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ARYA Atherosclerosis

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2. Bonow RO, Mann DL, Zipes DP, Libby P. Braunwald's Heart Disease E-Book: A Textbook of Cardiovascular Medicine. 7th ed. Philadelphia, PA: Elsevier Health Sciences; 2007. p. 1976, 1981, 1982.

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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* All the words of the article containing the references; each table is considered as 300 words.

There will be a 50% discount of publication fee if both the first and the corresponding author are affiliated to Isfahan University of Medical Sciences (IUMS).

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Oral health status, knowledge, attitude and practice of patients with heart disease

Amir Alireza Rasouli-Ghahroudi[(1)], Afshin Khorsand[(1)], Siamak Yaghobee[(1)], Amirreza Rokn[(2)], Mohammad Jalali[(3)], Sima Masudi[(4)], Hamed Rahimi[(5)], Ali Kabir[(6)]

Original Article

Abstract

BACKGROUND: The aim of this study was to investigate knowledge, attitude and practice (KAP) of cardiovascular disease (CVD) patients about their oral health status.

METHODS: In this cross-sectional study, we analyzed the data of 150 CVD patients that collected by a self-administered questionnaire consists of demographic characteristics and KAP. Oral health indicators calculated based on the results of oral examination by an expert dentist.

RESULTS: CVD patients had an overall moderate level of knowledge and attitude, but their practice was lower than moderate. There were important associations between knowledge scores with gender, education, residential area and financial status, between attitude scores with education and residential area, and between practice scores with education and financial status. There were no associations between KAP and age, marital status or job. Significant positive correlations were found between KAP components. Significant negative correlations were found between oral hygiene index with knowledge and practice.

CONCLUSION: The practice of heart disease patients about their oral health was poor, and declares that increasing awareness and attitude may not promote practice. Efficient programs are needed to promote oral health practice of adult populations in special groups.

Keywords: Health Knowledge; Attitudes; Practice; Oral Health; Cardiovascular Diseases

Date of submission: 29 Apr 2015, ***Date of acceptance:*** 07 Oct 2015

Introduction

In the past two decades, rapid increase has been occurred in the prevalence of cardiovascular disease (CVD) in many developing countries around the world, along with the obvious changes in lifestyle in terms of diet and physical activity.[1,2] CVDs with more than 45.0% of deaths are the first cause of mortality in Iran.[3] The prevalence of CVD in Iran is 37.5 and 22.2% in women and men, respectively.[4] Moreover, premature coronary heart diseases are increasing in Iran.[5]

Due to the high prevalence and significant social effects, oral disease can be considered as a public health problem.[6] An evidence is not adequate to support the hypothesis of oral infections as an independent risk factor for CVD events.[7] However, some studies have shown evidence of a weak association between the potential roles of periodontal infection as a risk factor for CVDs.[8-11] Based on these studies periodontal infection can increase the risk of CVD about 15-19%.[10,11] Furthermore, most of the drugs that used to treat CVDs have the potential to cause adverse reactions in the oral cavity and compromise oral health of these patients.[12]

In some cases, individual health status greatly depends on his/her knowledge, attitude and practice (KAP) in that area. Smyth et al.[6] showed better oral practice in the persons with strong knowledge of oral health. In planning and promoting oral health programs, it is important to recognize the knowledge and beliefs of the population about oral and dental health. Without the doubt, to rectify the oral and dental problems of the cardiac patients, the first thing is to evaluate

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their level of KAP. Oral health status and KAP of these patients have not been sufficiently studied yet, and we have assessed them in cardiovascular inpatients and outpatients of Tehran Heart Center, Iran, in this study.

Materials and Methods

In this cross-sectional study, 167 patients with heart diseases were interviewed, 17 of them were excluded from the analysis because of missing data of more than 40.0% of their data in every one area of the KAP. Patients were cases referring to Tehran Heart Center, Tehran University of Medical Sciences, between February 2011 and August 2012.

Subjects answered a self-administered questionnaire of KAP about oral health and its association with CVDs. This questionnaire has been standardized in a separate study, and the results have been published.[13] Reliability was 0.82 according to Cronbach's alpha score. A face validity was higher than 80.0%. A content validity of the whole parts of the questionnaire was 86.0% for clarity, 78.0% for relevancy, 85.2% for simplicity, and 82.3% for consistency of each question with the questions' set. Factor analysis showed that 15 components explain 74.0% of the total variance.[13]

Then, an expert dentist carried out the physical examination to determine oral health indicators.[14] He determined these indices: oral hygiene, debris, calculus, periodontal disease, and decayed, missed, and filled surfaces (DMFs), in addition, to exam for the presence and extent/severity of gingivitis, periodontitis, plaque, artificial teeth, loosed teeth, and gingival bleeding. One assistant helped assessment of the files of the hospitalized patients for completing demographic variables consist of age, gender, height, weight, marital status, education level, job, financial status, dental insurance, living place (rural/urban), were among our demographic variables.

Oral health indices (OHIs) consist of OHI, periodontal disease index (PDI), and DMFs were calculated for patients based on dentists' examination. Their definition and calculation described in details elsewhere.[13]

PDI (Ramfjord periodontal index) is a thorough clinical examination of the periodontal status of six teeth, with an evaluation of the gingival condition, pocket depth, calculus and plaque deposits, attrition, mobility, and lack of contact. Individuals with clinically normal gingiva have an index of 0-0.2. The index reaches a maximum of 8.0 in persons with severe terminal destructive periodontitis.[13,15]

In this study, heart disease is consisted of patients with ischemic heart disease (unstable angina and myocardial infarction).

Cases were defined as inpatient or outpatient cases with ischemic heart diseases. The oral disease was defined as any dental, gingival and periodontal problem according to physical examination.

In this study, sample size was estimated based on $\alpha = 0.05$, the percentage of cases with low dental health status equal to 11% (according to our pilot study), the accuracy around this prevalence equal to 5%, and considering 10% loss of the cases (due to different causes like drop out during the research and missing data) and according to the one proportion estimation formula. Hence, a total sample size was equal to 167 cases with ischemic heart disease. Selecting more than 70 cases in each group of inpatient or outpatient cases was only based on to consider relatively equal percentage (near 50%) in these two groups.

We used mean ± standard deviation (SD) for expressing quantitative variables. We calculated a modified standardized score for KAP components. We summed the scores of each part and subtracted the one-third of missing items from it because we assumed that not answering to three questions is equal to have one negative score for one question (as is usual in many exams like USMLE or TOEFL). Then, we divided the result by the number of questions and multiplied in 100. Hence, we obtained a score between 0 and 100 for all components. Therefore, the number of questions and missed answers did not affect the total scores and the scores of each part of KAP and each patient were comparable with other parts of the questionnaire in each patient or a total score of other participants. We used these modified standardized scores for all analysis. The difference in mean scores of 10 points was considered clinically important. We also categorized modified standardized scores of the KAP components into three categories to poor, moderate and good based on modified standardized scores under 40, 40-69 and 70 or more, respectively. One-way analysis of variance and independent t-test were used for comparison of mean scores of the KAP components by socio-demographic characteristics of participants. The correlations were evaluated by Pearson and partial correlation coefficients. Stepwise linear regression was also used for determining predictors of KAP and health status of participants. SPSS software (version 17, SPSS Inc., Chicago, IL, USA) was used for analysis the data.

All cases signed an informed written consent before entering to the study. This project is reviewed and accepted by Ethics Committee of Dental Implant Research Center, Faculty of Dentistry, Tehran University of Medical Sciences, with the code number: 90-03-104-17668.

Results

Sample characteristics

Demographic characteristics were no significantly different between those who remained in the analysis and those who excluded. Among them who remained in the study, 72 were outpatients and, 78 were in patients in Tehran.

The mean age (± SD) of the participants was 52.7 (± 8.8). Most of the participants were male (58.7%), married (90.0%), without university education (83.4%), residing in urban area (86.0%). More than 76.0% of them had good or very good financial status, but only about 9.0% of them had dental insurance. 93 patients (62.0%) had periodontitis (Table 1).

Table 2 shows the health status of the participants. 74.0% of participants reported their general health status as moderate, about 33.0% had co-morbidities, and 45.0% took medication. More than 37% of the study subjects had hypertension (HTN), 34.7% hypercholesterolemia/hypertriglyceridemia, and 28.0% diabetes mellitus (DM). 46.0% of them reported a family history of CVDs.

KAP about oral health

Participants' mean (± SD) score of knowledge was 57.7 (± 21.7). Among them, 69 (46.0%) had moderate and 48 (32.0%) had good knowledge about oral health. 44.0% of the respondents knew that gingivitis causes gingival bleeding, whereas about 17.0% did not know and the rest of them gave wrong answers. About 27.0% of them knew the cause of adding fluoride to toothpaste. 74.0% of the participants knew that dental plaque causes devastated teeth, and 75.3% were aware of the adverse effects of fizzy drinks on teeth.

For attitude, their mean (± SD) score was 52.3 (± 19.0). Most of the participants had moderate and good scores for attitude questions (55.3 and 19.3%, respectively). Three questions that had the most wrong answers were CVDs cause oral diseases (75.7%), what the dentist cares about is treatment not prevention (56.3%), and regular dental visits is not necessary (56.9%). 55.0% agreed that oral diseases cause CVDs and about 38.0% had not any idea.

Table 1. Socio-demographic characteristics of the participants

Participants (n = 150)	n (%)
Age (year)	
≤ 49	48 (32.0)
> 50	97 (64.7)
Not specified	5 (3.3)
Gender	
Male	88 (58.7)
Female	55 (36.7)
Not specified	7 (4.7)
Marital status	
Single	4 (2.7)
Married	135 (90.0)
Divorced	2 (1.3)
Widowed	6 (4.0)
Not specified	3 (2.0)
Education	
Illiterate	29 (19.3)
Primary school	46 (30.7)
Secondary school	16 (10.7)
Diploma	34 (22.7)
University	23 (15.3)
Not specified	2 (1.3)
Job	
Retired	23 (15.3)
Householder	37 (24.7)
Employed	11 (7.3)
Private	57 (38.0)
Unemployed	15 (10.0)
Not specified	7 (4.7)
Residential area	
Rural	13 (8.7)
Urban	129 (86.0)
Not specified	8 (5.3)
Financial status*	
Very good	17 (11.3)
Good	95 (65.3)
Moderate	34 (22.7)
Poor	1 (0.7)
Not specified	3 (2.0)
Dental insurance	
Yes	13 (8.7)
No	127 (84.7)
Not specified	10 (6.7)
Periodontitis	
Yes	93 (62.0)
No	57 (38.0)

*We judge for this variable according to both self-assessment by the patients and their monthly income

Mean (± SD) of practice score was 44.9 (± 15.5). 58.0% of participants had moderate scores, whereas only 3.3% had good scores. About 42.0% of participants stated that brushed their teeth once a day and 15.5% of them twice or more a day. Remaining participants do not brush regularly.

Moreover, 71.0% of cases spent 1-2 minutes or more to brush their teeth. Different questions about patterns of washing their mouths showed that 80.0% of the participants reported using of toothbrush and toothpaste, 55.8% used fluorinated toothpaste, and 74.1% reported using mouthwash. 9.0% of participants reported regular dental visits, whereas 61.5% visited their dentists only when they had a toothache. The high cost of dental visit singly or along with other causes was expressed by 53.0% of respondents as one of the common causes of not visiting the dentist.

Association between socio-demographic characteristics and KAP of oral health

The difference of the separate parts of KAP scores with socio-demographic characteristics included age, gender, education, residential area, and financial status had been shown in table 2. Mean scores of KAP for females were higher than males but only the difference for knowledge was significant ($P = 0.001$). There were significant difference for mean scores of KAP among different levels of education ($P = 0.006$, $P = 0.004$, and $P < 0.001$, receptively) (Table 2). The higher the education level of people, the greater the scores of KAP, except for attitude score of the participants who had university education. The participants who lived in urban area had higher mean scores than residents of the rural area; but, the differences were statistically significant only for knowledge and attitude scores ($P = 0.005$ and $P = 0.002$, respectively). Furthermore, there were significant differences for mean scores of knowledge and practice among different levels of financial status ($P = 0.009$ and $P = 0.004$, respectively), but the difference for mean scores of attitude was not significant ($P = 0.348$). There were no significant differences between mean scores of KAP in different levels of marital status and different job groups.

Correlation of dental indices and KAP scores

As table 3 illustrates, Pearson correlation coefficient between age and DMFs was moderate and significant ($r = 0.40$, $P < 0.001$). There were similar strength significant correlation between OHI and knowledge ($r = -0.32$, $P < 0.001$), knowledge and attitude ($r = 0.40$, $P < 0.001$), and knowledge and practice ($r = 0.32$, $P < 0.001$) too. Furthermore, there were significant but small correlations between OHI and attitude, OHI and practice, attitude and practice ($r = -0.20$; $P = 0.012$, $r = -0.26$; $P < 0.001$ and $r = 0.18$; $P = 0.024$, respectively) (Table 3).

Table 2. Comparison of mean scores of knowledge, attitude and practice (KAP) by socio-demographic characteristics of participants

Characteristics	Knowledge score (mean ± SD)	P	Attitude score (mean ± SD)	P	Practice score (mean ± SD)	P
Age* (year)		0.707		0.862		0.820
≤ 49	58.8 ± 21.4		52.1 ± 20.5		44.5 ± 16.2	
> 50	57.4 ± 21.9		52.7 ± 18.5		45.1 ± 15.1	
Gender*		0.001		0.214		0.309
Male	53.8 ± 23.2		50.9 ± 18.4		43.9 ± 15.8	
Female	65.7 ± 16.8		55.1 ± 20.2		46.7 ± 15.4	
Education**		0.006		0.004		< 0.001
Illiterate	47.1 ± 25.6		42.0 ± 16.7		35.3 ± 13.1	
Primary school	56.5 ± 21.1		51.1 ± 20.8		39.2 ± 14.7	
Secondary school	53.5 ± 19.9		57.0 ± 11.4		48.7 ± 8.9	
Diploma	62.5 ± 18.7		59.7 ± 18.0		52.8 ± 11.9	
University	67.5 ± 17.7		53.6 ± 19.6		52.6 ± 16.6	
Residential area*		0.005		0.002		0.162
Rural	41.3 ± 24.9		37.5 ± 18.5		39.1 ± 19.0	
Urban	58.8 ± 20.9		54.2 ± 18.6		45.2 ± 14.6	
Financial status**		0.009		0.348		0.004
Very good	64.7 ± 17.7		58.1 ± 23.8		55.7 ± 12.4	
Good	59.6 ± 21.7		52.2 ± 18.4		43.8 ± 14.8	
Moderate and poor	48.2 ± 20.8		49.9 ± 18.9		41.5 ± 15.9	
Total	57.7 ± 21.7		52.3 ± 19.0		44.9 ± 15.5	

*Independent t-test, **One-way analysis of variance; SD: Standard deviation

In regard to inter-correlations among KAP, we used partial correlation to obtain the correlation between two scores with control for the third one. After controlling for attitude, the correlation coefficient for knowledge and practice was 0.27 (P = 0.001). The correlation coefficient for attitude and practice after controlling for knowledge was 0.06 (P = 0.450) and for knowledge and attitude after controlling for practice was 0.37 (P < 0.001).

We also evaluated the relationships between OHIs and KAP components with control for education level and financial status with multiple linear regression models in men and women separately. Significant relationships were seen between OHI with attitude (β = -0.024, P = 0.030) and DMFs with knowledge and attitude (β = 0.493, P = 0.050 and β = 0.428, P = 0.040, respectively) in women. But in men, all KAP components were removed from the model and only education level and/or financial status were related with OHIs.

Association between patient's co-morbidities and KAP and oral indices

Table 4 shows the health status of the participants based on their self-reporting. About 37.0% of participants stated that had HTN, 34.7% had hyperlipidemia (HLP), and 28.0% had DM. 46.0% of the participants expressed that had family history of CVDs. 74.0% of participants had evaluated their health status as moderate.

Table 5 shows the comparison of mean scores of dental indices in HTN, DM, and HLP patients. There were significant differences in mean scores of DMFs and PDI indices in patients with HLP (P = 0.003 and P < 0.001, respectively), and in mean scores of OHI in patients with DM (P = 0.020).

Table 3. Pearson correlation (P) of knowledge, attitude and practice (KAP) with each other, age and oral health indicators

Variable	Age		Knowledge		Practice		Attitude	
	Pearson correlation	P	Pearson correlation	P	Pearson correlation	P	Pearson correlation	P
DMFs	0.407	< 0.001	0.006	0.944	−0.094	0.262	0.132	0.114
PDI	0.164	0.049	−0.109	0.187	−0.167	0.042	0.040	0.624
OHI	−0.004	0.967	−0.320	< 0.001	−0.268	< 0.001	−0.207	0.012
Age			0.037	0.663	−0.029	0.728	0.031	0.707
Knowledge					0.321	< 0.001	0.407	< 0.001
Practice							0.184	0.024

DMFs: Decayed, missed, and filled surfaces; OHI: Oral hygiene index; PDI: Periodontal disease index

Table 4. Health status of the participants based on self-reporting

Variable	Yes [n (%)]	No [n (%)]	Do not know [n (%)]	Not specified [n (%)]
Co-morbidity	50 (33.3)	53 (35.3)	25 (16.7)	22 (14.7)
Medication	68 (45.3)	65 (43.3)	-	17 (11.3)
HTN	56 (37.3)	68 (45.3)	13 (8.7)	13 (8.7)
HLP	52 (34.7)	81 (54.0)	8 (5.3)	9 (6.0)
DM	42 (28.0)	98 (65.3)	8 (5.3)	2 (1.3)
Family history of CVD	69 (46.0)	71 (47.3)	5 (5.3)	5 (5.3)
	Good	**Moderate**	**Without problem**	**Not specified**
General health status	14 (9.3)	111 (74.0)	5 (3.3)	20 (13.3)

CVD: Cardiovascular disease; HTN: Hypertension; HLP: Hyperlipidemia; DM: Diabetes mellitus

Table 5. Comparison of mean scores of dental indices in patients with hypertension, diabetes mellitus, and hyperlipidemia

Patients	DMFs			PDI			OHI		
	n	Mean ± SD	P	n	Mean ± SD	P	n	Mean ± SD	P
HTN			0.283			0.758			0.573
Yes	54	57.6 ± 32.4		56	3.8 ± 1.5		56	4.2 ± 2.1	
No	66	57.6 ± 32.4		68	3.7 ± 3.2		67	4.4 ± 1.5	
DM			0.533			0.909			0.020
Yes	40	53.0 ± 34.1		42	3.5 ± 1.7		42	5.0 ± 2.2	
No	94	49.1 ± 29.8		97	3.6 ± 2.8		96	4.2 ± 1.7	
HLP			0.003			< 0.001			0.192
Yes	51	59.8 ± 31.7		52	4.6 ± 3.2		52	4.7 ± 1.9	
No	76	43.1 ± 28.7		80	2.9 ± 1.6		79	4.3 ± 1.7	
Total	150	51.4 ± 31.7			3.6 ± 2.4			4.5 ± 1.9	

DMFs: Decayed, missed, and filled surfaces; DM: Diabetes mellitus; HLP: Hyperlipidemia; HTN: Hypertension; OHI: Oral hygiene index; PDI: Periodontal disease index

Table 6. Comparison of mean scores of knowledge, attitude and practice (KAP) in patients with hypertension, diabetes mellitus, and hyperlipidemia

Patients	Knowledge			Attitude			Practice		
	n	Mean ± SD	P	n	Mean ± SD	P	n	Mean ± SD	P
HTN			0.890			0.120			0.360
Yes	56	58.5 ± 21.7		56	49.9 ± 19.1		56	46.9 ± 15.5	
No	68	58.0 ± 20.9		68	55.2 ± 17.9		68	44.4 ± 14.9	
DM			0.041			0.096			0.101
Yes	42	51.9 ± 24.4		42	48.3 ± 19.2		42	42.2 ± 13.9	
No	98	60.2 ± 20.8		98	54.1 ± 18.2		98	46.8 ± 15.9	
HLP			0.867			0.617			0.003
Yes	52	58.5 ± 21.8		52	51.8 ± 18.5		52	39.8 ± 16.3	
No	81	59.1 ± 21.5		81	53.5 ± 19.3		81	47.8 ± 14.1	

DM: Diabetes mellitus; HLP: Hyperlipidemia; HTN: Hypertension

Table 6 shows the comparison of mean scores of KAP in HTN, DM, and HLP patients. There were no significant differences between mean scores of KAP with HTN, DM, and HLP except for DM and knowledge (P = 0.041) and HLP and practice (P = 0.003).

