, total fat, cholesterol and processed foods and low intake of fruits, vegetables, and dietary fiber have been associated with higher risk of coronary heart disease (CHD).[4-6] When micronutrients were investigated, the protective effect of folate, vitamin B_6, vitamin B_{12}, and vitamin E has been shown.[7] However, the role of minerals is not well-known.

Prior studies indicate that some dietary minerals,[8-10] such as selenium intake may affect the risk of CHD and related mortality.[11-13] Although, the prevalence of zinc deficiency is estimated to be high among all population worldwide,[14] and its role in developing some chronic diseases has been shown recently,[15] the role of zinc in developing CHD is not clear.[8,16,17]

There are different methods for evaluating zinc status in nutritional epidemiology such as nutrient intake assessment through questionnaire and biochemical measurement. Biochemical measures or biomarkers are attractive because they are objective and less suspicious to forgetful and biased human answers to the questionnaire.[18] In addition, within-food variation may occur due to geographical difference in soil zinc content. Consequently, since the concentration of Zn in most foods is not inherent and more important, Zn absorption may be affected by some physiologic and dietary factors

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such as phytate,[19] observational studies of Zn status may benefit from the use of biochemical measures of zinc levels in hair, nail, serum or plasma Zn concentrations more than its dietary intake.[20] While, serum and urine zinc usually inhibits recent intake,[14] nails and hairs slow growth have been shown to be a reliable biomarker for trace element status, especially reflecting past year exposure.[21]

Since the role of zinc is not clear in such a common disease and dietary recommendations are cost-effective and safe[22] and usually work even in developing countries,[23] the objective of this study was to review the results from studies of the association of Zn biomarkers with CHD, systematically.

Materials and Methods

Database MEDLINE was searched for observational studies and randomized trials investigating the relationship between Zn biochemical measurement and CHD. The following Medical Subject Headings (MeSH) terms were applied (cardiovascular OR myocardial infarction OR peripheral arterial disease OR stroke OR mortality OR coronary); and were combined with each of the terms ("zinc," "Zn," "zinc gluconate," "zinc sulfate," "zinc acetate," "zinc oxide"). The articles published in recent 5 years were included. The potentially relevant articles were included if the full paper had been obtained. Studies were restricted to human studies and publications in English. References of identified articles and reviews were also searched for additional relevant articles.

We aimed to identify all observational and randomized trials studies that assessed the association of Zn with CHD. Articles met the following criteria were excluded:

1- Not original research (reviews, editorials, non-research letters);

2- Case reports or case series;

3- Ecologic studies;

4- Studies lacking a biochemical measurement of Zn status;

5- Cellular or molecular studies;

6- Studies which their outcomes were a specific risk factor of CHD (for example lipid profile) or total mortality.

Data extraction and quality assessment

One investigator reviewed search results. Abstract of 209 retrieved articles were studied, and articles which met exclusion criteria were excluded. Although the stringent criteria were used for inclusion and exclusion, the studies which were finally included in the study, had different methodology and biochemical measurements. Therefore, the results were summarized and tabulated. For the included articles, some important information were extracted and tabulated including study design, first author, year of publication, country, patient characteristics (gender and mean age), sample size, case and control definition and the reported Zn status from studies (Tables 1 and 2). All biochemical measurement including hair, nail, urine, serum and plasma were included in the study. Case-control studies were concluded in table 1 and cohort studies were concluded in table 2. The quality of observational studies was assessed according to the criteria used by Flores-Mateo et al.[11] to minimize including of articles which have bias (Appendix 1).

Results

Six case-control studies and two prospective cohort studies were included in the study (Figure 1). The studies were published between 2009 and 2013 (Table 1). The number of case subjects varied between 24[24] and 457.[25] The quality scores varied widely. In almost all studies, serum Zn concentration was less in CHD patients as compared to control subjects, but this difference was not significant in all studies (Table 1). In the study of Islamoglu et al.[26] 67 patients with CHD were compared with 26 clinically healthy individuals. The serum Zn was found to be significantly lower in patients than in healthy control ($P < 0.010$). In the study of Bayir et al.[27] patients with diagnosed acute coronary syndrome (ACS) ($n = 100$) were compared with their age-matched controls ($n = 100$). Serum Zn concentration was significantly less in the CHD group compared to the control group ($P < 0.010$).

However, in the study of Giannoglou et al.[28] 40 patients with diagnosed CHD were compared with 32 controls. Serum Zn was not significantly associated with CHD risk and severity ($P = 0.320$). However, urinary Zn concentration was significantly higher in patients with CHD ($P = 0.030$). In the study of Cebi et al.[29] which compared 30 patients with diagnosed CHD with 20 healthy subjects, serum Zn was not statistically different in two groups ($P = 0.650$).

Hair Zn was assessed in two studies with contradictory results.[24,25] In the study of Afridi et al.[25] who investigated Zn status in hair, urine, and blood, 457 male CHD patients were enrolled and compared with 536 healthy individuals.