Discussion

Oral health is one of the important indicators of individual and public health. For planning in the areas of health education and health services, it is substantial to have accurate information of oral health status among different population groups, particularly patients, students, children, and adults.

Our study showed that the overall level of knowledge and attitude of our participants were moderate, but their practice was lower than 50.0%. Based on categorized scores, about half of the respondents had moderate scores in all components of KAP. Most of the patients with a moderate and good knowledge had similar attitude scores while their practice was poor and moderate. This indicates knowledge can affect the attitude. Furthermore, most of the respondents with poor and moderate attitude had a similar level of practice, too. In our study, only five people had good practice. This is inconsistent with the results obtained in pregnant women in Iran[16] that 34.4% of them had good practice. It might be due to the impact of their ill-health that can affect other aspects of their daily life. In addition, they are people in older age groups and it is possible that they simply did not acquire appropriate healthy behavior in their childhood and adolescence.

In our study, women's knowledge about oral health was better than men. Since the proportion of both groups in younger and old age groups were approximately equal, and a higher proportion of women had lower literacy level than men, thus the difference might be attributable to the women's interest to their health status. In addition, attitude and practice of females were better than males, but the differences were not significant. Furthermore, higher proportion of females had moderate and good practice scores than males.

In regard to high scores of knowledge in patients with CVDs, and the questions about dental decay, gingivitis, brushing the teeth, the role of dental plaque in the distraction of teeth and the relationship between general health and oral health, it seemed that these patients had background information about oral health. This can be due to repeated health education programs, especially oral health in the community.

In terms of educational level, patients with a higher education had higher levels of KAP, except for knowledge of secondary school education and attitude for academic degree. Illiterate persons had the lowest mean scores for each component of KAP. In every level of education, women had higher scores than men. In a study on KAP of pregnant women about oral and dental care, women with high school diploma had higher scores than women with an educational level under high school diploma.[16] These confirm that people in higher levels of education has more knowledge, better attitude and practice than those with lower levels of education.

In our study, 41.3% of respondents believed that regular dental visits every 6-12 months are necessary, but only 8.7% of them had a regular dental visit. In regard to knowledge and attitude of our participants, this showed that good knowledge and even good attitude did not influence dental practice. Low dental visit in our study might be due to not having dental insurance and high costs of dental services so that 84.7% of respondents had not dental insurance and about 53.0% of them specified high costs as one of the causes of referring to dentist. Zhu et al.[17] showed that about 67.0% of

Chinese adults in urban areas and 50.0% of them in rural areas had economic support for dental visits and treatments. While, in our study, 84.7% of the cases had not any insurance (Table 1).

Brushing the teeth, twice daily with fluorinated toothpaste recommended by dentists to promote the oral health and prevent the decay. In our study, 15.5% of the respondents stated that brushed their teeth once daily. This was a very lower than the results that Kelly et al.[18] reported for the UK (74.0%) and the results that reported for Kuwait adults of 84.6%.[19] The difference between the results for Kuwaiti adults is most likely due to special group of our study-heart disease patients- and the high proportion of low educational level of them. Although just 27.0% of our participants knew the cause of adding fluoride to toothpaste, about 56.0% of the respondents used fluorinated toothpaste. This might be due to the fact that the most available toothpaste in markets and drugstores are fluorinated ones.

Studies have shown that people mostly estimate the time they brush the teeth longer than actual time.[20,21] In our study about 30.0% of respondents stated that they brushed their teeth more than 2 minutes. However, there were no significant differences in their OHI or PDI with others.

The level of KAP of our respondents based on having the status of co-morbidities of interest in this study did not differ meaningfully. There were statistically significant differences for knowledge based on DM status and for practice in patients with and without HLP. The difference observed in DM could be due to a small number of diabetic patients in comparison with non-diabetics ones. The observed difference in HLP group was not clinically important and it could be because of the higher proportion of HLP patients with poor practice compared with a higher proportion of non-HLP respondents with moderate practice. So, having another disease along with CVDs did not influence the KAP of our participants.

In the evaluation of the effects of co-morbidities of the participants-HTN, HLP, and DM- on their oral health, our study revealed that DMFs and PDI of our patients differed significantly according to the status of HLP. Participants with HLP had higher DMFs and PDI than those without that. Since, DMFs shows the past experience of the patients, HLP could not cause increased DMFs. As an indicator of the present oral health, PDI score of the patients with HLP were higher than patients without that and the difference was significant. On the other hand, as mentioned above, HLP patients had poor practice in comparison with patients without HLP. Therefore, the difference might be due to the relatively better practice of later patients. This can be the case in a significant difference that was seen between OHI and DM status. Patients with diabetes mellitus had a lower mean score in practice, although it was not significant.

Our study indicated a relationship between KAP components. The relationship between knowledge and attitude was stronger than the attitude-practice and knowledge-practice relationships. We controlled the correlations between two areas for the third one, the relationship between attitude and practice were very weak and non-significant. In usual KAP model, that attitude has an intermediate role in the causal relationship between the knowledge and attitude. But in our study, it seemed that knowledge affected attitude and practice directly. When we considered the relationships in men and women independently and with control for the third factor, we saw the similar pattern in men. In women, however, the correlation between attitude and practice was stronger than the correlation between knowledge and attitude. In addition, there was a relationship between knowledge and practice. These showed in women knowledge influenced the practice of respondents directly and indirectly, and attitude was the intermediate variable in the causal relationship between knowledge and practice. This is consistent with the fourth type of the relationship between KAP that Schwartz[22] suggested. Anyway, we should be cautious in interpreting these results because these are the results of partial correlation and did not adjust for any other confounder.

In the context of oral health, without controlling for the effect of determinants such as education level and financial status, negative and significant correlations existed between KAP with OHI. These correlations were stronger in women than men. These relationships could indicate that the people who had high scores in KAP had better oral health, too. In women, despite their higher scores in knowledge and attitude, there were positive and significant relationships between knowledge and attitude with DMFs. The reason could be that in this study participants were adult and sick people and their high scores in DMFs could be in result of their lifestyle, lack of knowledge, and inappropriate practice in the past, especially in childhood and adolescence. On the other hand, women usually experience hormonal changes during their life,

because of pregnancy that can affects their oral and dental health, and make their teeth prone to decay. But after considering education level and financial status, in most of the models, KAP components were not related to oral health status. The reason could be that KAP components are related to education level and financial status of people.

This study was based on self-administered questionnaire on KAP of participants and dental and oral examination by a dentist. Therefore, one of our major limitations is that their performance assessed by self-reporting rather than monitoring. Another limitation of our study is that we evaluated the relationships among the three components of KAP by Pearson correlation coefficient and partial correlation rather than statistical modeling hence it is possible that relationships confounded by some confounding factors such as residential area or the education levels, and some unmeasured cultural and social factors.

Conclusion

These findings clearly showed that despite the moderate and good knowledge and attitude of 75.0% of patients about oral health, about half of them had poor practice. The score of OHIs confirm poor practice of these patients in the past and present. Co-morbidities did not associate with meaningful differences in KAP levels and OHIs. This study revealed that in adult patients, an increase in knowledge and attitude does not necessarily accompany with better practice or behavior.

We recommend other researchers design some new teaching techniques for patients at risk of CVDs to promote their knowledge and improve their attitude and practice for caring about their dental health. Our result showed that current educational system by academicians and media is not working.

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Conflict of Interests

Authors have no conflict of interests.

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The effect of low dose versus standard dose of arterial heparin on vascular complications following transradial coronary angiography: Randomized controlled clinical trial

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Original Article

Abstract

BACKGROUND: The potential risk of vascular complications associated with heparin, the dose of heparin therapy has not been exactly examined in patients undergoing transradial angiography. Thus, this study was aimed to compare referral arterial thrombosis, hematoma and hemorrhagic complications with 2500 and 5000 IU arterial heparin and the association of these complications with predictors in patients undergoing diagnostic angiography.

METHODS: This prospective, randomized, double-blind controlled trial was carried out on 441 patients aged ≥ 18-year-old in Isfahan, Iran. They were referred for diagnostic coronary angiography with radial access. First participants were randomized into to inject either 2500 IU (group A) or 5000 IU (group B) of heparin. Study's primary endpoints were thrombosis, hematoma, and hemorrhage.

RESULTS: The frequency of thrombosis was 25.5% in group A vs. 2.3% in group B ($P < 0.001$), while the frequency of hematoma had no significant differences in group A and B. None of patients in both groups had hemorrhage. Using 5000 IU of heparin protected the occurrence of thrombosis by 95% [odds ratio (OR): 0.05, 95% confidence interval (CI): 0.02-012] after adjustment for confounders.

CONCLUSION: The low dose (2500 IU) versus standard dose (5000 IU) of heparin use increased the risk of thrombosis following trans-radial diagnostic coronary angiography, with no effect on hematoma and bleeding.

Keywords: Coronary Angiography; Thrombosis; Hemorrhage; Hematoma

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Introduction

Cardiovascular diseases (CVDs) are the first leading cause of mortality in Iran and worldwide over the last decades.[1,2] The improving in primary and secondary prevention approaches and more access to invasive and non-invasive treatments have reduced CVD mortality in developed countries.[3] However, definite diagnosis is suggested before doing any coronary aggressive treatment. The most precise technique for final interpretation of coronary diseases is coronary angiography.[4] Although the transfemoral approach (TFA) has some vascular complications including bleeding, hematoma and arteriovenous fistula or pseudoaneurysm, it is the first option for diagnostic and therapeutic percutaneous coronary intervention (PCI).[5] Transradial approach (TRA) which was initiated by Campeau[6] in 1989 for a diagnostic procedure and improved by Kiemeneij and Laarman[7] for PCI, is the next alternative.

The radial artery is an increasingly utilized access site for coronary arteriography, now used in up to 20% of diagnostic procedures in the United States.[4] Although it is routine to use intense antiplatelet and anticoagulant treatment in coronary angiography via TRA, this approach is as safe as TFA,[8] and vascular access site complications are less common than TFA.[9] On the other hand, the prevalence of radial artery occlusion (RAO) was 2-18% in some studies after TRA coronary procedures.[10] Several factors including gender, body weight, the duration of procedure and compression, the dose of the

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anticoagulation agent and catheter numbers are can effect on vascular complication with TRA.[11] However, the potential risk of vascular complications associated with heparin. The dose of heparin therapy has not been exactly examined in patients undergoing TRA. Thus, this study was performed to evaluate the incidence and comparing the arterial thrombosis and hemorrhagic complications with 2500 and 5000 IU atrial heparin and the association of these complications with predictors in patients who underwent diagnostic angiography.

Materials and Methods

This was a two-center prospective, randomized, double-blind controlled trial (RCT) registered in Iranian Randomized Clinical Trial Center by ID number of IRCT138905124497N1. This study had a parallel design which was done in two specialized governmental and referral hospitals including Chamran and Nour on 441 subjects in Isfahan, Iran, from April 2014 to March 2015. The sample size was determined based on 95% confidence interval (CI), 80% power of the test and the frequency of thrombosis in low and a high dose of heparin in the same previous study[12] and 10% of effect size was estimated about 200 samples in each group. We recruited subjects aged > 18-year-old, who referred for diagnostic coronary angiography with radial access by nonprobability sampling method. The indications for angiography were intermediate to high risk in non-invasive test, stable ischemic heart disease with severe angina, deposit of optimal treatment and left ventricle (LV) dysfunction (LV ejection fraction < 50) with ischemic heart disease in noninvasive tests. The participants were randomized based on simple randomization using flipping a coin method. The randomization was done by a statistician, who was unaware of the different treatment. We excluded participants who patients were suggested to urgent angiography, angioplasty, having bleeding disorders, prior radial intervention, pathological Allen tests and chronic renal failure. Patient undergoing radial angiography the average fluoroscopy duration (from the first to the last rays radiation) was 8 minutes but the average whole TRA duration was 18 minutes.

The Ethics Committee of Isfahan University of Medical Sciences was approved and followed of the Declaration of Helsinki (Ethic Committee Code: 394080). Written informed consents were obtained from subjects.

All subjects underwent a medical history and clinical examination. Socio-economic demographic data including gender, age, and occupation as well as smoking status were obtained by a physician of treatment group. Physician acquired medical history such as acute coronary syndrome and peripheral vascular diseases and CVD risk factors including diabetes mellitus (DM) and using relevant drugs. Height and weight were measured using standard methods. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). A trained nurse measured blood pressure (BP) with a mercury sphygmomanometer according to a standard protocol,[13] twice each from right and left arms in sitting position after 5 minutes of rest. The first Korotkoff sound was recorded as the systolic BP (SBP) and the disappearance of the sounds (V phase) was considered as the diastolic BP (DBP). The values of BP used in the analysis were the recorded mean level of measured BP in the higher arm. According to the Joint National Committee (JNC) and World Health Organization (WHO) guideline criteria, hypertension was defined as an SBP ≥ 140 mmHg and/or a DBP ≥ 90.[14] In addition, sheath size, the number of catheters, procedure duration, and compression time after the procedure are some factors associated with RAO and hemorrhagic complication were reported.

Transradial catheterization procedure: Under sterile conditions, local anesthesia was achieved by an injection of 2% lidocaine at the puncture site. A 20-gauge needle was used to puncture the radial artery 2-3 cm proximal to the crease of the wrist. On appearance of pulsatile flow, a wire (0.025 inch, 45 cm) was advanced into the radial artery lumen. A glide sheath (Merit's) was then advanced over the wire into the radial artery using Seldinger technique in this study. For diagnostic coronary catheterization, a 5-French sheath system was used in all patients. Total 200 µg of nitroglycerin and 2.5 mg verapamil and 2500 (group A) or 5000 IU (group B) unfractionated heparin was injected via the arterial sheet before the wire into the radial artery through the sheath. Diagnostic angiography was performed with 5-French standard diagnostic coronary catheters (tiger).

Patients were randomized to receive either 2500 IU (group A) or 5000 IU (group B) of unfractionated heparin by another staff that was unaware of the patient's history.

Homeostasis procedures: All introducer sheaths were immediately removed following the angiography. A radial compression device (TR band, Terumo Europe, Leuven, Belgium) was

placed tightly around the wrist. The band was inflated with 15 ml air after removal of the sheath to obtain homeostasis.

Inflation pressure was reduced after 15, 30 and 60 minutes by removing 3-5 ml of air of the inflation chamber of the TR band, respectively. The band was left in place for at least 1 hour. A light dressing was applied to the site after removal of the compression device.

Endpoints: Study's primary end points were thrombosis, hematoma and hemorrhage record by one cardiology resident who was unaware of the study group. Thrombosis was assessed by patient's pulse Q30 minute until 4 hour (time of discharge) and then 24 hours after angiography and patient with radial pulseless investigated by color Doppler sonography. Radial artery flow was assessed at the access site at the wrist and the complete forearm up to the brachial artery in the cross section and in the longitudinal axis. The absence of radial artery flow was defined as complete occlusion. The partial flow was defined as a reduced flow velocity in a partial occluded vascular lumen in the distal, middle and/or proximal part of the radial artery. The hematoma was examined in 4 and 24 hours and hemorrhage in 1 and 4 hour after angiography. We defined hematoma as localized swelling and bruising in place of sheath and hemorrhage as active bleeding in place of the sheath. To achieve double-blind condition, the patients and the physician who examined the endpoints were unaware of the treatment.

The data normality of data was checked and approved. For the descriptive data analysis, categorical variables were expressed as absolute frequencies and percentages and were compared using the chi-square test. Continuous variables were expressed as the mean and standard deviation (SD) and compared using Student's t-test. Primary endpoints were compared between groups A and B by chi-square test. Logistic regression was utilized to examine odds ratio (OR) (95% CI) of any complications and some indicators including, age (year), gender (male/female), BMI (kg/m^2), current smoking status (yes/no), DM (yes/no), hypertension (yes/no), number of catheters (1/2 or 3), fluoroscopy duration (minute) and heparin use (2500 or 5000 IU). SPSS software (version 18, SPSS Inc., Chicago, IL, USA) was used for the statistical analyses, and $P < 0.050$ was considered statistically significant.

Results

We recruited 512 patients who were a candidate for TRA diagnostic angiography. Of total 71 were excluded because of not meeting inclusion criteria (n = 49) or refused to participate (n = 22). The flow chart showing number of eligible and excluded participants, the number of participants allocated to 2500 and 5000 IU of heparin is presented in figure 1.