Table 1. Case-control studies of biochemical measurement of zinc and coronary heart disease (CHD)

Author	Country	Men among control (%)	Mean age of case subjects (years)	Mean age of control subjects (years)	Type of case subjects	Source of control subjects	Number of case subjects/control subjects	Zinc assessment (technique)	Zinc concentration		P
									Case subjects	Control subjects	
Tan et al.[24]	China	50	36-81	24-72	ACS	Healthy volunteers	24/100	Hair (ICP-AES)	168.12 ± 69.74 ng/ml	166.60 ± 68.24	NR
Giannoglou et al.[28]	Greece	53	66	61	ACS (diagnosed with angiography)	Healthy volunteers (R/O ACS with angiography)	40/32	Serum, urine (AAS)	Serum = 626.5 µg/l Urine = 620 µg/24 h	Serum = 628.5 Urine = 469.4	0.830 0.014
Afridi et al.[25]	Pakistan	100	31-60	31-60	ACS (diagnosed with angiography)	Healthy volunteers	457/536	Serum, hair, urine (AAS)	NR	NR	< 0.050
Cebi et al.[29]	Turkey	NR	59.1 ± 11.0	57.5 ± 10.0	ACS (diagnosed with angiography)	Healthy volunteers (R/O ACS with angiography)	30/20	Serum (AAS)	0.85 µg/dl	0.90 µg/dl	0.650
Islamoglu et al.[26]	Turkey	73	58 ± 12.0	53 ± 12	ACS (diagnosed with angiography)	Healthy volunteer (R/O ACS with angiography)	67/26	Serum (AAS)	0.61 ng/l	0.96 ng/l	< 0.010
Bayir et al.[27]	Turkey	56	61.4 ± 12.0	61.6 ± 18.0	ACS	Healthy volunteers	100/100	Serum (AAS)	0.72 ppm	1.3 ppm	< 0.010

ACS: Acute coronary syndrome; AAS: Atomic absorption spectrometry; ICP-AES: Inductively coupled plasma atomic emission spectroscopy; NR: Not reported

Table 2. Prospective studies of biochemical measurement of zinc and coronary heart disease

Author	Country	Population	Men (%)	Mean age (Years)	Endpoint ascertainment	Follow-up (years)	Outcome	Number of case subjects/non-case subjects	Zinc assessment (technique)	Unadjusted HR (95%CI)/P	Adjusted HR (95%CI)/P
Bates et al.[31]	Britain	British National diet and nutrition survey	51	76.6 ± 7.4	Death certificate	14	CHD mortality	1054	Plasma (colorimetric assays)	0.73 (0.61-0.88)/ 0.001	0.83 (0.65-1.07)/ 0.150
Lobo et al.[30]	Brazil	Brazilian cohort	62	54.6 ± 12.7	Death certificate	2	CHD mortality of hemodialysis patients	45	Plasma (AAS)	NR	NS

HR: Hazard ratio; CHD: Coronary heart diseases; AAS: Atomic absorption spectrometry; NR: Not reported; NS: Not significant; CI: Confidence interval

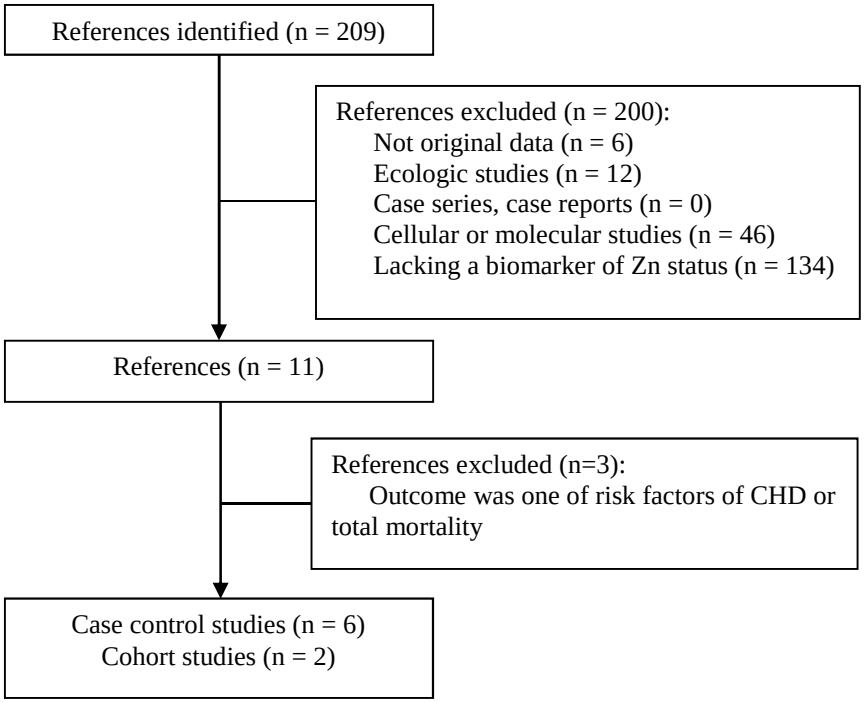

Figure 1. Flow of study selection process
CHD: Coronary heart diseases

The results showed that the concentrations of Zn were lower in CHD patients in both blood and hair samples (P > 0.001). However, the excretion of Zn was higher in CHD patients. Tan et al.[24] enrolled 24 CHD patients and 100 healthy persons aged 24-72. The concentration of hair Zn was not different significantly in case and control groups. Urine Zn was reported in two studies, and it was significantly higher in CHD patients than controls.[25,28]

In cohort studies included into this review study, serum Zn was not associated with CHD. Lobo et al.[30] followed 45 hemodialysis patients for 2 years to investigate the risks for CHD mortality. During the 24 months, 24.4% of the patients died, all due to CHD. In Lobo et al.[30] study, decreased plasma Zn was associated with increased tumor necrosis factor alpha (TNF-α) levels and oxidized low-density lipoprotein (LDL) in patients, but analysis by the Cox model showed that plasma Zn was not a significant predictor of mortality. In Bates et al.[31] prospective study, mortality status and its underlying causes were studied in 1054 subjects aged more than 65 years in the British National Diet and Nutrition Survey in 1994-2008. Primary vascular disease mortality comprised about 26% of all mortality. Model adjustment for sex and age, plasma Zn was suggested to be protective against vascular mortality, but after adjusting for all known risk factors (body mass index, systolic blood pressure, smoking, number of prescribed drugs, health score, physical activity score, and poverty) it was not significant.

Discussion

According to our knowledge, this study is the first systematic review evaluating the association between Zn status and CHD. Eight studies were included in this study, and the majority of the case-control studies showed an inverse association between Zn status through different indicators and CHD. This inverse association was observed in populations with different baseline Zn concentrations and in persons from different countries. Prospective cohort studies did not protect this association. However, we found no intervention studies to summarize.

In almost all studies, serum Zn concentration was less in CHD patients as compared to control subjects, but this difference was not significant in all studies (Table 1). Zn deficiency may have a roll in CHD risk. This theory is consistent with cellular and molecular findings. There are evidences that Zn may suppress apoptosis.[28,32-34] Therefore, Zn depletion may affect myocardial reperfusion injury by induction of apoptosis.[35] Zn deficiency can alter angiotensin-conversion enzyme activity adversely and cause hypertension due to vasoconstriction.[36] In addition, Zn may affect inflammatory response in humans

thorough affecting the production of inflammatory cytokines such as interleukin-1 (IL-1) and TNF-α.[37] Poor Zn status has been shown to be associated with inflammation.[38,39] Inflammation has been shown to play a role in the pathogenesis of myocardial ischemia[40,41] and anti-inflammatory strategies which reduce myocardial tissue damage are challenges in interventional cardiology.[42-46] Inflammation response will be initiated after releasing of inflammatory cytokines and absorbing neutrophils to the injury site, which lead to injury to the endothelial cells by the production of reactive oxygen species.[41,47] Moreover, the gene IL-6 which regulates the amount of circulating proteins involved in inflammatory responses, may be influenced by zinc status.[48] This gene has been shown to be associated with CHD.[49]

Although Zn deficiency could be a risk factor for CHD, decreased serum Zn in these patients could be caused by CHD. Evidence has shown that plasma Zn is a negative acute-phase reactant and after ACS plasma Zn may decrease in response to inflammation. Plasma Zn is affected by metallothioneins homeostasis, which is itself influenced by proinflammatory cytokines. Metallothionein which is expected to be increased in chronic inflammation causes low Zn availability in inflammatory conditions.[37] Thus, impaired Zn homeostasis in CHD patients may be due to chronic inflammation in these patients versus a risk factor of CHD. Therefore we could not determine which one comes first based on case control studies which is a limitation of case control studies. However, ignoring which comes first, CHD patients have poor Zn status and it is recommended to investigate if improving Zn status in these patients could improve their survival.

Urine Zn was reported in two studies and it was significantly higher in CHD patients than controls[25,28] which indicate zinc excretion and it is in consistent with studies shows lower level of zinc in serum. Hair Zn was assessed in two studies with contradictory results.[24,25] The Afridi et al. study is limited to men and this difference may be related to sex.[25] Tan et al. study might have not enough power to detect the difference between two groups because of low sample size in this study (only 24 cases).[24]

Careful consideration of choice of biochemical indicators will be valuable. All biochemical indicators of Zn, such as hair, urine, nails or plasma may reflect Zn exposure to some degree.[14,50,51] However, the interpretation of biomarkers is not simple because circulating plasma or serum Zn concentrations respond to conditions such as inflammation, infection, and time of last meal. Nails are susceptible to soil contamination. Contamination by coloring dyes and anti-dandruff shampoos may limit the suitability of hair.

In cohort studies included into this study, serum Zn was not associated with CHD. Lobo et al. have evaluated the association of plasma Zn and oxidized LDL and TNF-α.[30] It was concluded that decreased plasma Zn were associated with increased TNF-α levels and oxidized LDL in patients who undergone hemodialysis. It can be concluded that there is a relationship between Zn deficiency with inflammation and lipid peroxidation in hemodialysis patients, but serum zinc was not a predictor of CHD mortality. It should be mentioned that the follow-up for mortality was 2 years in this study, and it could be not enough for evaluating the effect of this mineral. Small sample size (45 hemodialysis patients) could be another reason for failure in finding significant relationship. Large prospective studies with enough sample size are needed for strong conclusion.

In another prospective study, it was suggested plasma Zn could be protective against vascular mortality, but after adjusting for all known risk factors it was not significant.[31] In this study, four model were used, and the protective effect of Zn was significant in all models except the full model which all confounders were entered into the model. However, the hazard ratio was very similar to other three models and paying attention to a confidence interval (0.65-1.07) shows the protective effect of zinc. The Bates et al. study investigated risk factors in elderly. However, the predictive value of risk factors for disease and mortality appears to decrease with age.[52] Moreover, the association between Zn and CHD might be underestimated in this study.

The discrepancy between most case-control studies and prospective studies may be related to the fact that this is inflammation of post-CHD which causes low plasma Zn which could be detected in case-control studies.

In assessing the association between Zn and CHD, different confounders should be considered. Zinc depletion could be due to a strict vegetarian diet (a diet which is limited to plant products)[53] or alcohol or drug addiction which all of them have relation with CHD and may confound the relation between Zn and CHD. Moreover, physical activity and age may affect Zn absorption and Zn loss.[14] They should be also taken into account because they may also confound this relationship.