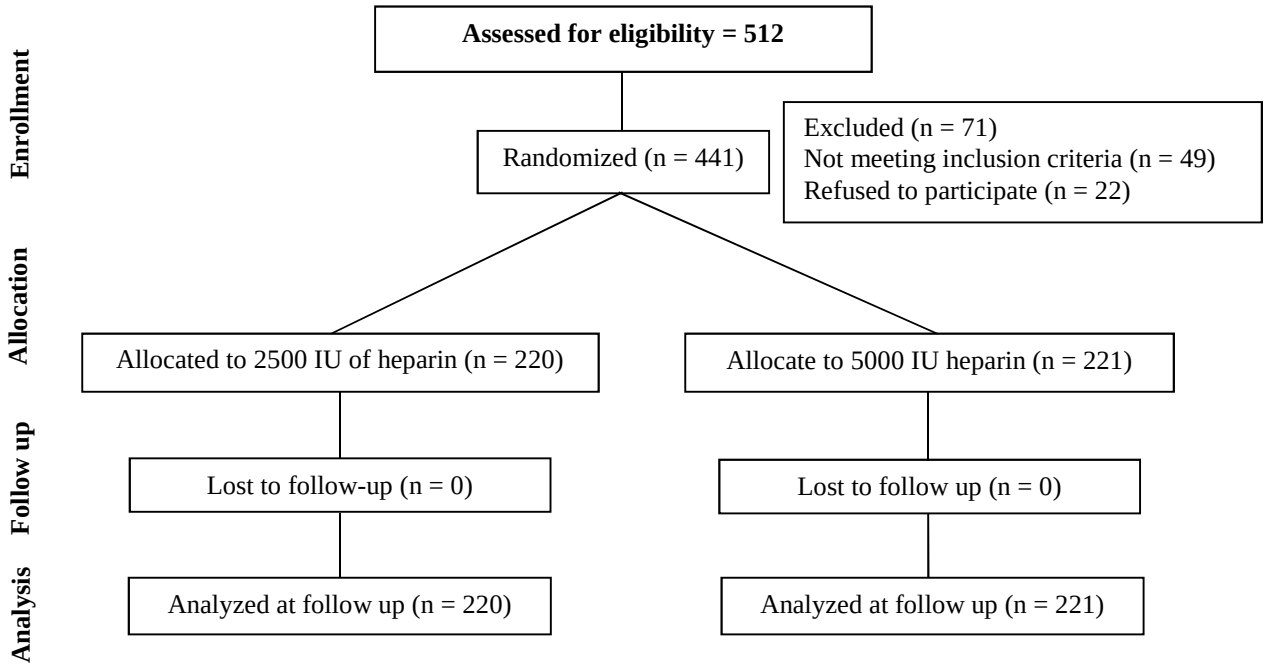

Figure 1. Flow chart showing number of eligible and excluded participants, number of participants allocated to 2500 and 5000 IU of heparin

Table 1 shows baseline characteristics and procedure status of patients based on study groups. Of 441 patients participated in this study 220 and 221 subjects were in group A and B, respectively. There is no significant differences in mean age and BMI of participants in group A vs. group B (P = 0.149 and P = 0.066, respectively). Totally 240 patients were male in both groups, however, there was no significant difference between two groups (P = 0.567). The frequency of hypertension, DM and smoking status were similar in both groups (all P more than 0.050).

The frequency of patients in group A, who had one catheter in the procedure was significantly less than group B [182 (82.7) vs. 202 (91.4); P = 0.007], while the fluoroscopy duration had no significant difference between two groups (P = 0.059). The baseline characteristics of patients were compared in subjects with and without events including thrombosis and hematoma based on the dose of heparin. This comparison shows the thrombosis was more frequent in female gender and smokers (P < 0.001 and P = 0.001, respectively). In addition, the hematoma was more frequent in diabetic patients (P = 0.047). There were no significant differences in the other variables between the patients with and without thrombosis and hematoma.

Table 2 demonstrates that injecting 2500 IU of heparin increased the occurrence of thrombosis in unadjusted and after adjustment for all potential confounders were more than 14 and 21 times than standard heparin dose (OR: 14.75, 95% CI: 5.78-37.65; P < 0.001) and [21.87 (8.12-56.93); P < 0.001], respectively. The risk of thrombosis was 2.25 times more in female than male (OR: 2.25, 95% CI: 1.02-4.94). After adjustment of potential confounders, hypertension, DM, current smoking, a number of catheters and fluoroscopy duration increased the risk of thrombosis by 2.11, 1.79, 2.281.12 and 2.84 times, respectively. However, the BMI inversely associated with incidence of thrombosis [0.82 (0.72-0.93); P = 0.002] (Table 3). However, there is no association of the amount of injected heparin as well as other risk factors with hematoma incidence (Table 3). The frequency of thrombosis was 25.5 against 2.3% in group A vs. group B (P < 0.001), while the frequency of hematoma had no significant differences in group A and B (Figure 2). Furthermore, there was no bleeding occurrence in patients of both groups.

Discussion

In this two-center RCT study, we examined the incidence of RAOs following TRA access coronary angiography with 2500 against 5000 IU heparin injection. TRA access occlusions are often asymptomatic and consequently underdiagnosed, thus it seems logical, that anticoagulant therapy should be used to decline these events.[14] We found that the risk of thrombosis was more than 21 times in low dose group versus standard dose. However, the risk of hematoma had no difference in low and standard dose of heparin injection. Furthermore, there was no minor and major bleeding incidence after 1 and 4 hours in both groups. Our findings were consistent with Mohandes et al.[15] and the accumulating evidence which suggests TR access is associated with significant reductions in bleeding compared with a TFA.[14,16,17] Patients' baseline and angiographic characteristics were well balanced in two groups and had no significant differences except for the number of catheters which was less in high dose group.

Table 1. Baseline characteristics and procedural data of the study population based on study group

Characteristics	Group		P
	Group A* (n = 220)	Group B** (n = 221)	
Age (year) (mean ± SD)	62.87 ± 9.10	62.48 ± 9.40	0.149
BMI (kg/m²) (mean ± SD)	26.09 ± 3.60	25.59 ± 3.10	0.066
Gender (female) [n (%)]	97 (44.1)	104 (47.1)	0.567
Hypertension [n (%)]	48 (21.8)	43 (19.5)	0.558
DM [n (%)]	29 (13.2)	20 (9.0)	0.176
Smoking [n (%)]	39 (17.9)	35 (15.8)	0.611
Number of catheters [n (%)]			0.007
1	182 (82.7)	202 (91.4)	
2 or 3	38 (17.3)	19 (8.6)	
Fluoroscopy duration (min) (mean ± SD)	8.11 ± 0.70	8.23 ± 0.47	0.059

*Group A: Group who injected 2500 IU heparin, **Group B: Group who injected 5000 IU heparin. Categorical variables were analyzed by chi-square test and continuous variables by independent t-test.
BMI: Body mass index; DM: Diabetes mellitus; SD: Standard deviation

Table 2. Odds ratio and 95% confidence interval of thrombosis and hematoma according to different characteristics

Characteristics	Thrombosis		Hematoma	
	OR (95% CI)	P	OR (95% CI)	P
Crude				
Heparin*	14.75 (5.78-37.65)	< 0.001	0.82 (0.13-4.97)	0.819
Age (year)	0.99 (0.96-1.02)	0.674	1.02 (0.93-1.13)	0.621
BMI (kg/m²)	0.82 (0.74-0.91)	< 0.001	1.02 (0.79-1.31)	0.882
Gender (female)**	2.94 (1.58-5.45)	0.001	2.85 (0.31-25.79)	0.351
Hypertension (no/yes)	1.93 (1.06-3.52)	0.031	5.76 (0.94-35.16)	0.058
DM (no/yes)	2.27 (1.11-4.65)	0.025	5.35 (0.87-33.08)	0.071
Current smoker (no/yes)	2.92 (1.59-5.37)	0.001	3.29 (0.29-37.10)	0.334
Number of catheters (2 or more)***	1.39 (0.66-2.92)	0.386	9.16 (1.49-56.28)	0.017
Fluoroscopy duration (minutes)	2.00 (1.04-3.08)	0.001	5.26 (1.26-21.95)	0.023
Adjusted†				
Heparin	21.87 (8.12-56.93)	< 0.001	0.26 (0.01-3.99)	0.332
Age (year)	0.99 (0.96-1.03)	0.784	1.08 (0.91-1.30)	0.375
BMI (kg/m²)	0.82 (0.72-0.93)	0.002	1.06 (0.67-1.69)	0.794
Gender (female)	2.25 (1.02-4.94)	0.044	7.04 (0.05-20.34)	0.443
Hypertension (no/yes)	2.11 (1.02-4.39)	0.045	2.54 (0.36-12.02)	0.206
DM (no/yes)	1.79 (1.04-4.53)	0.021	3.38 (0.32-14.51)	0.181
Current smoker (no/yes)	2.28 (1.03-5.07)	0.043	3.9 (0.13-15.92)	0.277
Number of catheters (2 or more)	1.12 (1.01-1.14)	0.048	4.5 (0.70-16.23)	0.078
Fluoroscopy duration (minutes)	2.84 (1.58-5.10)	< 0.001	1.86 (0.13-10.67)	0.649

*Group B, who injected 5000 IU heparin considered as a reference group, **The reference group was male gender, ***The reference group was using 1 catheter, †Each variable was adjusted by the others one
BMI: Body mass index; CI: Confidence interval; OR: Odds ratio; DM: Diabetes mellitus

Table 3. Baseline characteristics and procedural data in patients with and without thrombosis and hematoma based on study group

Characteristics	With thrombosis	Without thrombosis	P	With hematoma	Without hematoma	P
Group A*						
Age (year) (mean ± SD)	62.89 ± 10.30	62.86 ± 8.70	0.186	66.00 ± 2.10	62.81 ± 9.20	0.070
BMI (kg/m²) (mean ± SD)	24.33 ± 2.70	26.69 ± 3.70	0.016	26.37 ± 2.60	26.08 ± 3.60	0.419
Gender (Female) [n (%)]	29 (51.8)	35 (21.4)	< 0.001	2 (66.7)	93 (43.1)	0.083
Hypertension [n (%)]	17 (30.4)	31 (18.9)	0.057	2 (66.7)	46 (21.3)	0.122
DM [n (%)]	11 (19.6)	18 (11.0)	0.080	2 (66.7)	27 (12.5)	0.047
Smoking [n (%)]	19 (33.9)	20 (12.3)	0.001	1 (33.0)	39 (18.1)	0.820
Number of catheters (2 or 3) [n (%)]	8 (14.3)	30 (18.3)	0.322	1 (33.0)	37 (17.1)	0.437
Fluoroscopy duration (minutes) (mean ± SD)	8.27 ± 0.49	8.21 ± 0.40	0.204	8.19 ± 0.56	8.24 ± 0.43	0.224
Group B**						
Age (year) (mean ± SD)	54.60 ± 8.20	62.67 ± 9.40	0.393	64.50 ± 3.50	64.29 ± 9.50	0.094
BMI (kg/m²) (mean ± SD)	24.42 ± 2.30	25.6 ± 3.1	0.514	25.79 ± 2.70	25.59 ± 3.10	0.684
Gender (female) [n (%)]	2 (60.0)	101 (46.8)	0.444	102 (86.4)	1 (50.0)	0.264
Hypertension [n (%)]	41 (19.0)	2 (40.0)	0.251	1 (50.0)	23 (19.5)	0.361
DM [n (%)]	1(20.0)	19 (8.8)	0.381	1 (50.0)	10 (8.5)	0.140
Smoking [n (%)]	1(20.0)	34 (15.7)	0.581	5 (4.2)	1 (50.0)	0.098
Number of catheters (2 or 3) [n (%)]	8 (14.3)	30 (18.3)	0.322	1 (50.0)	10 (8.5)	0.140
Fluoroscopy duration (minutes) (mean ± SD)	8.08 ± 0.69	8.12 ± 0.61	0.213	8.17 ± 0.72	8.10 ± 0.64	0.237

*Group A: Group who injected 2500 IU heparin, **Group B: Group who injected 5000 IU heparin, Categorical variables were analyzed by chi-square test and continuous variables independent t-test.
BMI: Body mass index; SD: Standard deviation; DM: Diabetes mellitus

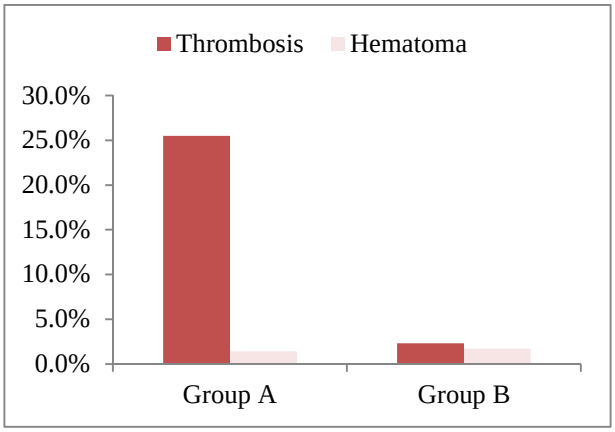

Figure 2. Comparison of the incidence of thrombosis and hematoma in group A (2500 IU heparin injection) and group B (5000 IU heparin injection)

Although TRA has some advantages against TFA, increasing fluoroscopy duration lead to fluoroscopy and radiation time extension which is the TRA disadvantages.[18] The average of fluoroscopy duration was more than 8 minutes in both groups in the current study, which was higher than previous studies.[19,20]

Thrombosis risk following TRA access diagnostic and interventional coronary procedures raged between 1 and 5%.[7,20] Thrombolytic therapy on ischemic hand symptoms after right atrium cannulation had a favorable effect in Geschwind et al. study.[21] In our study, this post-procedural symptom following TRA diagnostic angiography was higher than previous studies in low dose, but not in the high dose heparin group. Moreover, the incidence rate of RAO, as the most common post-procedural complication of TRA ranged from 2 to 18% event in evidence.[22-25] It seems that creation of thrombus involves in the early RAO occurrence.[26]

Consistent to our study, Moody et al.[14] reported that application of higher dose of heparin (100 IU/kg body weight) against 5000 IU in the patients who underwent coronary angiography led to less rate of RAO development. They proposed that the using higher heparin doses with average of 9000 IU inversely associated with the occurrence of RAO.[14] In addition, Spaulding et al.[27] found that RAO rates were 24 vs. 4.3% in the patients with 2000-3000 and 5000 IU of heparin use, respectively, which was similar to the incidence of post-procedural thrombosis in our study. In another study of RAO incidence was 30% in patients receiving 1000 IU of heparin during diagnostic angiography.[28] However, in the study of Manoukian et al.[29] with TRA access, the incidence of RAO had no difference between two groups with 50 IU/kg and 5000 IU heparin.

No anticoagulant therapy, increased pressure of the radial artery compression, low ratio of radial artery to sheath and smoking are some important risk factors of RAO development.[22-24]

The risk of thrombosis positively associated to female gender, hypertension, DM, current smoking, number of catheters and procedure duration while inversely had relationship with BMI. Contrary to our findings, several studies reported that RAO occlusion was associated with body weight, however, these studies had similar results about gender.[22,23,30] Gender difference might be due to less radial artery to sheath diameter ratio in females.[14] However, in line with our results Plante et al.[31] found inverse association between body weight and RAO occurrence. They believed that body weight could be as effective as heparin in RAO risk reduction.[31,32] Furthermore inconsistent to our findings Moody et al.[14] found no association between hypertension and the smoking status with RAO development.

Limitations

Our strength was examining three events including thrombosis, hematoma, and hemorrhage at the same time. In addition, determining the potential confounders consist of age, gender, number of the catheter, BMI, presence of DM and hypertension. This study had some limitations. First, study sample size was small, thus, we could not conduct subgroup analysis; Not performing this study as a multi-center RCT was our second limitation.The other limitation was using only 2 heparin doses for all patients with no consideration of their weights.

Conclusion

The low dose (2500 IU) of heparin use against standard dose (5000 IU) increased the risk of thrombosis following TRA diagnosis coronary angiography. While, it had not any influence on hematoma and hemorrhagic complications. Further studies in multi-center with more study population are required to confirm our observations.

Acknowledgments

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Conflict of Interests

Authors have no conflict of interests.

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Overweight and obesity prevalence and its predictors in a general population: A community-based study in Kerman, Iran (Kerman coronary artery diseases risk factors studies)

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Original Article

Abstract,

BACKGROUND: The aim of this study was to present age-sex standardized prevalence of overweight and obesity as well as central obesity and its associated variables in an adult population of Iran.

METHODS: Around 5900 adult individuals aged 15-75 years enrolled to the study from 2009 to 2011 applying randomized cluster household survey in Kerman, southeastern of Iran. Overweight was defined as body mass index (BMI) 25-29.9 kg/m², obesity was considered as BMI ≥ 30 kg/m², and central obesity was regarded as waist circumference (WC) > 88 cm for women and 102 cm for men.

RESULTS: The overall age-sex standardized prevalence of overweight, obesity and central obesity was 29.6% (29.5% men, 29.7% women), 13.0% (9.3% men, 16.9% women) and 14.4% (7.5% men, 21.5% women), respectively. "Overweight/obesity" increased by age, [adjusted odds ratio (AOR): 7.9 95% confidence interval (CI): 5.8, 10.7)] for 65-75 years old, 11.7 (95% CI: 9, 15.3) for 55-65 years old, 10.1 (95% CI: 7.8, 13) for 45-54 years old compared with the first age group), female gender [AOR: 1.5 (1.3, 1.8); P < 0.001], higher education (AOR > 1.5 compared with illiterate individuals; P < 0.001), and low physical activity [AOR: 1.4 (95% CI: 1.1, 1.8); P = 0.006] and decreased by smoking [AOR: 0.4 (95% CI: 0.3, 0.6); P < 0.001] and opium using [AOR: 0.5 (95% CI: 0.4, 0.7); P < 0.001]. Female gender [AOR: 4.1 (95% CI: 3.3, 5); P < 0.001], advanced (AOR > 7 for age groups ≥ 35 years old; P < 0.001) positively, while smoking [AOR: 0.6 (0.4, 0.8); P = 0.004] negatively were the most significant predictors for abnormal WC.

CONCLUSION: Our data reveal that overweight and obesity affected almost half of the adult population (43.0%), and central obesity was around 15.0%, which reflect the high prevalence of this abnormality. In addition, several demographic, social and lifestyle factors were associated with obesity. Appropriate interventions and strategies with a concentration of the general population are needed to deal with its potential subsequent consequences.