The competency for absorption among nutrients and such interactions should be considered too, as they may affect Zn utilization.

Conclusion

In conclusion, the results from observational studies evaluating the association between Zn status and risk of CHD are controversial; however, case-control studies with sufficient sample size could find a significant inverse association between serum Zn concentration and CHD risk. None of the prospective studies confirmed this association. More cohort studies with CHD mortality endpoint and appropriate biologic samples which have collected in the beginning of the study are needed to be able to conclude about this association in future.

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Conflict of Interests

Authors have no conflict of interests.

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Appendix 1. Quality criteria for observational studies on zinc and CHD (coronary heart disease)

Reference number	24	28	25	31	29	26	30	27
All observational studies								
Exposure was assessed at the individual level	√	√	√	√	√	√	√	√
Outcomes were based on objective tests or standard criteria in 90% of study participants	√	√	√	√	√	√	√	√
The authors presented internal comparisons within study participants		√	√	√				√
The authors controlled for potential confounding risk factors in addition to age	√	√		√				√
Prospective cohort studies								
Loss to follow-up was independent of exposure								
The intensity of search of disease was independent of exposure status				√				
Case-control studies								
Data were collected in a similar manner for all participants	√	√				√	√	√
The same exclusion criteria were applied to all participants		√				√		√
The selection process for Non-cases was described		√						
Samples were collected ≤ 24 hour after the onset of symptoms for all cases				√				√
The study was based on incident cases of disease	√							√
Non cases were persons who would have been excluded if they had developed CAD								

CAD: Coronary artery diseases

Acute myocardial infarction in a young male wrestler: A case report

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Case Report

Abstract

BACKGROUND: Anabolic steroids have been widely used in recent years. It could adversely affect the cardiovascular system. Non-traditional risk factors for coronary heart diseases (CHDs) have raised great concern.

CASE REPORT: A young bodybuilder was presented with crushing retrosternal chest pain, excessive diaphoresis, and vomiting. The symptoms began during wrestling. The patient did not have a history of traditional cardiovascular risk factors. He was using large quantities of nutritional and bodybuilding supplements with multiple intramuscular injections of dexamethasone during past 6 months. The electrocardiography (ECG) revealed ST-segment elevation in the precordial, I and aVL leads consistent with acute extensive myocardial infarction (MI). Lipid profile, cardiac troponin, and creatine phosphokinase-MB (CPK-MB) was abnormal. Transthoracic echocardiography (TTE) revealed mild left ventricular (LV) enlargement and reduced global systolic dysfunction with regional wall akinesia. The patient received thrombolytic therapy which was resulted in symptomatic relief and resolution in ST-T changes. Significant smoke was seen in LV cavity without clot formation on the discharge day. About 1 week later, large fresh clots were seen in the apex. He was admitted again, and the burden of clots was reduced significantly after initiation of oral warfarin. Other laboratory tests were as follows: High-sensitivity C-reactive protein (CRP): 25.9 mg/dl, homocysteine: 26.2 µmol/l. The patient was discharged with specific medication. Clots were disappeared after 6 weeks of warfarin therapy. Later, the patient was evaluated again, and there was not any symptom and LV clots.

CONCLUSION: Hyperhomocysteinemia could be induced by steroid abuse and may cause atherosclerotic and thrombotic effects in healthy athletes. We suggest clinicians to take a careful history of young athletes presented with MI or thrombotic events and also pay special attention to their homocysteine levels in their follow-ups.

Keywords: Hyperhomocysteinemia, Anabolic Agents, Thrombosis

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Introduction

Although the importance of conventional risk factors is well established, it is commonly suggested that more than 50% of patients with coronary heart disease (CHD) lack any of the conventional risk factors. This claim implies that other factors play a significant role in CHD and have led to considerable interest in non-traditional risk factors and genetic causes of CHD.[1]

Hyperhomocysteinemia has been proposed as a risk factor for increased tendency of vessel thrombosis and cardiac ischemia.[2,3] Elevated levels of homocysteine can also affect coagulation cascade or even cause multivessel coronary artery disease.[3,4] On the other hand, anabolic androgenic steroids can directly affect cardiovascular system by inducing left ventricular (LV) hypertrophy and dysfunction or even indirectly causing hyperhomocysteinemia.[5] Here, we discuss a 23-year-old male wrestler with a 6 months history of excessive anabolic steroid use presenting with crushing retrosternal chest pain.

Case Report

The 23-year-old man was referred to the emergency department with a 4 hours history of crushing retrosternal chest pain, excessive diaphoresis, and

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vomiting. The symptoms began during wrestling. The patient had a previous history of retrosternal chest discomfort ascribed to gastric upset which always relieved spontaneously. He did not have traditional cardiovascular risk factors (cigarette smoking, diabetes, and hypertension). The patient was a bodybuilder and wrestler, who was continually using large quantities of nutritional and bodybuilding supplements with multiple intramuscular injections of dexamethasone during past 6 months. The vital signs were as follows on admission: Blood pressure: 140/90 mmHg, pulse rate of 72/minutes, respiratory rate: 14/minutes. The third and fourth heart sounds were prominent. The electrocardiography (ECG) which was recorded in emergency room revealed ST-segment elevation in the precordial, I and aVL leads consistent with acute extensive myocardial infarction (MI) (Figure 1).

Increased serum level of cardiac troponin was detected. Lipid profile was abnormal [high-density lipoprotein (HDL): 20 mg/dl, low-density lipoprotein (LDL): 101 mg/dl, triglycerides (TG): 305 mg/dl, cholesterol: 317 mg/dl]. Transthoracic echocardiography (TTE) revealed mild LV enlargement and reduced global systolic function (ejection fraction: 35-40%) with akinesia of all apical segments and mid-anterior and anteroseptal regions. The door to needle-door to balloon time was estimated to be long lasting. Hence, thrombolytic (streptokinase) was prescribed which was resulted in symptomatic relief and resolution in ST-T changes. About 4 days later, coronary angiography was done, showing non-significant stenosis in mid portion of left anterior descending artery (Figure 2). In the last day of admission, significant smoke was seen in LV cavity without clot formation.

The patient was reassessed 1 week after discharge and TTE was done. LV ejection fraction was 40%, and large fresh clots were seen in the apex (Figure 3-A). He was admitted again for better cardiac monitoring and initiation of anticoagulation. The size of the clots was reduced significantly after initiation of oral warfarin (Figure 3-B). Other laboratory tests were as follow: High-sensitivity C-reactive protein (CRP): 25.9 mg/dl, homocysteine: 26.2 µmol/l. The patient was discharged on warfarin, folic acid, vitamin B_{12} in addition to carvedilol, atorvastatin, losartan, and low dose furosemide. In the follow-up visits, the patient underwent echocardiography. The clots were disappeared after 6 weeks of warfarin therapy (Figure 3-C).

Six months later, the patient was evaluated again and there was not any symptom and the LV clots were disappeared. Serum level of homocysteine was within the normal limits. Vitamin B_{12} and folic acid drugs were discontinued. During 3 years follow-up, there was not any clot formation in LV cavity in TTE and the patient had occasionally non-angina chest pain, exertional dyspnea (New York Heart Association I/II) without worsening of global LV function or any thromboembolic events. Lipid profile was normal in repeated assessment. The patient is now taking carvedilol, captopril, aspirin, atorvastatin, spironolactone, and warfarin and involved regularly in cardiac rehabilitation programs.

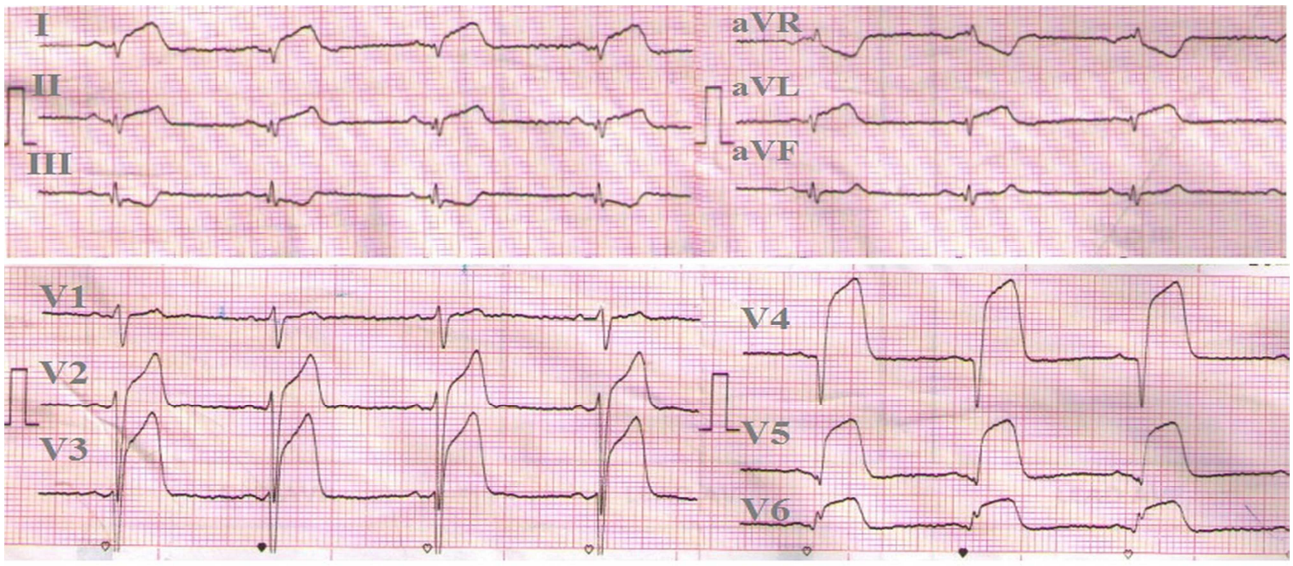

Figure 1. Twelve-leads electrocardiogram revealed significant ST elevation in precordial (tombstone sign), I and aVL leads (compatible with acute extensive anterior myocardial infraction)