Keywords: Body Mass Index; Overweight; Obesity; Central Obesity; Risk Factors, Iran

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Introduction

Abnormal body mass index (BMI) which can be in the forms of overweight and obesity has been one of the most health challenges worldwide. Recent studies have also indicated the increasing trend of overweight and obesity in both developed and developing countries.[1,2] There is no doubt that obesity has been associated with plenty of diseases such as type 2 diabetes mellitus (DM), cardiovascular diseases, hypertension and cancers.[3]

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According to the World Health Organization (WHO) report in 2005, approximately 1.6 billion people suffered from overweight, and around 400 million people were clinically obese, although it is expected to increase these figures to 2.3 billion people and 700 million people, respectively.[4-9]

The problem of obesity involved Asian countries and the Persian Gulf countries, especially Iran, and it becomes one of the top priorities in such countries.[1,5,6] WHO reported the prevalence of obesity and overweight in the Middle East countries at 54.2% among women and 31.4% in men which annually resulted in 150000 deaths.[1] WHO in 2002 also reported that about 70.0% of all mortalities (268000 cases) in Iran resulted from chronic diseases, of which overweight and obesity were the most significant reasons. The prevalence of overweight among Iranian men and women by WHO reports were 54.0 and 70.0%, respectively, which projected to raise this prevalence to 74.0% among women, but constant among men during the period of 2005-2015.[7] Studies in Iran have also proven the projections and numerous researches have implied the upward trend of obesity prevalence[8-10] as well as metabolic syndrome[11] in all age groups of older than 15 years old.

Iran, with plentiful differences of sociocultural issues in all provinces across the country, and due to considerable variations in both lifestyle and dietary/nutritional culture in recent years has observed a varied pattern of overweight and obesity prevalence. Several studies regarding obesity and overweight have been performed across the country so far, the last and recent one is a systematic review[12] which compiled different study related to overweight and obesity in Iran. However, Kerman, Iran, lacks from a population-based study with appropriate sample size to show its condition. The current study is a part of the first phase of a population-based research named Kerman coronary artery diseases risk factors studies (KERCADRs) in Kerman to determine the prevalence of overweight, obesity, and central obesity in an adult population aged 15-75 years old.

Materials and Methods

The first phase of the study known as KERCADRs, which is a population-based cohort study, was initiated from 2009 to 2011 among 5900 adult subjects aged 15-75 years old in Kerman. Using a non-proportional to size one-stage cluster sampling household survey, the study samples were recruited. The methodology of the KERCADRs has been published elsewhere in detail.[13] The study protocol of the study was approved by the Ethics Committee of the Kerman University of Medical Sciences (Ethic code 88/110KA). An informed consent was to participate was given by all subjects' prior participation in the study.

Interview and measurements

Interviews were conducted by trained interviewers. In addition, a specialist physician evaluated the study participants for various coronary artery diseases (CAD) risk factors using a standard and structural questionnaire. The data were consisted of socio-demographic variables such as age and sex, and the highest level of achieved education [in three categories: illiterate (no attended school), primary to high school (grades 1-8), and above high school (> grade 8)], the status of the participants in terms of cigarette smoking (two categories: currently smoking cigarette/non-current or past smoker), and their status regarding opium use (three categories: non-current or past daily user/occasional as using for recreational purposes/and currently consuming opium). The level of depression and anxiety was assessed using Beck questionnaire. Global Physical Activity Questionnaire (GPAQ) and Metabolic Equivalents (METs) were used to evaluate the level of physical activity in the present study. Hence, the total metabolic equivalent time (per minute) was computed for the status of the activity in work, transport and recreation. Therefore, it was categorized into three levels of low, moderate and high levels.[14] Likewise, the more detailed explanations of the selected variables utilized in the current study have been already published.[13]

Definition of overweight and obesity

In the process of interviewing and conducting clinical examination, three anthropometric measurements of height, weight, and waist circumference (WC) were also gauged by a standard method. Using a tape measure, through measuring of waist diameter of the level of the midpoint between iliac crest and lower border of tenth rib, WC was obtained. WC more than 88 cm for women and 102 cm for men were considered as an inappropriate measurement. BMI was calculated by dividing weight in kg to height in meter squared (kg/m^2), which was according to the WHO standard recommended method.[15] Based on the WHO definition, BMI was classified into three categories of normal (BMI 18.5-24.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2), and obese (BMI $\geq$ 30 kg/m^2).[16]

Data management and all statistical analyses

were conducted using STATA (version 12, StataCorp. 2011 College Station, TX: Stata Corp LP.). Survey data analysis package was used for the analysis of the data collected from this study. Then, census statistics of Kerman population in 2006 was utilized for age and sex direct standardizations.[17] We reported weighted prevalence[18] for overweight, obesity and central obesity. Data were reported as relative frequencies along with 95% confidence interval (CI). A univariate and multiple logistic regression models were performed to determine the potential predictors of overweight and obesity, and central obesity and then, crude and adjusted odds ratio (AOR) were presented. The prevalence of co-morbidities including type 2 DM, hypertension, hypercholesterolemia, hypertriglyceridemia, levels of depression and anxiety were also reported. $P < 0.050$ was considered as statistically significant.

Results

Overweight, obesity and central obesity

In total, the age- and sex-standardized the prevalence of overweight and obesity was 29.6% (men 29.5% vs. women 29.7%; $P < 0.001$) and 13.0% (men 9.3% vs. women 16.9%; $P < 0.001$), respectively, whereas the prevalence of central obesity was 14.4% (men 7.5% vs. 21.5%; $P < 0.001$) (Table 1). Overall, a mean BMI was 25.8 kg/m^2 (men 24.8 vs. women 26.7 kg/m^2) and overall mean WC was 85.5 cm (men 87.4 vs. women 83.4 cm) (Table 2).

The overweight prevalence constantly increased from 14.9% in young subjects (aged 15-24 years) to its highest level at 43.4% among group of 55-64 years old. Obesity among the first age group was 5.6% and significantly increased by advanced age (24.0% for 45-54, 23.0% for 55-64 and 17.6% for 65-75 years old; $P < 0.001$). We also found that there was a significant increase in the prevalence of central obesity by advanced age; from 3.6% among subjects aged 15-24 years to 31.9 and 30.9% among elderly adults aged 55-64 and 65-74 years old ($P < 0.001$), respectively (Table 1). Mean BMI from 22 kg/m^2 among 15-24 years old reached to its maximum at 27.3 among 45-54 years old and decreased to 25.9 among the highest group of age. Mean of WC for the first age group was 73.7 cm and reached to 90.7 cm among 55-64 years old (Table 2).

Around 40.0% of people in the lowest level of education had overweight, which went down to 28.1% among people in the moderate level of education (primary and high school), while it was vice versa for obesity prevalence; 5.1% for illiterate people and 13.9% for the second category of education. The prevalence of central obesity ranged from 11.8 to 14.8% in different education groups. Cigarette smoker had a lower prevalence of overweight while slightly higher prevalence of obesity. Central obesity was almost similar among smokers (15.4%) and non-smokers (14.9%). In regard to those who were addicted to opium, in comparison with occasional users, people with no using and also dependent users had more prevalence of overweight (18.0 vs. 30.2% and 26.4%) and obesity (9.1 vs. 13.5% and 14.4%). In terms of central obesity, dependent users had a higher prevalence. Overweight was observed among 26.5% of depressed people and 29.2% of those with anxiety signs, whereas it was 12.4 and 13.2% for obesity status and 14.9 and 14.7% for the status of central obesity. People with higher physical activity had lower overweight, obesity and central obesity (Table 1).

Predictors of abnormal BMI and WC (Table 3)

Multiple logistic regression analysis showed that the odds of abnormal BMI (both overweight and obesity) significantly increased in women [AOR 1.5 (95% CI: 1.3, 1.8)], advanced age [OR ranged from 3.2 (95% CI: 2.5, 4.1) to 11.7 (95% CI: 9, 15.3) vs. 1 for 15-24 years old as reference group], higher education level [AOR 1.6 (95% CI: 1.3, 2) for the second level and 1.8 (95% CI: 1.4, 2.3) for the third level) and low physical activity (AOR 1.4 (95% CI: 1.1, 1.8)], conversely decreased significantly among cigarette smokers [AOR 0.4 (95% CI: 0.3, 0.6)] and dependent opium users [AOR 0.5 (95% CI: 0.4, 0.7)]. These analysis for central obesity revealed that odds of abnormal WC significantly increased in women gender [AOR 4.1 (95% CI: 3.3, 5)], advanced age groups [AOR ranged 3.7 (95% CI: 2.3, 6) to 15.7 (95% CI: 9.9, 24.7) vs. the first age group], anxious people [AOR 1.2 (95% CI: 1, 1.5)], while significantly decreased by the status of cigarette smoking [AOR 0.6 (95% CI: 0.4, 0.8)].

Co-morbidities (Table 4)

On the whole, anxiety (75.5% with overweight and 77.2% with obesity) was the most prevalent co-morbidities in the total society, but the lowest one was hypertriglyceridemia (18.9% with overweight and 24.2% with obesity). The range of prevalence of other co-morbidities including hypertension, hypercholesterolemia, and depression with overweight was 30-37%, and for obesity ranged 19-39%. Similar prevalence of co-morbidities with inappropriate WC ranged 28.3 for hypertriglyceridemia to 78.0% for anxiety.

Table 1. The standardized prevalence of obesity (body mass index) and central obesity (waist circumference), community-based cohort study (KERCADR-1st Round, n = 5895) in Kerman

Subgroups	BMI			P	Normal WC	Inappropriate WC	P
	Normal	Overweight	Obese				
Overall	57.4 (55.7, 59.1)	29.6 (28.1, 31.1)	13 (12.0, 14.1)		85.6 (84.6, 86.6)	14.4 (13.4, 15.4)	
Sex							
Men	61.2 (59.9, 62.5)	29.5 (28.3, 30.7)	9.3 (8.6, 10.1)	< 0.001	92.5 (91.8, 93.1)	7.5 (6.9, 8.2)	< 0.001
Women	53.5 (52.4, 54.5)	29.7 (28.7, 30.6)	16.9 (16.1, 17.6)		78.5 (77.7, 79.2)	21.5 (20.8, 22.3)	
Age groups (year)							
15-24	79.4 (78.2, 80.6)	14.9 (13.9, 16.0)	5.6 (5.0, 6.4)	< 0.001	96.4 (95.8, 96.9)	3.6 (3.1, 4.2)	< 0.001
25-34	56.6 (55.8, 57.5)	31.8 (31.1, 32.6)	11.5 (11.0, 12.1)		88.1 (87.5, 88.7)	11.9 (11.3, 12.5)	
35-44	37.8 (37.2, 38.3)	43.5 (42.9, 44.1)	18.7 (18.2, 19.2)		79.4 (79.0, 79.9)	20.6 (20.1, 21.0)	
45-54	35.9 (35.5, 36.3)	40.1 (39.7, 40.5)	24 (23.7, 24.3)		70.4 (70.0, 70.7)	29.6 (29.3, 30.0)	
55-64	33.7 (33.5, 33.9)	43.4 (43.2, 43.6)	23 (22.8, 23.1)		68.1 (67.9, 68.2)	31.9 (31.8, 32.1)	
65-75	42.6 (42.4, 42.7)	39.8 (39.6, 40.0)	17.6 (17.5, 17.8)		69.1 (69.0, 69.3)	30.9 (30.7, 31.0)	
Education							
Illiterate	54.6 (44.0, 64.8)	40.2 (30.2, 51.2)	5.1 (3.8, 6.9)	< 0.001	88.2 (79.7, 93.4)	11.8 (6.6, 20.3)	< 0.001
Primary to high school	58.0 (56.1, 59.9)	28.1 (26.4, 29.9)	13.9 (12.7, 15.3)		85.2 (83.9, 86.3)	14.8 (13.7, 16.1)	
Above high school	51.7 (48.3, 55.2)	36.5 (33.1, 39.9)	11.8 (9.8, 14.1)		86.1 (83.9, 88.1)	13.9 (11.9, 16.1)	
Current cigarette smoker							
No	55.8 (54.0, 57.5)	31.0 (29.4, 32.7)	13.3 (12.2, 14.4)	0.058	85.1 (84.0, 86.2)	14.9 (13.8, 16.0)	< 0.001
Yes	63.6 (55.9, 70.7)	19.5 (13.6, 27.0)	16.9 (10.3, 26.5)		84.6 (76.8, 90.1)	15.4 (9.9, 23.2)	
Opium addiction							
No	56.3 (54.5, 58.1)	30.2 (28.6, 31.9)	13.5 (12.3, 14.7)	0.029	85.3 (84.2, 86.4)	14.7 (13.6, 15.8)	0.590
Occasional user	72.9 (68.4, 77.0)	18.0 (14.9, 21.6)	9.1 (6.3, 12.8)		87.1 (83.1, 90.2)	12.9 (9.8, 16.9)	
Depended user	59.2 (50.8, 67.1)	26.4 (19.9, 34.2)	14.4 (8.9, 22.3)		82.8 (74.5, 88.8)	17.2 (11.2, 25.5)	
Depression							
No	55.9 (53.8, 57.9)	30.9 (29.1, 32.9)	13.1 (11.9, 14.5)	0.064	85.8 (84.6, 87.0)	14.2 (13.0, 15.4)	< 0.001
Yes	61.1 (58.2, 64.0)	26.5 (24.0, 29.2)	12.4 (10.6, 14.4)		85.1 (83.1, 86.8)	14.9 (13.2, 16.9)	
Anxiety							
No	56.3 (52.6, 60.0)	31.3 (28.0, 34.8)	12.4 (10.2, 15.0)	0.180	86.2 (83.5, 88.5)	13.8 (11.5, 16.5)	0.001
Yes	57.7 (55.7, 59.6)	29.2 (27.4, 30.9)	13.2 (12.0, 14.5)		85.3 (84.1, 86.4)	14.7 (13.6, 15.9)	
Physical activity							
Low	53.9 (51.1, 56.8)	31.0 (28.5, 33.7)	15.0 (13.2, 17.1)	< 0.001	84.0 (82.3, 85.6)	16.0 (14.4, 17.7)	< 0.001
Moderate	58.3 (55.8, 60.8)	30.0 (27.8, 32.4)	11.6 (10.2, 13.2)		86.7 (85.3, 87.9)	13.3 (12.1, 14.7)	
High	62.2 (56.9, 67.3)	26.5 (22.2, 31.3)	11.2 (8.0, 15.5)		88.8 (84.9, 91.7)	11.2 (8.3, 15.1)	

Numbers are reported as % and [95% CI (confidence interval)]; Normal: BMI < 25, Overweight: 25 ≤ BMI < 30, and Obese: BMI ≥ 30. Central obesity was defined as > 88 cm for women and > 102 cm for men. KERCADR: Kerman coronary artery diseases risk factors; BMI: Body mass index; WC: Waist circumference

Table 2. The mean body mass index and waist circumference according to sex and age groups, community-based cohort study (KERCADR-1st Round, n = 5895) in Kerman

Subgroups	Mean BMI	Mean WC
Overall	25.8 (25.7, 26.0)	85.5 (85.1, 85.9)
Sex		
Men	24.8 (24.6, 25.0)	87.4 (86.8, 87.9)
Women	26.7 (26.5, 26.9)	83.9 (83.4, 84.4)
Age groups (year)		
15-24	22.0 (21.6, 22.4)	73.7 (72.8, 74.6)
25-34	24.7 (24.3, 25.0)	81.0 (80.1, 82.0)
35-44	26.6 (26.3, 27.0)	85.7 (84.9, 86.5)
45-54	27.3 (27.0, 27.6)	88.5 (87.7, 89.2)
55-64	26.9 (26.6, 27.2)	90.7 (89.9, 91.5)
65-75	25.9 (25.5, 26.3)	89.9 (88.8, 91.0)

BMI: Body mass index; WC: Waist circumference; KERCADR: Kerman coronary artery diseases risk factors

Table 3. Crude and adjusted odds ratio for different associated factors of obesity and central obesity, community-based cohort study (KERCADR-1st Round, n = 5895) in Kerman

Subgroups	Overweight and obesity		Adjusted P	Central obesity		Adjusted P
	Crude OR	AOR		Crude OR	AOR	
Sex						
Men	1	-		1	-	
Women	1.9 (1.7, 2.1)	1.5 (1.3, 1.8)	< 0.001	4.6 (3.8, 5.4)	4.1 (3.3, 5.0)	< 0.001
Age groups (year)						
15-24	1	-		1	-	
25-34	3.0 (2.3, 3.8)	3.2 (2.5, 4.1)	< 0.001	3.6 (2.3, 5.7)	3.7 (2.3, 6.0)	< 0.001
35-44	6.9 (5.4, 8.8)	7.9 (6.1, 10.2)	< 0.001	7.6 (4.9, 11.8)	7.6 (4.8, 12.0)	< 0.001
45-54	7.7 (6.0, 9.8)	10.1 (7.8, 13)	< 0.001	12.8 (8.3, 19.7)	13.9 (8.9, 21.7)	< 0.001
55-64	7.8 (6.1, 10.1)	11.7 (9.0, 15.3)	< 0.001	12.7 (8.2, 19.6)	15.7 (9.9, 24.7)	< 0.001
65-75	5.1 (3.8, 6.7)	7.9 (5.8, 10.7)	< 0.001	10.8 (6.8, 17.1)	14.4 (8.8, 23.5)	< 0.001
Education						
Illiterate	1	-		1	-	
Primary to high school	1 (0.9, 1.2)	1.6 (1.3, 2.0)	< 0.001	0.5 (0.4, 0.6)	1.0 (0.8, 1.3)	0.990
Above high school	1 (0.8, 1.2)	1.8 (1.4, 2.3)	< 0.001	0.4 (0.3, 0.5)	1.0 (0.7, 1.4)	0.980
Current cigarette smoker						
No	1	-		1	-	
Yes	0.4 (0.4, 0.5)	0.4 (0.3, 0.6)	< 0.001	0.3 (0.2, 0.4)	0.6 (0.4, 0.8)	0.004
Opium addiction						
No	1	-		1	-	
Occasional user	0.9 (0.7, 1.2)	0.9 (0.7, 1.2)	0.390	0.7 (0.5, 0.9)	1.0 (0.7, 1.4)	0.880
Depended user	0.5 (0.4, 0.6)	0.5 (0.4, 0.7)	< 0.001	0.6 (0.4, 0.8)	0.7 (0.5, 1.0)	0.058
Depression						
No	1	-		1	-	
Yes	1.1 (0.9, 1.2)	0.9 (0.8, 1.1)	0.290	1.7 (1.4, 1.9)	1.0 (0.9, 1.3)	0.560
Anxiety						
No	1	-		1	-	
Yes	1.1 (0.9, 1.2)	1.0 (0.9, 1.2)	0.630	1.7 (1.4, 2.0)	1.2 (1.0, 1.5)	0.091
Physical activity						
High	1	-		1	-	
Moderate	1.8 (1.4, 2.2)	1.1 (0.9, 1.5)	0.270	2.5 (1.8, 3.4)	1.2 (0.8, 1.7)	0.420
Low	2 (1.6, 2.5)	1.4 (1.1, 1.8)	0.006	2.8 (2.0, 3.9)	1.4 (1.01, 2.1)	0.073

OR: Odds ratio; AOR: Adjusted odds ratio; KERCADR: Kerman coronary artery diseases risk factors
Numbers are reported as OR and [95% CI (confidence interval)]

Sex, age, physical inactivity on obesity

Overweight and obesity among male subjects were slightly higher before the age of 25 years, but it became similar in the age group of 25-29 for both sexes. From this age point, the differences between males and females became more evident so that the prevalence of obesity among women grew higher than men. The prevalence trend was constantly upward in both sexes until the age of 59 years. The trend decreased in both sexes after thus age, while it was still more prevalent among women. However, the pattern of physical inactivity prevalence was different, because the prevalence among females was higher in the first age groups; afterward it became similar with a stable trend, although it was partially greater among men. After the age of 59 years, by decreasing trend of overweight and obesity in both sexes, the prevalence of physical inactivity among females increased and among males decreased (Figure 1).

The prevalence of central obesity among females was remarkably higher in all age groups. There was an increasing pattern of central obesity prevalence among females and it started to become rising from the age group of 25 years old (around 15.0%) and with an upward trend reached to its highest prevalence in the last age group; 70-74 years old (around 60.0%), but there was a stabilized trend for male subjects ranged from 3.2 to 15.4%. while the prevalence of physical inactivity from the first age groups by 49 years old was greater than central obesity prevalence. Since 49 years old, the prevalence of central obesity and physical inactivity with a similar trend simultaneously increased (Figure 2).

Table 4. The prevalence of different co-morbidities with obesity and central obesity, community-based cohort study (KERCADR-1st Round, n = 5895) in Kerman

Co-morbidities	BMI			Normal WC*	Inappropriate WC
	Normal	Overweight	Obese		
DM	7.0 (6.0, 8.2)	10.2 (9.0, 11.7)	11.6 (9.4, 14.1)	7.7 (7.0, 8.6)	12.8 (10.0, 16.3)
BP	22.6 (19.9, 25.6)	37.4 (31.6, 43.6)	19.7 (18.5, 20.9)	16.5 (15.4, 17.7)	40.9 (32.8, 49.6)
Hypercholesterolemia	23.9 (22.1, 25.8)	37.2 (33.7, 40.8)	39.4 (33.3, 46.0)	28.1 (26.5, 29.6)	33.8 (28.4, 39.7)
Hypertriglyceridemia	9.4 (8.1, 10.8)	18.9 (16.3, 21.7)	24.2 (19.0, 30.2)	12.5 (11.4, 13.6)	28.3 (20.8, 37.2)
Depression	36.2 (33.9, 38.6)	30.5 (27.1, 34.0)	32.2 (26.3, 38.7)	34.3 (32.5, 36.3)	35.6 (27.3, 44.8)
Anxiety	77.4 (75.3, 79.4)	75.5 (71.8, 78.9)	77.2 (70.8, 82.6)	76.8 (75.1, 78.5)	78.0 (70.6, 83.9)

Numbers are reported as % and [95% CI (confidence interval)], Normal: BMI < 25 kg/m^2, Overweight: BMI 25-29.9 kg/m^2, Obese: BMI ≥ 30 kg/m^2. *Normal WC: WC < 88 cm for women and 102 cm for men; Inappropriate WC: WC > 88 cm for women and 102 cm for men.

BMI: Body mass index; WC: Waist circumference; DM: Diabetes mellitus; BP: Blood pressure; KERCADR: Kerman coronary artery diseases risk factors

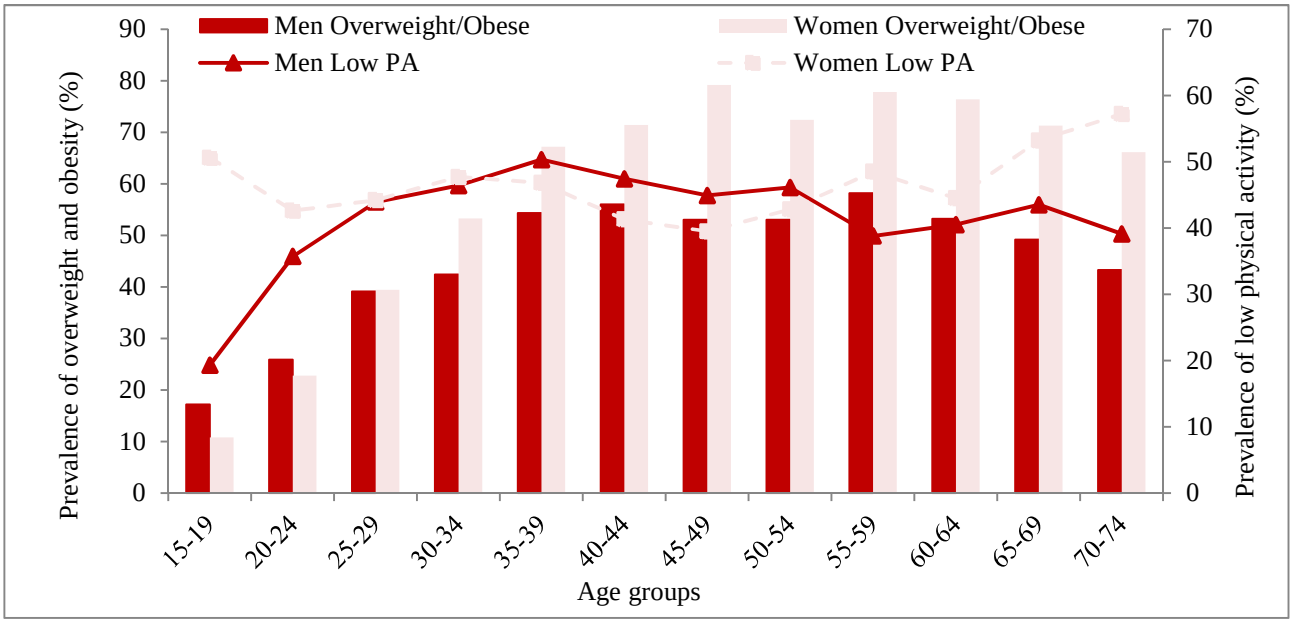

Figure 1. Prevalence of obesity (body mass index) and low physical activity by age group and sex in Kerman, 2009-2011 community-based cohort study [KERCADR (Kerman coronary artery diseases risk factors)-1st Round, n = 5895]

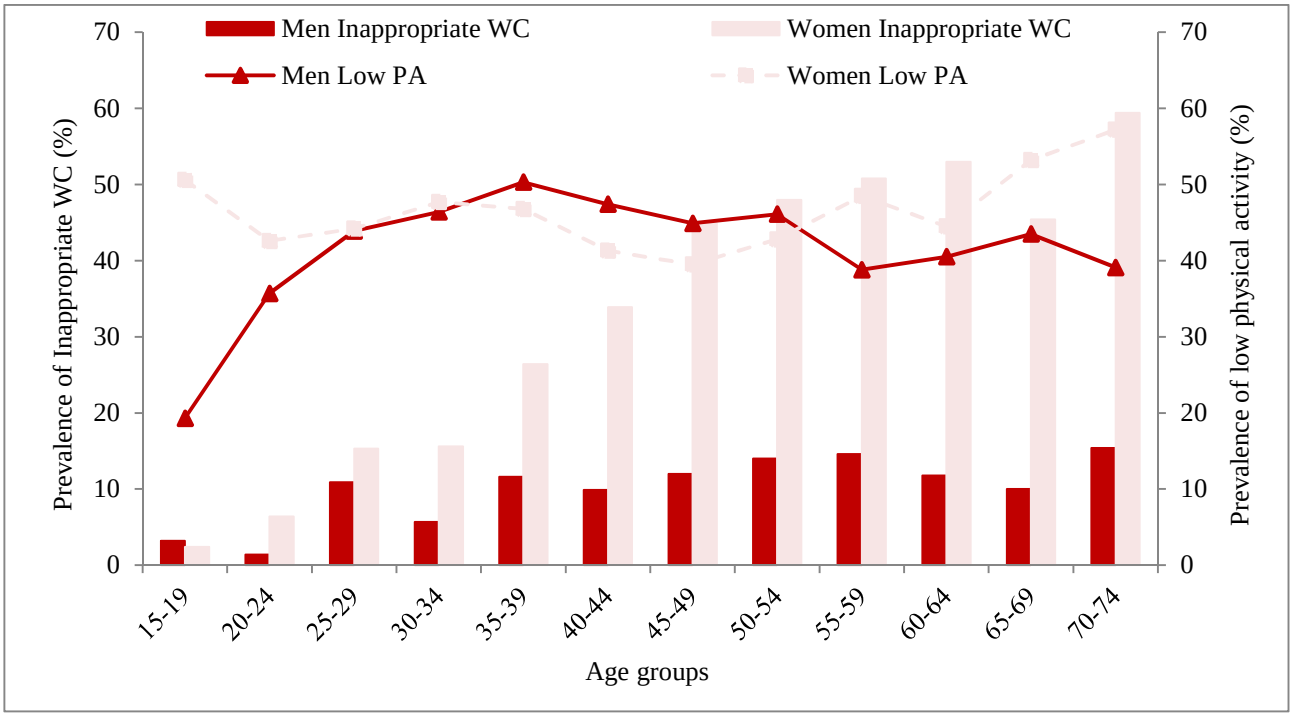

Figure 2. Prevalence of central obesity (waist circumference) and low physical activity by age group and sex in Kerman, 2009-2011 community-based cohort study [KERCADR (Kerman coronary artery diseases risk factors)-1st Round, n = 5895]
WC: Waist circumference

Discussion

Our data showed that prevalence of overweight and obesity was 43.0%, and central obesity was around 15.0%. In addition, several demographic, social and lifestyle factors including gender, age, anxiety, physical inactivity and cigarette smoking and opium use were associated positively or negatively with obesity. In a recent systematic review, it has been shown that prevalence of overweight in sub-national studies among adults ranged 12.8-76.4% and obesity ranged 2.4-35.4%, while for the national studies it was from 27.0 to 38.5% for overweight and from 12.6 to 25.9% for obesity prevalence.[12]

We could show a notable association between the two baseline variables of female gender and advanced age and occurring overweight and obesity. The authors believe that the main reasons for a higher rate of obesity in these baseline subgroups include improper lifestyle such as unhealthy dietary habit, and tend to inactivity style. Interestingly, the patterning of obesity worldwide is gendered and has been showed to be greater in women compared with men.[19] As of 2008 the WHO estimates that at least 500 million adults (< 10%) are obese, with higher rates among women than men.[20] Most of the studies in Iran have shown the greater prevalence of overweight and obesity among women,[21-23] which physical inactivity can be introduced as one the main reason of this discrepancy between men and women.[24]

The rate of obesity also increases with age at least up to 50 or 60 years old.[20] According to a report published, 26.0% of women and 19.0% of men were classed as inactive and 46.0% of men and 37.0% of women reported walking of at least moderate intensity for 10 minutes or more on at least 1 day in the last 4 weeks. In this regard and to link dietary habit to the cause of increasing trend of obesity, it can be noted that different contextual factors drive gender differences in food consumption in our society so men often report consuming healthier foods, while women consume more fat-rich foods and fast foods than men.[25]

Similar reports to our results have been also in previous studies on Iranian population. In a study by Janghorbani et al.,[26] the age-adjusted prevalence of overweight or obesity was 42.8% in men and 57.0% in women; 11.1% of men and 25.2% of women were obese while 6.3% of men and 5.2% of women were underweight. In this regard, advanced age, low physical activity, low educational attainment, marriage, and residence in urban areas were strongly associated with obesity. In another

study by Bahrami et al.[27] The age-adjusted prevalence rates of overweight and obesity in this Iranian population were 62.2 and 28.0%, respectively. Both overweight and obesity were a more common in women than men. Ghadiri-Anari et al.[28] also found that in both genders, the rate of obesity and overweight raised by increasing of age up to 50 years old. Overall, the prevalence of obesity was higher in women compared with men in all ages. In total, an unhealthy diet and sedentary lifestyles are concerns for all adults especially for women.

Our study could clearly show a direct link between obesity and lower educational level. In this regard, those men and women with less than a college degree were more likely to be obese than those with a lower educational degree. It may be well explained by this fact that those with higher socioeconomic level have more appropriate lifestyle regarding daily activities, and dietary behaviors as well as less tending to smoking and drinking behaviors. In fact, higher educational level keys to better health. Cutler found that those with more years of schooling are less likely to smoke, drink a lot, to be overweight or obese or to use illegal drugs. Similarly, the better educated are more likely to exercise.[29] A review by Grossman and Kaestner concluded that years of formal schooling is the most important correlate of good health.[30]

A cross-sectional estimate from a study of twins conducted by Webbink et al.[31] also confirms the negative relationship between education and the probability of being overweight. Similar observations could be found in Iranian reports. In a study by Veghari et al.,[32] the prevalence of obesity was seen in 24.0% of subjects and significantly was seen in 3.1 and 14.1% of uneducated people more than in 1-9 years schooling and in high school or college-educated people, respectively with a significant difference. After adjusted for location area, gender, age, and economic stats, the risk of obesity was 2.044 in uneducated people compared to high school or college-educated subjects. Moreover, in another study carried out by Veghari et al.[33] an inverse association between educational level and prevalence of central obesity was revealed; 50.1% for uneducated people, 35.1% for individuals with 1-9 years of schooling and 19.0% for those educated higher than high school. In addition, compared with educated participants, OR of having an abnormal central obesity among uneducated people was 4.214 and among individuals with 1-9 years of schooling was 2.2. Overall, education can play a role in tackling overweight and obesity due to its strong link to better lifestyle and nutritional habits.

Similar to previous reports, both overweight and obesity are less frequent in smokers than in non-smokers. Smoking has a significant effect on an individual's weight. Those who quit smoking gain an average of 4.4 kg for men and 5.0 kg for women over 10 years.[34] Nicotine acutely increases energy expenditure[35] and could reduce appetite, which likely explains why smokers tend to have lower body weight than do nonsmokers and why smoking cessation is frequently followed by weight gain.[35,36] Similarly, in our survey, opium use led to decreasing body weight. In some experimental studies, the use of opioids such as morphine lower food intake.[37] This association can be mediated by activation of some opioid receptors affecting overeating.[38]

Overall, overweight and obesity are major public problems in Iran with a significant heterogeneity between the genders (more in women than in men), age subgroups (more in the elderly than in the younger), education levels (more in lower education levels), and smoking habit (less in smokers and opium users). In this regard, the effect of each of these baseline parameters can be mediated by poorer lifestyle and nutritional behaviors.

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Conflict of Interests

Authors have no conflict of interests.

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In-hospital and six-month outcomes of elderly patients undergoing primary percutaneous coronary intervention for acute ST-elevation myocardial infarction

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Original Article

Abstract

BACKGROUND: Elderly patients constitute a rapidly growing proportion of the population, and hence the increasing rises in the number of patients with ST-segment-elevation myocardial infarction (STEMI). Primary percutaneous coronary intervention (PCI), which is now established as the preferred reperfusion strategy in STEMI patients, has been inadequately investigated in this high-risk group. The aim of the present study was to investigate the in-hospital and 6-month outcomes of primary PCI in elderly patients (≥ 75 years) with STEMI.

METHODS: A total of 100 elderly patients with STEMI including those with cardiogenic shock were included. Primary PCI procedures were performed in a tertiary referral center between 2009 and 2014. In-hospital and 6-month outcomes of patients were recorded and analyzed.

RESULTS: The average age of the patients was 79.6 ± 3.8 years (range = 75-90 years) and 27.0% were women. Cardiovascular risk factors and prior events were common. Nearly, half of the patients had three-vessel disease and the left anterior descending artery (LAD) was the most common infarct-related artery. The presence of cardiogenic shock but not the other variables was associated with less anatomic and procedural success (P < 0.001). It was also the major independent predictors of 6-month mortality in the patients aged ≥ 75 years, [hazard ratio (HR) = 8.02; 95% confidence interval (CI): 1.75-25.97, P < 0.001]. In-hospital mortality was 2.4% in the patients without and 83.0% in those with cardiogenic shock.

CONCLUSION: Primary PCI in aged patients could be associated with low complication rates and improved survival if performed in high-volume centers with experienced operators. Considering the very high rate of mortality in patients with cardiogenic shock, there should be measures to treat these patients before the onset of hemodynamic instability.

Keywords: Cardiogenic Shock; Elderly; Percutaneous Coronary Intervention

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Introduction

Population growth and advanced health care have conferred an increase in life expectancy among elderly patients. It is predicted that the proportion of octogenarians will probably have tripled by the year 2050.[1] Coronary artery diseases (CADs) and its associated acute events such as ST-segment-elevation myocardial infarction (STEMI) are very frequent in the aged population and cause significant morbidity and mortality. Primary percutaneous coronary intervention (PCI) is currently the method of choice and the best reperfusion strategy for patients presenting with STEMI in that it has reduced the rates of cardiac mortality and re-infarction over the last decades.[2,3] Even though elderly patients constitute a major high-risk population of patients with STEMI who might benefit from more invasive therapies, they are frequently excluded from clinical trials owing to higher morbidity and mortality associated with the primary PCI.[4] Worse outcome is influenced not only by the extensive CAD but also by more complex comorbidities.[5] In addition, elderly patients are more likely to suffer from complications following revascularization procedures.[6] The existing literature contains no research on the

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outcome of primary PCI in elderly Iranian patients. We, therefore, sought to evaluate the in-hospital and mid-term outcomes of primary PCI in patients aged ≥ 75 years old, who presented with acute STEMI in a high-volume tertiary center.

Materials and Methods

A retrospective evaluation of the primary PCI database was performed between April 2009 and May 2014. The local Ethics Committee of Rajaie Cardiovascular, Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran, approved the trial design.