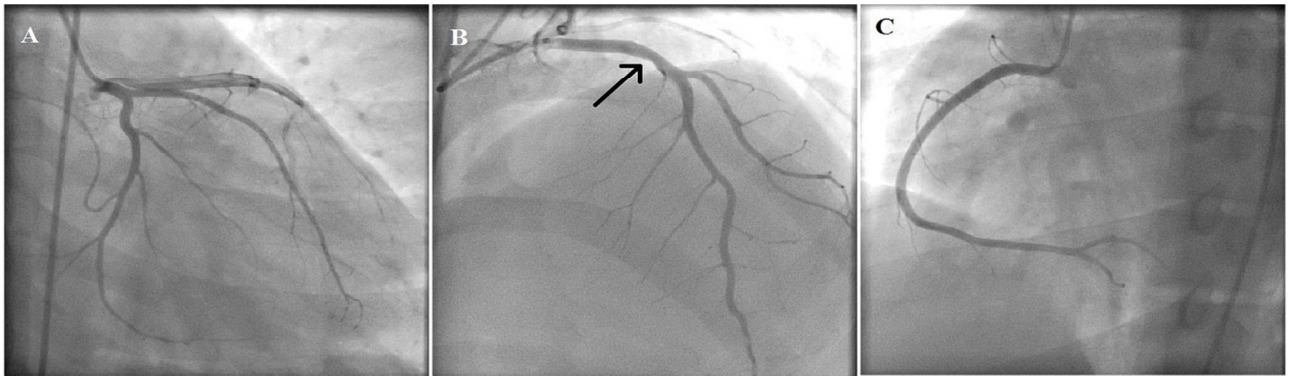

Figure 2. (A, B and C) Coronary angiography showing just a non-significant lesion in mid portion of left anterior descending (arrow in B), Left circumflex and right coronary artery were normal

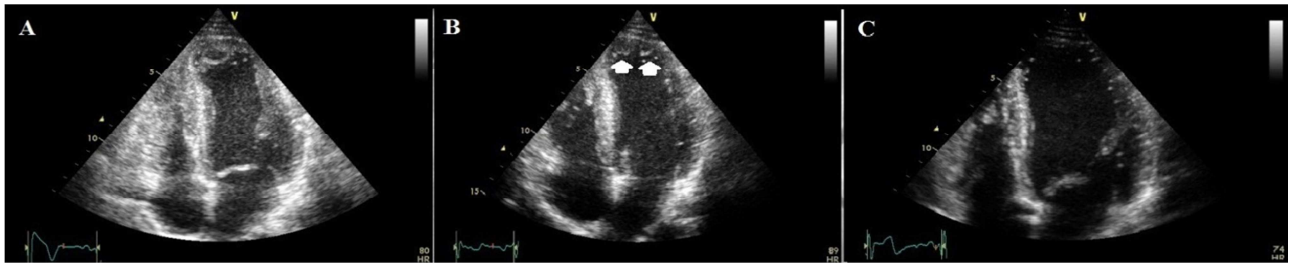

Figure 3. Echocardiographic images in apical four chamber views, (A) Large fresh clots in the apex (1 week later), (B) arrows denting the residual but small clots and (C) no residual clots

Discussion

In this report, we presented a case of acute chest pain in a young wrestler who uses bodybuilding supplements and intramuscular dexamethasone. ECG, echocardiographic and laboratory data were considered to be a more compatible with MI. However, not every chest pain and rises in cardiac biomarkers are due to acute coronary syndromes. Chest pain with associated increase in cardiac biomarker could be found in acute pulmonary embolism. ECG and echocardiographic findings were not compatible with such diagnosis in this patient. Myocarditis should also be considered as a possible diagnosis in young patients with acute coronary syndrome presentation especially in the absence of atherosclerosis risk factors or with normal coronary angiogram. In one series of patients with chest pain and ECG abnormalities, 32% of the cases have myocarditis on myocardial biopsy.[6] Wall motion abnormalities could also be seen in echocardiography in myocarditis, but it is more global rather than segmental. ECG abnormalities or segmental distribution of wall motion abnormalities extend beyond a single coronary artery territory in the typical cases.[7] This was in contrary to the presented case in which the ECG changes and regional wall motion abnormalities were comparable and suggesting the involvement of anterior coronary circulation.

Anabolic steroids have various effects on cardiovascular system. Atherosclerosis, systemic hypertension, impaired diastolic, and systolic ventricular function and disturbances in lipid metabolisms have all been reported with anabolic steroid abuse.[8] Increased platelet activity is also observed in such patients, and might be responsible for MI or even stroke.[8]

There are many cases of androgenic anabolic steroid abuse in young athletes showing cardiovascular problems such as MI or thrombosis of different vessels such as renal artery.[5]

LV dysfunction is the other effect of long-term androgenic anabolic steroid abuse and could increase the risk of sudden death in these patients.[9] Pathologic studies in such patients revealed small arteriole wall thickening and intimal hyperplasia, which could be responsible for causing ischemic myocardial damage and subsequent ventricular dysfunction.[10]

Use of anabolic steroid can induce acute hyper homocysteinemia and associated thrombotic events.[2] A higher level of homocysteine could be seen with lower HDL concentration, higher plasma LDL, and triglycerides.[5]

Homocysteine is a sulfhydryl amino acid, absent

in human natural dietary sources.[11] It can be toxic to endothelial cells leading to the smooth muscle proliferation in vessel wall and affecting the coagulation cascade.[3] Multivessel coronary artery disease and acute MI have been reported in the setting of the high level of homocysteine.[4] Anabolic steroids can affect the absorption of B_6 and B_{12} vitamins and cause an elevation in homocysteine levels.[12] This effect might be responsible for the elevation of homocysteine levels in our patient; causing potential stenosis and thrombosis.