A total of 656 primary PCI-treated patients were initially evaluated. The inclusion criteria were comprised age > 75 years and chest pain accompanied by ST-segment-elevation in at least two contagious leads presenting within the first 12 hours after the symptom onset or after 12 hours in the case of persistent chest pain. Notably, patients with hemodynamic instability or cardiogenic shock at the time of presentation or during the hospital course were not excluded from the study. Cardiogenic shock patients were considered eligible if they presented within 36 hours after the initiation of chest pain and no more than 18 hours after the development of shock. Patients with inability to receive dual antiplatelet therapy, the presence of the left main involvement, severe CAD or mechanical complications of MI requiring surgical intervention and extreme comorbidities precluding primary PCI as a therapeutic option were excluded. Finally, a total of 100 consecutive elderly patients were selected and analyzed.

The study patients received the same routine preparation protocol for coronary angiography and primary PCI, including 325 mg of the loading dose of aspirin and 300-600 mg of the loading dose of clopidogrel before the procedure. Primary PCI procedures were performed via routine standards by an experienced team. The intention to treat was for culprit lesions, and multivessel PCI was performed in cardiogenic shock patients who were unresponsive to the culprit PCI. The in-hospital and 6-month clinical outcomes of the patients were recorded using the hospital data registry, patients' files, and telephone calls. Anatomical success was defined as the attainment of a residual diameter stenosis < 20% and normal epicardial flow based on thrombolysis in myocardial infarction grading (TIMI-3 flow). Procedural success was considered as anatomical success without the occurrence of major complications (i.e. death, MI, or urgent revascularization) during the hospital course.

Statistical analysis was performed using SPSS software (version 16, SPSS Inc., Chicago, IL, USA). The results are presented as means ± standard deviation (SD) for the continuous variables and as percentages for the categorical data. The chi-square test was used to compare the numerical variables. 6-month cumulative survival rates were assessed with the Kaplan-Meier curve. Cox regression model was implemented to determinate the independent predictors of 6-month cumulative mortality and clinical success. A P <0.050 was considered a significant.

Results

About 100 primary PCI patients over the age of 75 were included. The average age of the patients was 79.6 ± 3.8 years (range = 75-90 years) and 27% were women. The baseline clinical characteristics of the study patients are summarized in table 1. Hypertension was the most common risk factor (53%), and 74% of the cases had, at least, one of the four known risk factors for atherosclerosis. 18% of the patients presented with or developed cardiogenic shock on admission or during the hospital course. Previous cardiovascular events and interventions were also fairly common. The procedural angiographic and interventional characteristics of the patients are depicted in table 2.

Table 1. Baseline characteristics of the patients

100 patients	Prevalence
Age (year) (mean ± SD)	79.60 ± 3.86
Sex (%)	
Male	73
Female	27
Risk factors (%)	
Smoking	18
Hypertension	53
Dyslipidemia	30
Diabetes	37
Past medical history (%)	
MI	31
PCI	13
CABG	4
CVA	6
CKD	8
Cardiogenic shock (%)	18

MI: Myocardial infarction; PCI: Percutaneous coronary intervention; CABG: Coronary artery bypass grafting; CVA: Cerebrovascular accident; CKD: Chronic kidney disease; SD: Standard deviation

Table 2. Angiographic and procedural data

Variables	Prevalence (%)
Disease extension	
Single-vessel disease	25
Two-vessel disease	28
Three-vessel disease	47
Infarct-related artery	
LAD	50
RCA	33
LCX	14
Venous graft	3
Post-procedural TIMI flow	
III	73
II	17
0-I	10

LAD: Left anterior descending artery; RCA: Right coronary artery; LCX: Left circumflex artery; TIMI flow: Thrombolysis in myocardial infarction

The involvement of more than one coronary vessel was common, and 47% of the cases were diagnosed to have three-vessel disease. The left anterior descending artery (LAD) was the most common infarct-related artery, followed by the right coronary artery (RCA) (50 and 33%, respectively). Anatomical success was achieved in 73% of the patients. The no-reflow phenomenon (TIMI-0 and TIMI-1) occurred in 10% of the study population and the slow flow (TIMI-2) in 17%. Age, presence of risk factors and baseline morbidities were not associated with the occurrence of the no-reflow/slow flow phenomenon. This was also the case for the extension of the vessel involvement and the culprit artery (Table 3). However, there was a meaningful association between the anatomical success rate and the presence of cardiogenic shock ($P < 0.001$). Cardiogenic shock was also the sole parameter significantly associated with less procedural success. Neither the number of the diseased vessels nor a specific culprit artery had a significant influence on the procedural success rates. The mean duration of hospital stay was 6.3 ± 3.0 days in those discharged alive (range = 2-17 days).

The rate of in-hospital mortality was 17%: 2 (2.4%) cases in the patients without cardiogenic shock and 15 (83%) cases in those with cardiogenic shock. The presence of cardiogenic shock was significantly associated with the occurrence of death during hospitalization ($P < 0.001$). The probability of being free from the occurrence of death was investigated via Kaplan-Meier method which presented in figure 1. The in-hospital and 6-month adverse events are shown in table 4. In a multiple cox regression model, cardiogenic shock [hazard ratio (HR): 8.02, 95% confidence interval (CI): 1.75-25.97; $P < 0.001$], anatomical success rate (HR: 6.7, 95% CI: 1.16-22.7; $P < 0.001$), and post-procedural stroke (HR: 3.01, 95% CI: 1.01-7.6; $P = 0.026$) were identified as the independent predictors of mortality during the follow-up.

Discussion

Elderly people are the most rapidly growing proportion of the world population, and acute MI is the leading cause of cardiac death in this group. Despite the extensive implementation of mechanical reperfusion therapy, it may be difficult to choose the best reperfusion strategy for elderly patients, who are more likely to have additional comorbidities and risk factors. Although most studies have shown the relative superiority of primary PCI over the other reperfusion strategies or no reperfusion, there are several important factors which limit the widespread use of the former in elderly patients. Elderly patients with acute MI are less often treated with reperfusion therapy than younger patients.[7] These patients frequently present late after the initiation of MI because of atypical symptoms, impaired pain perception, and delays relating to the family members and health care system. It is also worth bearing in mind that even if primary PCI is performed, it is associated with high rates of early and late complications and limited survival.[8]

Meanwhile, it has been shown that reperfusion therapy, compared with conservative therapies, has significantly reduced 30-day and 1-year mortality rates in elderly acute MI patients.[9-12] Another reason that renders arriving at a final conclusion complex is that elderly patients with acute MI are frequently excluded from randomized clinical trials.[13] By comparison with similar studies, ours showed a large proportion of male patients treated with primary PCI. The difference may be due to ethnic differences and the exclusion of the aged and perhaps more disable women from invasive strategy. The elderly patients in the present study had multiple risk factors and advanced CAD; however, primary PCI was associated with an acceptable anatomical and procedural success rates. In addition, the in-hospital mortality rate was considerably low and comparable with that of the younger patients. In those who survived the hospital course, 6-month follow-up also showed improved survival and an event-free course, underscoring once again the importance of the timely application of primary PCI in this high-risk group.

Table 3. Anatomical and procedural success rates

Variable	Anatomical success rate (%)	P	Procedural success rate (%)	P
Sex		0.880		0.780
Male	72.6		56.2	
Female	74.1		59.3	
Diabetes		0.990		0.380
Yes	73.0		51.4	
No	73.0		60.3	
Hypertension		0.880		0.190
Yes	73.6		50.9	
No	72.3		63.8	
Hyperlipidemia		0.590		0.690
Yes	76.7		60.0	
No	71.4		55.7	
Smoking		0.270		0.890
Yes	83.3		55.6	
No	70.7		57.3	
Prior CABG		0.920		0.770
Yes	75.0		50.0	
No	72.9		57.3	
Prior PCI		0.310		0.120
Yes	84.6		76.9	
No	71.3		54.0	
Prior MI		0.750		0.770
Yes	71.0		54.8	
No	73.9		58.0	
Prior CVA		0.550		0.720
Yes	83.3		50.0	
No	72.3		57.4	
CKD		0.330		0.240
Yes	87.5		37.5	
No	71.7		58.7	
Disease extension		0.950		0.760
Single-vessel disease	72.0		60.0	
Two-vessel disease	71.4		60.6	
Three-vessel disease	74.5		53.2	
Culprit artery		0.500		0.610
LAD	68.0		52.0	
RCA	78.8		57.6	
LCX	71.4		71.4	
Venous graft	100		66.7	
Cardiogenic shock		< 0.001		< 0.001
Yes	27.8		11.1	
No	82.9		67.1	

All the associations were assessed via Pearson's chi-square test. P < 0.050 considered as statistically significant.
CABG: Coronary artery bypass grafting; PCI: Percutaneous coronary intervention; MI: Myocardial infarction; CVA: Cerebrovascular accident; CKD: Chronic kidney disease; LAD: Left anterior descending artery; RCA: Right coronary artery; LCX: Left circumflex artery

The SHOCK trial (SHould we emergently revascularize Occluded Coronaries in cardiogenic shocK) found no benefit with revascularization in patients over 75 years of age complicated by cardiogenic shock; nevertheless, several large observational studies have shown the advantages of early revascularization in the elderly with cardiogenic shock.[14-17] There are also studies revealing extremely high mortality rates in patients aged > 75 years with cardiogenic shock even with the early interventional approach. In the Zeymer et al.[18] registry, 63% of the patients older than 75 years died. In our study, the cardiogenic shock was the most powerful independent risk factor for poor anatomical and procedural success and finally death following primary PCI. The high mortality rate in our elderly patients with cardiogenic shock might have additional reasons. Our hospital is a tertiary center and, as such, the majority of its patients are referred from other hospitals quite late after the initiation of chest pain or just after the occurrence of cardiogenic shock. In addition, apart from the intra-aortic balloon pump, no other supportive circulatory device was used in our patients.

Table 4. Short- and long-term adverse events

Variables	Without shock (n = 82)	With shock (n = 18)	P
Hospital stay (days)	6.6	17.3	0.001*
Major bleeding [n (%)]			
In-hospital	2 (2.4)	0 (0)	0.500
6-month	0 (0)	0 (0)	-
CVA [n (%)]			
In-hospital	0 (0)	1 (5.6)	0.480**
6-month	2 (2.5)	0 (0)	0.510**
MI [n (%)]			
In-hospital	2 (2.4)	6 (33)	0.100**
6-month	0 (0)	2 (67)	0.430**
Stent thrombosis [n (%)]			
In-hospital	2 (2.4)	0 (0)	0.500**
6-month	0 (0)	0 (0)	-
Mortality [n (%)]			
In-hospital	2 (2.4)	15 (83)	< 0.001**
6-month	0 (0)	1 (33)	0.330**

CVA: Cerebrovascular accident; MI: Myocardial infarction
*Student's t-test, **Pearson's chi-square test

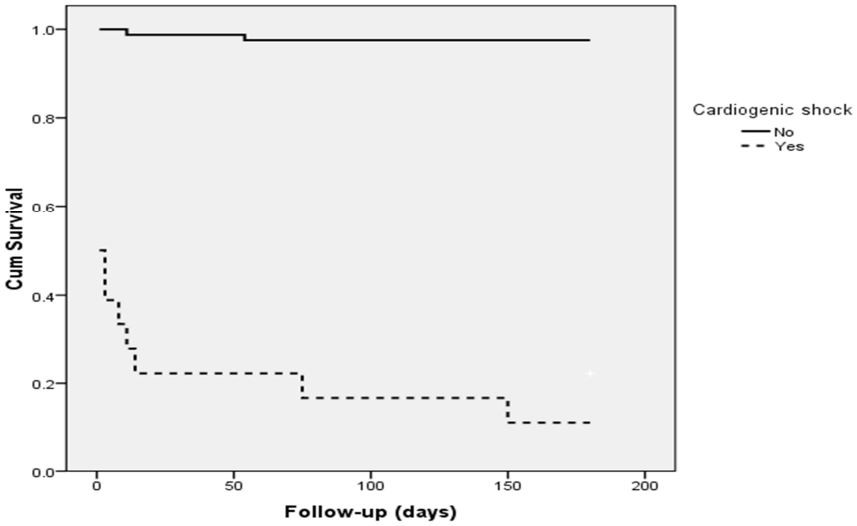

Figure 1. Kaplan-Meier estimate of cumulative in-hospital and 6-month survival rates

Limitations

First and foremost among the limitations of the present study is that it is not sufficiently powered because of the small number of the participants. Another shortcoming is that the results of this single referral Centre study may have been influenced by patient selection biases. Our treated patients probably had a high-risk profile compared with the real world presentation of patients with acute MI.

Conclusion

It is widely accepted that primary PCI in the elderly is more challenging, and future prospective studies in the elderly with STEMI are needed to evaluate the effectiveness and safety of primary PCI in this patient population.[19] Our study showed that primary PCI in aged patients could be associated with low complication rates and improved survival if performed in high-volume centers with experienced operators. Given the very high rate of

mortality in patients with cardiogenic shock, there should be measures to treat these patients before the onset of hemodynamic instability.

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Conflict of Interests

Authors have no conflict of interests.

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Effect of aqueous extract of Vernonia amygdalina on atherosclerosis in rabbits

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Original Article

Abstract

BACKGROUND: Extracts of Vernonia amygdalina (V. amygdalina) have been shown to affect the serum lipid profile of some laboratory animals in previous studies. Its impact on serum lipid profile and the histological changes in atherosclerosis has not been studied. Our aim was to determine the effects of V. amygdalina on atherosclerotic lesions induced in rabbits on high-cholesterol diet.

METHODS: 18 male rabbits were randomly divided into three groups of control, atherogenic diet, and atherogenic diet + 200 mg/kg of V. amygdalina. The rabbits were fed a normal diet (control group) or a diet supplemented by 0.5% cholesterol and 1% methionine (second and third groups, respectively) for 12 weeks. The fasting sera of all animals were collected at baseline and at the end of the 12 weeks, to determine the levels of lipid profile and the aortas underwent pathomorphological examination.

RESULTS: The two groups on the atherogenic diet had significantly increased serum total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) compared to the control group. The serum triglyceride (TG) was not statistically different in all three groups. High-density lipoprotein cholesterol (HDL-C) was significantly increased in the V. amygdalina group, compared to the control group but there was no statistically significant difference between the two groups on atherogenic diet. The two groups of rabbits that were on high-cholesterol diet (atherogenic diet group, as well as the atherogenic diet + 200 mg/kg of V. amygdalina) developed histological evidence of atherosclerosis. However, there was no histological difference between the lesions observed in these two groups.

CONCLUSION: The use of 200 mg/kg of aqueous extract of V. amygdalina in rabbits did not appear to exert a significant effect on the serum lipid profile. It also did not appear to have any beneficial effect on the development of atherosclerotic lesions.

Keywords: Vernonia; Rabbits; Atherosclerosis; Cholesterol; Alternative Medicine

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Introduction

Atherosclerosis is a major cause of mortality all over the world. It is characterized by high levels of serum lipids comprising total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) in the serum. Increased serum TC and particularly LDL-C have been implicated in the etiology of atherosclerosis. The atherosclerotic process involves the build-up of a waxy plaque on the inside of blood vessels, and it involves an ongoing inflammatory response. It can involve the entire vascular system and is characterized by plaques in the intima layer of arteries.[1,2]

High level of serum lipids is related to increased oxidative damage, which affects antioxidant status and lipoprotein levels.[3,4]

While orthodox medicine is generally accepted and preferred globally, the use of herbs and traditional medicine is often considered an equally acceptable alternative in many regions of the world. The traditional medicine is commonly used in the developing countries where the cost of orthodox medicine and access to medical care is unavailable to part of the populace. According to the World Health Organization (WHO), 80% of people in developing countries use traditional medicine, 85% of which are plant extracts.[5]

Some medicinal herbs have antioxidant effects and can also reduce the blood lipids. Some of these herbs have been shown to prevent atherosclerosis.[6] Vernonia amygdalina (V. amygdalina), is a member of the Asteraceae family. It is a shrub that grows in

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tropical Africa.[7] Leaves from this plant serve as food and culinary herb in soup in many parts of Africa. The aqueous extract of the leaves is used traditionally as treatment for anemia, nausea, diabetes, loss of appetite, dysentery, and other gastrointestinal tract problems.[8] In Nigeria, the plant is used in the control of tick and treatment of a cough, feverish condition, constipation, and hypertension.[9-11] Extracts of V. amygdalina has been shown to reduce serum LDL-C and TC.[12-14]

Some studies have reported that plants which lower serum lipid values are rich in flavonoids and tannins. These compounds play a significant role in the mobilization and metabolism of lipids. Phytochemical analysis of V. amygdalinas revealed high levels of flavonoids, saponin, tannins, and alkaloids.[15]

This study aimed to examine the effect of aqueous extract of V. amygdalina on the serum lipid profile and the histological changes in the aorta of rabbits on the atherogenic diet.

Materials and Methods

Preparation of plant extract

V. amygdalina leaves were purchased at a local market, Ibadan, Nigeria and authenticated at Department of Botany, University of Ibadan, Nigeria (Voucher number UIH-22432). The leaves were rinsed with water to remove extraneous materials. The leaves were subsequently spread to dry indoors until a constant dry weight was attained. The size was reduced via grinding it into powder with a mill. At the end of milling, 2.4 kg of ground leaves was obtained.

Aqueous extraction of the leaves was performed at Department of Pharmacy, University of Ibadan. The ground leaves were soaked in 6 liter of distilled water (using 2 glass jars containing 1.2 kg of leaves in 3 liter each) for 24 hours with 2 hourly stirring of the solution. The mixture was subsequently filtered through the first muslin bag and second using a Whatman filter paper. The extract was concentrated using a rotatory evaporator at 45 °C and then dried using a vacuum oven at 45 °C and pressure of 600 mmHg.

The resultant yield of extract was 122 g, giving a percentage yield of 5.1%. The resultant paste was stored in a glass jar in the refrigerator. It was reconstituted with distilled water, on a daily basis as required; to give a solution in which 1 ml contained 100 mg of extract. The extract was administered into the oral cavity of the rabbits with a metal gavage needle.

The dose of extract was set at 200 mg/kg per day based on the doses administered in previous studies conducted on rats which revealed beneficial effects on serum lipid profiles at this dose.[12,13]

Constitution of the atherogenic diet

Cholesterol powder was procured from AMRESCO (Ohio, USA) and methionine powder from Hard Eight Nutrition LLC (Nevada, USA). The chow was constituted by dissolving 12.5 g of cholesterol in 125 ml of groundnut oil, and mixing this with 25 g of methionine powder and 2350 g of chow. Thus, mixing 2.5 kg of chow was consumed in 2-3 days. The atherogenic diet consisted of chow supplemented with 0.5% cholesterol and 1% methionine and 5% groundnut oil by weight.[16,17]

A total of 18 male rabbits weighing 750-1200 g and aged 2-3 months were obtained. They were adapted to laboratory handling for a week and then randomly divided into three groups as follows:

- Group 1: Normal chow for 12 weeks
- Group 2: Normal chow and atherogenic diet for 12 weeks
- Group 3: Normal chow, atherogenic diet and 200 mg/kg of extract/day for 12 weeks.

The animals were housed in individual metal cages, in a well-ventilated room with natural 12-hour light/dark cycles. They were fed chow at 5.0% of the body weight (of the largest animal) per day and had free access to water. The weights of the animals at baseline and post-intervention were noted. Animals were handled in compliance with the ethical guidelines of the University of Ibadan.

At the end of 12 weeks, the animals were fasted overnight and a blood sample obtained for fasting lipid profile. Leadman reagents were used to analyze TC, TG and high-density lipoprotein cholesterol (HDL-C) using a Landwind auto-chemistry analyzer. LDL-C was calculated using the Friedewald equation.

Euthanasia was achieved under anesthesia using ketamine and xylazine followed by exsanguination. The aorta was excised from the root of the aorta, distal to the aortic valve to the bifurcation of the aorta. It was split open longitudinally, and the surface of the endothelium was examined. The presence of fatty streaks was seen on gross examination of the vessels of the animals on atherogenic diet.

These fatty streaks were more pronounced at the root of the aorta and around the ostia of the intercostals arteries. Sections of the aorta were obtained from the thoracic aorta and stained with hematoxylin-eosin stain.

Aortic histomorphometric study

The tunica intima of each section was carefully examined with an Olympus light microscope (CX41 model) for the presence of atherosclerotic lesions. The images of each slide were captured. The tunica intima and tunica media thickness were measured using computerized image analyzer (Motic Image plus Version 2.0).

The tunica intima thickness was measured from lumen to the internal elastic lamina while the tunica media thickness was measured from the internal elastic lamina to the external elastic lamina. This was used to calculate the intima-media ratio. Measurements were taken from four sections of the aorta of one rabbit each from the three groups. The average of these measurements was utilized for analysis.[18]

Results are expressed as mean ± standard deviation (SD). A statistical analysis was carried out using SPSS software (version 22, SPSS Inc., Chicago, IL, USA). Paired t-test was used to compare baseline and post-intervention weight and serum lipid profiles. Comparison across the groups of all parameters was done using analysis of variance (ANOVA) test. Bonferroni post-hoc analysis was performed on all parameters which ANOVA showed statistically significant differences (where $P < 0.050$). The level of statistical significance was set at 95% with $P < 0.050$.

Results

The summary of the serum lipid profile at baseline and post-intervention is presented in tables 1 and 2, respectively. The baseline parameters did not show a statistically significant difference across the three groups. The post-intervention parameters showed a significant difference in TC, HDL-C, and LDL-C. Table 3 shows the post-hoc Bonferroni analysis and indicates that TC and LDL-C were significantly different between the groups 1 and 2, also between the groups 1 and 3. However, these parameters were not statistically different between the groups 2 and 3.

Comparison of the weight and serum lipid profile within the experimental groups at baseline and post-intervention is shown in table 4. It revealed a significant change in the weight and TC in the three groups. It also showed that the HDL-C and LDL-C had significantly differences between the groups 2 and 3. The mean intima-media ratios in the three groups revealed 0 ± 0, 0.76 ± 0.13, and 0.63 ± 0.11, respectively. The statistical analysis revealed that the difference in the ratios of groups 2 and 3 was not statistically significant.

The hematoxylin-eosin stain of the aorta from the three experimental groups is represented in Figure 1 and reveals the presence of atherosclerotic lesions in groups 2 and 3. The lesions are characterized by several layers of foam cells and pools of extracellular lipid.

Table 1. Summary of mean weights and serum lipid profiles; and comparative ANOVA across the three groups at baseline

Variable	Group 1 (mean ± SD)	Group 2 (mean ± SD)	Group 3 (mean ± SD)	F statistic	P
Weight (g)	1000.0 ± 163.30	966.67 ± 143.76	808.33 ± 80.10	3.42	0.640
TC (mmol/l)	1.53 ± 0.77	2.03 ± 0.96	2.63 ± 1.69	0.95	0.410
TG (mmol/l)	2.00 ± 1.04	1.10 ± 0.97	1.45 ± 1.77	0.53	0.600
HDL-C (mmol/l)	0.48 ± 0.22	0.83 ± 0.60	0.70 ± 0.46	0.67	0.530
LDL-C (mmol/l)	1.18 ± 0.79	1.18 ± 0.70	1.82 ± 1.35	0.74	0.500

TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SD: Standard deviation

Table 2. Summary of mean weights and serum lipid profiles; and comparative ANOVA across the three groups post-intervention

Variable	Group 1 (mean ± SD)	Group 2 (mean ± SD)	Group 3 (mean ± SD)	F statistic	P
Weight (g)	1525.00 ± 150.00	1791.00 ± 253.80	1550.00 ± 164.32	2.96	0.870
TC (mmol/l)	3.73 ± 0.75	15.72 ± 0.27	15.68 ± 0.42	955.66	< 0.001*
TG (mmol/l)	1.06 ± 0.09	4.37 ± 3.53	1.49 ± 0.36	3.65	0.060
HDL-C (mmol/l)	0.98 ± 0.39	1.76 ± 0.44	2.31 ± 0.70	7.10	0.010*
LDL-C (mmol/l)	2.27 ± 0.79	11.97 ± 1.14	12.67 ± 0.42	213.67	< 0.001*

*Statistically significant

TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; SD: Standard deviation

Table 3. Post-hoc multiple comparison analysis of the three groups post-intervention

Variable	Multiple comparison	P
TC	Group 1 vs. Group 3	< 0.001*
	Group 1 vs. Group 2	< 0.001*
	Group 2 vs. Group 3	> 0.999
HDL-C	Group 1 vs. Group 3	0.010*
	Group 1 vs. Group 2	0.140
	Group 2 vs. Group 3	0.310
LDL-C	Group 1 vs. Group3	< 0.001*
	Group 1 vs. Group 2	< 0.001*
	Group 2 vs. Group 3	0.530

*Statistically significant
TC: Total cholesterol; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol;

Discussion

This study evaluated the effects of extracts of V. amygdalina on rabbits placed on atherogenic diet with assessments of serum lipid profiles as well as pathomorphological changes. The group exposed to V. amygdalina extract did not appear to have had a significantly different serum lipid profile as well as pathomorphological changes. This study is important as previous studies evaluating the effect of V. amygdalina had been conducted in rats, rather than rabbits, which are better suited animal models for atherosclerosis research.

At baseline, all the rabbits in the three groups did not have a statistically significant difference in mean weights, which assured that they were comparable across the groups. This was further buttressed by the mean weight gain across the groups over the course of the 12-weeks intervention, as their feeding regimen was standardized at 5-10% of the body weight of the rabbits. This feeding regimen was in keeping with the recommendations suggested feeding chow for rabbits on atherogenic diet should be restricted to prevent obesity.[19]

The post-intervention serum lipid profile results revealed a statistically significant increase in TC across all the groups (with baseline values as comparative standard). While this finding was altogether unsurprising for the groups on atherogenic diet, it was unexpected for the group on normal chow. However, a possible explanation is provided by Dontas et al.,[20] which reported age-related increase in TC of rabbits confined to cages over time, even when they are on normal chow. Thus, the observed statistically significant increase in TC for the control group of rabbits in this study may simply be an age-related finding. There was also no significant difference between the group on atherogenic diet compared with the group on both atherogenic diet and extracts of V. amygdalina. This may suggest that the extracts of the V. aymgdalina may not be protective against the increase in serum TC. The observed significantly increased mean TC values in groups 2 and 3 after 12 weeks of atherogenic diet is in agreement with previously reported studies such as Zulli and Hare.[17]

Table 4. Baseline and post-intervention within group comparison of mean weight and lipid profiles

Variable	Group 1	Group 2	Group 3
	t (P)	t (P)	t (P)
Weight	4.74 (0.020)*	8.20 (< 0.001)*	10.09 (< 0.001)*
TC	6.05 (0.010)*	30.92 (< 0.001)*	16.75 (< 0.001)*
TG	1.87 (0.160)	1.95 (0.110)	0.05 (0.960)
HDL-C	2.27 (0.110)	8.81 (< 0.001)*	4.44 (0.010)*
LDL-C	3.50 (0.040)	22.01 (< 0.001)*	17.53 (< 0.001)*

*Statistically significant
TC: Total cholesterol; TG: Triglycerides; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol

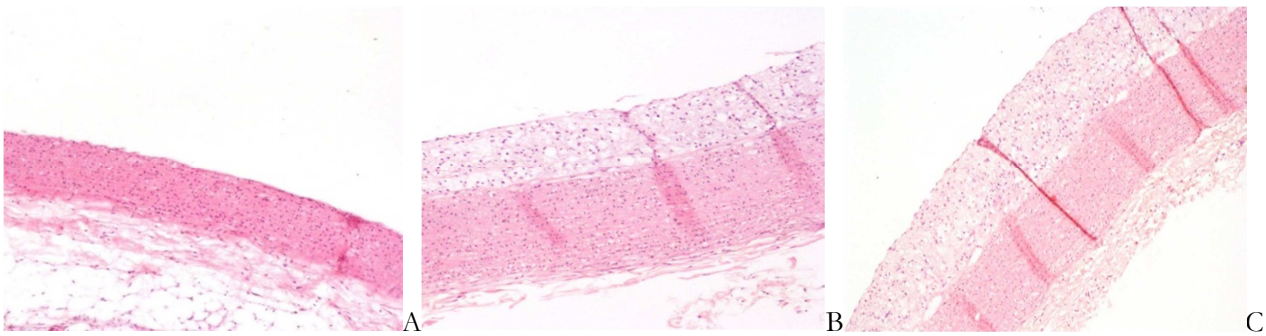

Figure 1. Hematoxylin-eosin stain of the aorta ×100 magnification
Group 1, normal diet (A), Group 2, atherogenic diet (B) and Group 3, atherogenic diet and 200 mg/kg/day V. amgdalina extract(C)

The pre- and post-intervention serum TG did not reveal any statistically significant difference across the groups. However, the mean scores of TG were higher in group 2 than both groups 1 and 3. This may suggest that the use of the aqueous extract of V. amygdalina may have had some beneficial effect on group 3 in terms of reducing the mean TG scores, even though this was not statistically significant. Previous studies conducted on rats and using 200 mg/kg of V. amygdalina reported a reduction in TG levels.[12,13] To our knowledge, no previous study has evaluated the effects of V. amygdalina on rabbits, and it may well be that the usage of an lethal dose 50 (LD50), as well as graded increasing doses of the extract may have shown or definitively confirmed that the extract of V. amygdalina has no beneficial effect on serum lipid profiles. This is therefore a limitation of this study.

The HDL-C was the highest in the group on extract as compared to the group on atherogenic diet only as well as the group on normal chow. The HDL-C was the highest in group 3, and there was a statistically significant different between groups 1 and 3. However, there was no such significance between groups 1 and 2 on the one hand, and between groups 2 and 3 on the other hand. This finding suggests that the HDL-C fraction which is protective against atherosclerosis was highest in the group which received aqueous extract of V. amygdalina. This suggestion of some possible benefit from the extract of V. amygdalina on HDL-C was not, however, reported by previous studies in rats.[17,18]

The use of the extract did not have a beneficial effect on the level of LDL-C across the groups. LDL-C was significantly higher in the groups that had atherogenic diet (groups 2 and 3 as compared to group 1). However, there was no significant difference between the values in groups 2 and 3. This implies that the use of the aqueous extract of V. amygdalina did not appear to have resulted in a significant reduction of LDL-C, as compared to group 2. This is in contrast with previous studies in rats[12,13] which reported otherwise. The reason for this observed difference in study findings may be due to the different animals used (rats versus rabbits) and the consequential physiologic differences in the metabolism of the extract.

Post-intervention histology

The post-intervention histological examination of the aorta in the three groups revealed that group 1 animals had a normal aortic wall while there was presence of atherosclerotic lesions in the aortic walls of animals in groups 2 and 3 (comprising rabbits that had atherogenic diet). A previous study that utilized rabbits as an exploratory model for atherosclerotic studies, and whose atherogenic diet was utilized as a template in this study also found atherosclerotic lesions.[17] Both studies also lasted for an equivalent duration of 12 weeks.

The features of atherosclerosis found in this study were similar in the two groups on atherogenic diet. These lesions consisted of thickened tunica intima with pools of extracellular lipids and several layers of foam cells. These features are consistent with the classification of atherosclerosis type III (intermediate lesions) as categorized by the American Heart Association.[21] Furthermore, statistical analysis comparing the mean intima-media ratio of these two groups (0.76 ± 0.13 and 0.63 ± 0.11, respectively) showed there was no statistically significant difference between them. This infers that the use of 200 mg/kg of aqueous extract V. amygdalina extract did not appear to have an ameliorating effect on the development of atherosclerosis in these rabbits.

Conclusion

In conclusion, this study showed that the use of atherogenic diet resulted in the induction of atherosclerotic lesions in rabbits. However, the use of 200 mg/kg/day of aqueous extract of V. amygdalina did not appear to exert a statistically significant effect on the serum lipid profile. It does not also appear to have exerted any beneficial effect on the lesions of atherosclerosis. Subsequent studies may explore the use of graded and increasing doses of the extract to ascertain if different doses may demonstrate an effect.

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Conflict of Interests

Authors have no conflict of interests.

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Infectious and coronary artery disease

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Review Article

Abstract

BACKGROUND: Atherosclerotic event is one of the most causes of death in the world. Coronary artery disease (CAD) is one manifestation of atherosclerosis. It is well-known that several risk factors, such as diabetes mellitus (DM), smoking, hypertension (HTN), have effects on it. It is proposed that infection can lead to atherosclerosis or even make its process faster. Here, we discuss about the effect of some of infectious agents on the atherosclerosis and CAD.

METHODS: In this study, first we did a comprehensive search in PubMed, Scopus, and Science Direct using some related keywords such as atherosclerosis, CAD, myocardial infarction (MI), infection, and name of viruses and bacteria. After finding the related papers, we reviewed the correlation between some microbial agents and risk of CAD.

RESULTS: Literature has reported several infectious agents (viruses, bacteria, and parasites) that can be associated with risk of CAD. This association for some of them like Helicobacter pylori (H. pylori), Chlamydia pneumonia (C. pneumoniae), and Cytomegalovirus (CMV) is a very strong. On the other hand, there are some other agents like influenza that still need to be more investigated through original studies. Furthermore, different mechanisms (general and special) have been reported for the association of each agent with CAD.

CONCLUSION: Based on the studies in databases and our literature review, it is so clear that some microbes and infectious agents can be involved in the process of atherosclerosis. Therefore, controlling each type of infections especially among people with a traditional risk factor for atherosclerosis should be taken into account for reducing the risk of CAD and atherosclerosis.

Keywords: Infection; Coronary Artery Disease; Atherosclerosis

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Introduction

Development of plaques related to the athermanous in the inner layer of arteries is called atherogenesis. The traditional risk factors for the process of atherosclerosis can act on the different places of this process. For instance hypertension (HTN) as major risk factors for this process can increase the tension of arterial wall. It can prevent from appropriate repair process. It is proposed that cigarette smoking and diabetes can effect on the biology of the vasculature, but there are not enough details about their mechanisms.[1] It is said that traditional risk factors such as smoking, diabetes mellitus (DM), and HTN cannot be considered alone for all cases of atherosclerosis.[2]

Today atherosclerosis is considered as a chronic inflammatory disease of blood vessels. Two mechanisms for the effect of inflammation on the atherosclerosis are considered. Direct mechanism is related to the inflammation at the site of vessel wall.[3] Many studies in databases suggest that microbes have an important role in vascular disease and atherosclerosis.[4] Infection in the vessel wall can act in the category of the direct mechanism. Infectious agents have effects on the formation of atherosclerotic plaque, making its process faster. Infectious agents can also lead to final complication of these plaques like plaque rupture and thrombosis.[2] The second and indirect mechanism is related to the inflammation at non-vasculature places that can lead to increase secretion of cytokines.[3] Until now impact of many infectious agents on the atherosclerosis are investigated, and there are many original and even secondary articles

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in this field.[2] Effects of some microbes such as Helicobacter pylori (H. pylori), Chlamydia pneumonia (C. pneumoniae), Cytomegalovirus (CMV), hepatitis C virus (HCV) on the atherosclerosis has been reviewed widely but evidence about some other agents seems to be inadequate. Table 1 shows some of the available meta-analyses in databases regarding the correlation of infection and atherosclerosis.

Materials and Methods

In this narrative review, electronic databases and resources including PubMed, Scopus and Science Direct and Google Scholar were searched using appropriate combination of some keywords like "atherosclerosis," "coronary heart disease (CHD)," "cerebrovascular disease (CVDs)," "microbe," "infection," "bacteria," "virus" and name of some infectious agents based on the literature review. Furthermore, in related papers, we investigated the references of them for finding other related papers. Before including each paper, we evaluated them regarding methodology and study design. After finding the related papers, the correlation between some microbial agents and coronary artery disease (CAD) were evaluated in 11 separate parts.

Results

H. pylori

Vcev et al.[10] in a randomized, multicenter study with evaluation of 180 subjects (90 CAD and 90 healthy parsons as a control group) observed that H. pylori has more seroprevalence in patients group compared to control group. They also investigated the association between this infection and CAD risk factors and showed that body mass index, smoking, HTN, DM, total cholesterol, and socio-economic status in both groups of study have not a significant association with H. pylori infection. And at the end, they suggested more studies in this field. But Jin et al.[11] in their study showed that some risk factors for CAD [gender, age, smoking, and high-density lipoprotein (HDL) cholesterol] have a meaningful difference in patients with CAD (n = 175) compared to control group (n = 88). They reported a non-significant difference between two groups about the presence of H. pylori infection.

In a cohort study, Zhu et al.[12] followed up 929 patients with CAD (antibodies to H. pylori were found in 56% of cases) for 3 years and investigated them for acute myocardial infarction (AMI) and death. Finally, they showed that there is no meaningful association between H. pylori infection and incidence of AMI or death and concluded that this infection cannot be a major risk factor for CAD, AMI or death.