While administration of folate supplement is somehow controversial, normalizing plasma homocysteine levels with healthy diet containing vegetables and fresh fruits accompanied by moderate exercise is more favorable.[11] Administration of high dose of vitamin B_6 with folic acid after acute MI does not reduce the risk of death or recurrence of cardiovascular disease.[13] On the other hands, it can adversely affect myocardial repair and increase morbidity and mortality among patients with cardiovascular disease.[13]

Use of anabolic steroid in young athletes is an important issue for clinicians. These substances have various effects on the cardiovascular system as well as other organs. Hyperhomocysteinemia could be induced by steroid abuse and may have atherosclerotic and thrombotic effects in healthy athletes. However, if a patient has the previous hyperhomocysteinemia, the risk of catastrophic cardiovascular events might be higher. We suggest clinicians to take history of young athletes presented with MI or thrombotic events carefully and also pay special attention to the homocysteine levels in their follow-up visits.

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None.

Conflict of Interests

Authors have no conflict of interests.

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Adherence to practice guidelines for coronary artery bypass graft surgery in Shiraz, Iran

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Short Communication

Abstract

BACKGROUND: There is an increasing tendency to use evidence-based medicine (EBM) and guidelines among physicians. This is also true for concordance of coronary artery bypass graft (CABG) surgery and guidelines; therefore, we aimed to address the adherence to 2011 American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) guideline for CABG.

METHODS: In this cross-sectional study, we assessed 246 patients who underwent CABG in Shiraz, Iran, during 2011-2012, using a data collecting form provided through studying ACCF/AHA guideline 2011. The patients were categorized into clinical subgroups and then grouped into appropriate, in-appropriate and uncertain classes. Chi-square was used to compare categorical variables and t-test was used for continuous variables.

RESULTS: Of the 246 patients, 70.3% were grouped into "class I," 12.6% into "class IIa," 6.9% into "class IIb" and 10.2% into "class III." Therefore, 82.9% of the patients were grouped into "appropriate," 6.9% into "uncertain," and 10.2% into group "inappropriate."

CONCLUSION: We suggest that more attention is needed to be paid to these guidelines. Using these guidelines may help surgeons to have a uniform approach for patients.

Keywords: Adherence, Guidelines, Coronary Artery Bypass Graft, Iran

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Introduction

Coronary artery bypass graft (CABG), as a category of coronary revascularization, is one of the most frequent procedures performed and annually about 50000 open-heart surgeries are performed in Iran, 50-60% of which is allocated to CABG.[1]

Despite the advantages of CABG in treating patients and increasing the chance of survival; we have increasingly encountered the public accusation of inappropriateness of this procedure.[2,3]

The rate of inappropriateness in different studies varied from 2 to 14%.[2,4,5] since CABG is very costly and can cause post-operation mortality and morbidity, we should always select the patients for this operation carefully and consider the benefits of this procedure for them.[6,7]

There is an increasing tendency to use the evidence-based medicine (EBM) and guidelines among the physicians, too.[8] EBMs can help physicians to select the best plan for the right patient in the right way.[9] We conducted this study to address the adherence to 2011 American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) guideline for CABG surgery in the current clinical care in Shiraz, Iran.

Materials and Methods

In this cross-sectional study, we assessed 246 patients who underwent CABG in Shiraz during 2011-2012. CABG was performed in Shiraz in six hospitals during the study period. These hospitals are of three types: governmental, private, and charity. Precisely, 3482 CABG operations were performed for a year in Shiraz, starting from March 2011. We selected patients based on random stratification of hospitals. We used a random numbers generation website to have randomized numbers according to our sample size to reach the

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proportional study sample. All selected patients, who were operated on in Shiraz in 2011, were included in this study. We only excluded 28 patients whose medical records were incomplete.

Primarily, a data collection form was provided through studying and investigating the ACCF/AHA guideline 2011. This form was modified based on the existing information of hospitalized patients in cardiac surgery wards. After the data were collected, we assigned patients into clinical subgroups according to ACCF/AHA guideline. According to these clinical subgroups, the patients were classified into four classes (class I, IIa and IIb, III). CABG was appropriate for all patients who were classified in class I, IIa. Patients classified in class IIb were uncertain, and operation for patients in class III was inappropriate. Finally, our classification can be summarized as follows: class I (useful and effective), class IIa (evidence favors usefulness), class IIb (evidence less well-established), and class III (not useful or effective).[10]

Chi-square was used to compare categorical variables and t-test was used for continuous variables. All statistical analyses were performed using the SPSS software (version 15, SPSS Inc., Chicago, IL, USA). $P \leq 0.05$ were considered significant, and the 95% confidence interval (CI) was calculated.

Results

In our study, 35.4% of patients were female and 64.4% male and there was a significant difference in the mean age between these two groups ($P = 0.01$ and 95% CI: -5 to -0.136). The mean age of all patients, men and women were 62.24 ± 10.01, 61.33 ± 10.7, and 63.90 ± 8.83 years, respectively.

Appropriateness of CABG procedure in all patients

According to the 2011 ACCF/AHA guideline for CABG surgery, of the 246 patients,70.3% were grouped into "class I," 12.6% into "class IIa," 6.9% into "class IIb," and into 10.2% "class III." Therefore, 82.9% of the patients were grouped into "appropriate," 6.9% into" uncertain" and 10.2% into group "inappropriate."

Appropriateness of CABG procedure based on hospitals

Appropriateness of CABG surgery into governmental, charity and private hospitals was 84.1, 83.8, and 77.4 percent, respectively. There was no statistically significant difference between kinds of hospital and appropriateness ($P = 0.40$).

Appropriateness of CABG procedure based on sex of patients

Table 1 shows the distribution of appropriateness classes for men and women. CABG surgery appropriateness was 83.6% for men and 78.2% for women. However, among men in the present study, 5.0% were grouped into uncertain and 10.6% into inappropriate, and 10.3% of women were grouped into uncertain and 9.2% into the inappropriate groups.

Inappropriateness of CABG procedure according to clinical subgroups

Of all patients, 10.5% were grouped in class III. Figure 1 shows the analysis of this class. Class III patients in our study were placed into one of the four clinical subgroups, respectively: ST-segment elevation myocardial infarction (MI), stable angina, and patients with poor left ventricular (LV) function and CABG after percutaneous coronary intervention (PCI) failure.

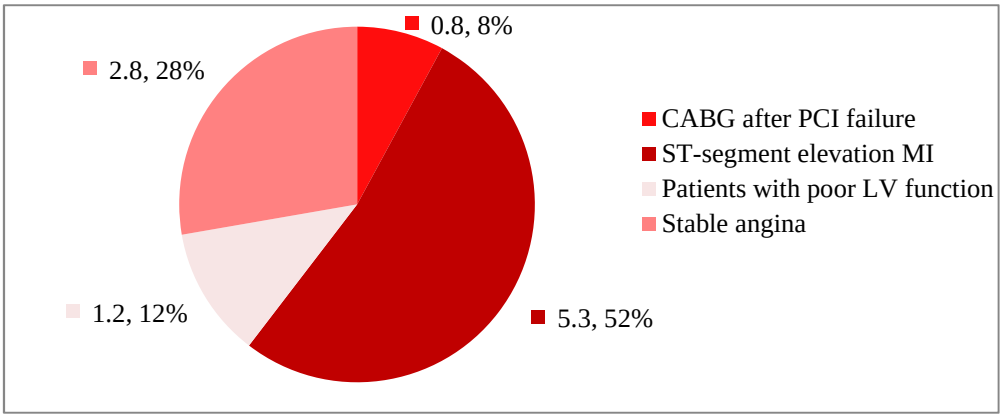

Figure 1. Proportion of class III based on clinical subgroup (n = 25)
PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass graft; LV: Left ventricular; MI: Myocardial infarction

Table 1. Distribution of coronary artery bypass graft (CABG) procedure based on patients' sex

Sex	Classification				
	Class I	Class IIa	Class IIb	Class III	Total
Male [n (%)]	113 (45.9)	21 (8.5)	8 (3.3)	17 (6.9)	159 (64.6)
Females [n (%)]	60 (24.4)	10 (4.1)	9 (3.7)	8 (3.3)	87 (35.4)
Total [n (%)]	173 (70.3)	31 (12.6)	17 (6.9)	25 (10.2)	246 (100)

Discussion

In our study, 70.3% of patients were grouped in class I and 12.6% in class IIa. These two groups are the ones who benefit from surgery. Hence, CABG was "appropriate" for 82.9% of the patients, 6.9% were grouped in the "uncertain" and 10.2% in the "inappropriate" subgroups. Our findings are different with study of O'Connor et al.[2] in Northern New England. In that study, 96.1% were grouped in the "appropriate," 2.5% in the "uncertain" and 1.4% in the "inappropriate" subgroups. As can be seen, the appropriateness of CABG surgery in our patients is lower. Hence, it is necessary to use guidelines properly and to select the patients carefully. It is important that the proper procedure be done for the right patient in the right way. Furthermore, appropriate patient selection may be helpful in improving the outcomes after treatment. However, it is obvious that these guidelines are unlikely to be enough for decision making. Physicians can use these guidelines as a means to support their decision because nothing can be a substitute for clinical judgment. Using these guidelines about which the experts have agreed together with physician's clinical judgment may mean a better outcome for the patient. In addition, we are able to use multidisciplinary approaches for patients to make the best decision. Not only overuse of procedures but also their underuse may harm the patients.

As shown, the maximum appropriateness was in governmental and charity hospitals. This may be due to the fact that governmental hospitals are academic centers, and training of medical students is done in these centers. Leape et al.[11] found that academic hospitals had a greater agreement with guideline and inappropriateness was 1.6% in these hospitals. These findings were in agreement with those of our study. Regarding the appropriateness of CABG surgery for men and women; there was no statistically significant difference between appropriateness of CABG surgery in men and women. The study of O'Connor et al.[2] demonstrated that there are no statistically significant differences between appropriateness of CABG surgery in men and women and this finding was consistent with our results. Bernstein et al.[12] also showed that inappropriateness of CABG surgery was 2.0% in men and 3.0% in women, and there was no statistically significant difference by gender. Of all the patients coded into class III, 52.0% were in ST-segment elevation MI clinical subgroup. This clinical subgroup included patients who presented with refractory ischemia, cardiogenic shock, life-threatening arrhythmia or failed PCI. These patients were often operated on in emergency or urgent conditions. Due to this condition, morbidity and mortality of patients increased.[7]

Bernstein et al.[13] showed that inappropriateness varied from 1.5 to 3.7%, and appropriateness was more in patients who were undergoing CABG than PCI. Patients with poor LV function benefit from CABG surgery if the reason of this problem is ischemic and the myocardium is viable as well. Hannan et al.[14] showed that most physicians recommend CABG surgery for patients with poor LV function. However, these guidelines may need to be revised over the years, but we recommend that clinical judgment of physicians, using guidelines and multidisciplinary approaches lead to the best decision.

Conclusion

We suggest that more attention is needed to be paid to these guidelines. Using these guidelines may help surgeons to have a uniform approach for patients. We recommend that clinical judgment of physicians, using guidelines and multidisciplinary approaches lead to the best decision.

Acknowledgments

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Conflict of Interests

Authors have no conflict of interests.

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