In some studies, it has been proposed a mechanism for the association of H. pylori with CAD that we explain it with more details here. It is understood that hyperhomocysteinemia can be an important risk factor for CAD and atherosclerosis.[13] This condition can result from inhibition of the methionine synthase reaction due to the low-level of folate serum.[14] On the other hand, we know that H. pylori infection can result in low ascorbic acid level in gastric juice[15] which reduces absorption of folate.[16] Furthermore, there is a meaningful association between folate level of serum and CHD.[17] Therefore, we think that effect of prescribing ascorbic acid on decreasing the atherosclerosis process can be studied and with consideration of all available data about the association of H. pylori and CAD, we suggest that these patients especially those with a conventional risk factor for CAD should take a good care for CAD. Another proposed mechanism for H. pylori infection is related to H. pylori strains with cytotoxin-associated gene A. However, a study revealed that colonization with this battery cannot considered as an independent risk factor for severe CAD.[18] Power full studies like meta-analysis studies in a different aspect of this association like the progression of atheroma, development of CAD and its effect on risk factors of CAD is helpful about this issue. A meta-analysis in 2012 showed that there is an association between H. pylori infection and ischemic stroke[6] while another one in 2014 rejected this correlation.[19]

Table 1. Some available meta-analyses regarding correlation of infection and atherosclerosis

First author	Publication year	Microorganism	Evaluated outcome	Reported results
Zhang et al.[5]	2008	H. pylori (Cag A)	IS and CAD	Significantly associated
Wang et al.[6]	2012	H. pylori	IS	Significantly associated
Chen et al.[7]	2013	C. pneumoniae	CVD	Significantly associated
Huang et al.[8]	2014	Hepatitis C	Carotid atherosclerosis	Significantly associated
Filardo et al.[9]	2015	C. pneumoniae	Atherosclerosis	Significantly associated

H. pylori: Helicobacter pylori; C. pneumoniae: Chlamydia pneumoniae; CAD: Coronary artery disease; CVD: Cardiovascular disease; IS: Ischemic stroke

Streptococcal pneumonia

Eurich et al.[20] in a population-based cohort study investigated 6171 patients of community-acquired pneumonia. During the follow-up, they observed acute coronary syndrome (ACS) events in 175 patients. They showed that pneumococcal polysaccharide vaccination can reduce the ACS events (about 60%) in patients with pneumonia. There is a possible mechanism for this protective effect of pneumococcal vaccination based on an experimental study. The similarity between epitope of S. pneumoniae and oxidized low-density lipoprotein (Ox-LDL) propose a molecular mimicry theory so that pneumococcal vaccination can result in a reduction of anti-Ox-LDL immunoglobulins (Igs) and finally decrease in the atherosclerosis process.[21]

There is a possibility for hereditary component-2 deficiency (C2D) that can play a role for progression of atheroma. On the other hand, Jonsson et al.[22] investigated 40 persons with C2D. They reported severe infection as the most clinical presentation for these patients. Septicemia or meningitis caused by S. pneumonia made up the majority of previous reported infections. Moreover, they also reported pneumonia and recurrent pneumonia in their follow-up of these patients.

Based on these studies, an association between S. pneumonia with CAD can be suggested but this association and its mechanism is still unclear and more original studies, and evidence is needed to clarify all aspect of this association.

C. pneumoniae

C. pneumoniae infection is another bacterial infection that is proposed for playing a role for developing CAD. In a cross-sectional study Haider et al.,[23] evaluated 63 patients with CVDs including angina and MI and 40 healthy subjects as control group for detection of C. pneumoniae IgA antibodies and interferon γ (IFN-γ) with enzyme-linked immunosorbent assays (ELISA). According to their observation C. pneumoniae, IgA was seen in 66.7% of subjects in control groups and in 41.4% in subjects in control groups. The mean amount of IFN-γ was 32.12 pg/ml in patients group compared to 11.32 pg/ml in control groups. An important finding in this study was about increased IFN-γ in patients group. We also know that the value of IFN-γ can be higher in patients with ACS and stable angina compared with healthy persons.[24] Hence, it can be said the C. pneumoniae can have some effects on the development of CAD especially by elevation of IFN-γ values. However, there are some studies that concluded this relationship cannot be very strong. For example, Sadeghian et al.[25] by a case-control study investigated 30 patients with coronary atherosclerosis and the same number in the control group. They observed only one patient with positive polymerase chain reaction (PCR) for C. pneumoniae in cases group. In the control group, there were no positive cases.

Also, it has been showed that there is a cross reactivity between Bartonella quintana and C. pneumoniae. Hence, there is possibility that the association between C. pneumoniae and CAD can be related to the B. quintana. But, Badiaga et al.[26] in a case-control study demonstrated that C. pneumoniae is an independent risk factor for CAD and only in some cases there is a co-infection not cross-reactivity.

These differences must be evaluated in more powerful studies like a meta-analysis. For instance in a meta-analysis in 2013 a significant association between CVDs and serum specific IgG for C. pneumoniae has been reported.[7] Different issues in this topic should be evaluated in other studies. One of them is related to the different methods (PCR, serological markers, culture from vascular tissue) that used in different studies. The other important problem is the use of standard method in studies.[27]

Mycoplasma pneumoniae (M. pneumoniae)

Basinkevich et al.[28] measured antibodies and antigen to M. pneumoniae in patients with CHD and persons without it and demonstrated that there is more seropositivity for M. pneumoniae in cases group compared with control group. So, they concluded that this type of infection can be associated with CHD.

M. pneumoniae and C. pneumoniae usually is reported together in different studies related to CAD.[28,29] Momiyama et al.[30] investigated the interaction of M. pneumoniae infection with chlamydial infection. They concluded that M. pneumoniae is a more prevalent in persons with CAD compared with control group and they showed that this prevalence can be dependent on co-infection by M. pneumoniae and C. pneumoniae. Therefore, this co-infection is considered as an important factor for development CAD.

For confirming the association of M. pneumoniae with CAD and also the interaction of M. pneumoniae infection with chlamydial infection, more original studies is still needed. But now consideration of reducing the CAD risk factors in

these patients should be noticed.

Human immunodeficiency virus (HIV)

Another important organism that is mentioned to have an association with atherosclerosis is HIV. Neumann et al.[31] investigated 101 HIV-infected patients with coronary angiography and demonstrated that there is CAD in 59.1% of all patients. Also, it has been said that some factors like simultaneous infections with other viruses or vitamin D deficiency/insufficiency can make a stronger correlation between HIV infection and CAD.[32] Escaut et al.[33] in a cohort of 840 patients showed that there were a higher proportion of coronary event in HIV-infected subjects and concluded that metabolic disturbances due to drugs and smoking of tobacco is the important factors for this association. Lai et al.[34] in their study demonstrated that long-term exposure to the antiviral therapy and use of cocaine is associated with the development of CAD. At this time, there are some studies proposed the relationship between HIV and CAD and each one suggests some factors affecting on this relationship so it seems that meta-analysis for doing subgroup analysis in this field can be more helpful. An available meta-analysis about this issue in 2009 revealed that HIV infection cannot be a strong risk factor for subclinical atherosclerosis.[35]

CMV

Basinkevich et al.[29] in their study measured the level of IgM antibody to CMV in patients with MI, unstable angina, stable angina and in healthy subjects as control group and showed that seropositivity frequency is more in patients group compared with control group. Furthermore, there are some studies have shown the presence of CMV and its replication in the atherosclerotic plaque.[36] There is a mechanism that has been proposed for the effect of CMV in the process of atherosclerosis. It has been said that antibodies specific for CMV can trigger a pathway and induce genes expressing the molecules implicated in the activation of endothelial cell apoptosis that this damage to the endothelial cell can be consider for atherosclerotic pathogenicity.[37] It is proved that poor control of glucose level in type 2 diabetic patients can lead to developing CMV infection of arterial wall.[38] Another important issue is related to the existence of CMV infection in immunosuppressive patients like kidney transplant patients. This infection also is related to the development of atherosclerosis among kidney transplant patients.[39,40] After all a meta-analysis in 2012 with inclusion of 55 studies showed that CMV infection can be effective in the process of atherosclerosis.[41]

Herpes simplex virus type 1 (HSV-1) and 2

Al-Ghamdi[42] for revealing the association of HSV-1 and atherosclerosis measured the level of IgG antibody specific for HSV-1 among 40 patients with acute and chronic CAD, 20 with peripheral arterial disease and 20 with cerebral stroke and compared it with 15 subjects as control group. In the results of this study, in spite of a high seropositivity for HSV, the seropositivity had not a statistically meaningful difference between the two groups. Also Sorlie et al.[43] reported that there is no association between HSV1 antibody level and CHD. Some studies have different results. For example, Siscovick et al.[44] in a nested case-control study observed that existence of antibody to HSV-1 can increase the risk of incident MI and CHD death 2 times in older patients. Some studies also proposed a mechanism for effect of HSV-1 on atherosclerosis process. A major receptor for Ox-LDL is lectin-like Ox-LDL receptor-1 (LOX-1) in the endothelial cell. It has been said that this receptor is more expressed in the atherosclerosis process and therefore there may be a possible role in the atherosclerosis for this receptor.[45]

On the other hand, it has been shown that in HSV-1 infected patients, due to the more expression of LOX-1, the uptake of Ox-LDL will increase and therefore it can lead to activation and dysfunction of endothelial cells and eventually atherosclerosis.[46] But ultimately with consideration of this available data, we suggest more original studies and long-term follow-up of HCV-1 infected patients for a better understanding of association between HSV-1 and CAD. Sun et al. in a cross-sectional study with evaluation of 1244 subjects (488 with essential HTN and 756 normotensive) demonstrated that HSV-2 can be considered as an independent risk factor for HTN[47] and we know that HTN is a traditional risk factor for CAD. So, it can be supposed that HSV-2 can develop CAD by HTN. Also it has been shown that seropositivity of HSV-2 antibody can be related to the risk of death due to the CVD in the future.[48]

Biopsies from CAD have been investigated for inflammatory cells and also for the antigen to HSV-2. And it is demonstrated that there is a meaningful correlation between the presence of antigen to HSV-2 and infiltrate.[49] But in some studies also reported that seropositivity to HCV-2 antibody is not different between ischemic heart disease (IHD)

patients compared with healthy subjects.[50] At this time, we need more original studies for clarifying the association of HSV-2 with atherosclerosis process and CAD.

Hepatitis viruses

Hepatitis viruses seem to be involved in the process of atherosclerosis. It has been shown that hepatitis A virus (HAV) can be related to the development of atherosclerosis process and therefore leading to CAD. Zhu et al.[51] showed in their study that CAD has statistically more prevalence among HAV-infected patients compared with patients without HAV seropositivity. So according to this conclusion, prevalence of CAD and HAV infection should be associated to each other but the prevalence of HAV infection and CVD is not similar in different places.[52] Furthermore, there are some studies with consideration of CAD prevalence have concluded that HAV infection cannot be a predictor for atherosclerosis and it's not related to CAD.[53,54]

Ishizaka et al. in their study concluded that hepatitis B virus (HBV) is not associated with C-reactive protein (CRP) level and atherosclerosis. In contrast, HBV infection and seropositivity to HBV surface antigen has been proposed as a risk factor for developing atherosclerosis.[55] About involving HBV in atherosclerosis process, there are some reasons. Infection with HBV can have some extra liver manifestation like vasculitis and there are some evidences that show the presence of HBV in endothelial cells.[56,57] Also, we know that chronic liver disease can lead to increase of oxidative stress level.[58] So by this ways, it seems that hepatitis B infection can help the atherosclerosis process. But it also has been said the effect of HBV on atherosclerosis is duo to the liver failure and it cannot be an independent risk factor for CAD.[59]

Arcari et al.[60] in their cohort study with the investigation of 582 subjects concluded that HCV infection has not any relationship with AMI. Also Butt et al.[61] showed that patients with HCV infection has a younger age, lower lipid level and lower HTN prevalence than healthy control subjects. Even after adjusting conventional risk factor for CAD they concluded that HCV infection can be associated with developing CAD. Another study in 2013, by Miyajima et al.[62] demonstrates that HCV can be associated with mild atherosclerosis. We know that presence of inflammatory markers like CRP and interleukin-6 (IL6) can be a trigger for atherosclerosis process[63,64] and on the other hand, it has been shown that these markers have a more level in the HCV-infected patients.[65,66] So, this can be a possible mechanism for developing atherosclerosis by HCV infection. Also a meta-analysis in 2012 showed that HCV infection is an independent risk factor for carotid atherosclerosis.[8]

Influenza A

It has been shown that level of IL-6 and IL-8 can increase due to infection of monocyte with influenza A\H1N1 and it can lead to systemic inflammation and further developing the atherosclerosis process.[67] Perhaps this can activate the second or indirect mechanism about the role inflammation in the process of atherosclerosis that we pointed it before. Some other studies have reported that infection with influenza (A or B) cannot be a risk factor for developing CAD.[68] on the other hand it is shown that vaccination against influenza can be a protective factor for developing atherosclerosis during the seasons related to the flu.[69,70] of course this is soon to be used generally for the suspected CAD patients and its effect should be investigated in further studies. Also more studies about relationship of CAD and influenza are still needed.

Organism causes dental infection

Some studies have suggested that oral and dental infection can be an important risk factor for CAD.[71,72] So that they have also mentioned some of the organisms that cause oral or dental infection can be found in the coronary arteries of patients with atherosclerosis. Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Prevotella intermedia, Tannerella forsythensis, are microorganisms implicated in dental infection and also have been seen in the coronary artery biopsy samples.[73] Zhang et al.[74] also reported in their study some other microorganism like T. forsythensis, Bacteroides forsythus, Campylobacter rectus, Fusobacterium nucleatum, Treponema spp. and Streptococcus sanguis simultaneously in both coronary atherosclerotic plaques and subgingival plaque in patients with CAD.[74] Based on these studies, the association between these infections and CAD can be concluded and dental health in particular in patients with CAD risk factors should be considered.

Conclusion

Based on the studies in databases and our literature review, it is so clear that some microbes and

infectious agents can be involved in the process of atherosclerosis. Some agents still need more studies for investigation of their effects on atherosclerosis and also secondary studies is required in some other agents. We think that the infectious agents can be involved in both direct and indirect mechanisms of inflammation effect on the process of atherosclerosis. On the other hand, it is shown that some other agents like H. pylori have some especial mechanisms for affecting on the process of atherosclerosis. We believe that infection should be considered as an important risk factor for atherosclerosis. Therefore, controlling each type of infections especially among people with a traditional risk factor for atherosclerosis should be taken into account for reducing the risk of CAD and atherosclerosis.

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Conflict of Interests

Authors have no conflict of interests.

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Left ventricular apical hypoplasia: Case report on cardiomyopathy and a history of sudden cardiac death

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Case Report

Abstract

BACKGROUND: Isolated left ventricular apical hypoplasia with several different unrecognized dimensions is a newly discovered congenital anomaly of the heart.

CASE REPORT: In this report, we describe a case of cardiomyopathy of this type occurring in a 13-year-old male with a history of mental retardation and sudden cardiac death (SCD) of second-degree relatives. The patient was referred for an evaluation of cardiac status. An echocardiography analysis demonstrated a spherical left ventricle (LV) appearance with mild mitral regurgitation. Cardiac magnetic resonance imaging (MRI) confirmed a spherical and truncated LV appearance. The right ventricle was found to have elongated and wrapped around the LV, and diverticulum was also seen in the cardiac MRI.

CONCLUSION: To the best of our knowledge, this is to present the first case of LV apical hypoplasia combined with LV diverticulum and a family history of SCD. As more cases featuring this cardiomyopathy type are recognized, it will be easier to elucidate the natural history and management of such cardiac anomalies.

Keywords: Cardiomyopathy; Hypoplasia; Magnetic Resonance Imaging Scan; Sudden Cardiac Death

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Introduction

Isolated left ventricular apical hypoplasia with several different unrecognized dimensions is a newly discovered congenital anomaly of the heart, as described for the first time by Fernandez-Valls et al.[1] This congenital anomaly was first hypothesized as isolated left ventricular hypoplasia with no specific symptoms such as atypical chest pain, fatigue, or breathlessness, and even as an asymptomatic anomaly. Magnetic resonance imaging (MRI) role in diagnosing cardiac anomalies or masses is strongly recommended.[2] This anomaly was first described in detail on the basis of an MRI modality. Initial evidence indicated that the symptoms of affected patients were fully relieved by anti-heart failure medications.[3,4] The first case of congenital left ventricular hypoplasia described was reported as an isolated phenomenon. However, it has been indicated in some reports in conjunction with other cardiovascular abnormalities such as cyanotic congenital anomalies, transposition of the cardiac valves, and aortic stenosis.[5-7]

In the present study, we investigate the other cardiac anomalies accompanying left ventricular apical hypoplasia.

Case Report

A 13-year-old male patient with a history of sudden cardiac death (SCD) in two of his second-degree relatives, referred to our clinic to evaluate a possible cardiac disease. He also had mental retardation from birth. The presenting symptoms were relatively mild and non-specific and included shortness of breath and chest discomfort. The patient's hemodynamic condition was evaluated through a physical examination and an assessment of his vital signs. The physical examination identified grade II systolic murmurs. Electrocardiography (ECG) analysis showed a normal sinus rate and rhythm, right axis deviation

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(110°), and a low precordial voltage with poor R-wave progression.

Transthoracic echocardiograms showed moderate to severe left ventricle (LV) systolic dysfunction. In addition, mild tricuspid regurgitation was presented. Besides enlargement of the left atrium and moderate mitral regurgitation, other cardiac valves showed no significant abnormality.

Since the LV apex was not clear in the four-chamber view of the echocardiographic evaluation (Figure 1) and to study the kinetic features of the congenital malformation and its morphological characteristics, we performed contrast-enhanced cardiac MRI, using a 1.5 T whole-body scanner (Avanto, Siemens, Erlangen). For signal reception, an eight-element cardiac phased-array receiver surface coil was used. We performed retrospective ECG-triggered steady-state free precession (SSFP) sequence for the evaluation of LV myocardial thickness, as well as kinetic, parietal segmental, and the global contractility. We oriented the sequences to the short-axis and long-axis (atrium-ventricular and four-chamber axes) using parameters as follows: TR 3.8 ms; TE 1.8 ms; flip angle (FA) 70°; matrix scan 256 × 256; field of view (FOV) 400; thickness 8 mm; gap 2 mm; 25 cardiac phases per cycle; and retrospective synchronization. Cine cardiac MRI with a four-chamber view showed a truncated appearance of the spherical LV with a bulging of the interventricular septum (IVS) toward the right ventricle (white arrow). It also indicated invagination of fatty material and elongation of a normally functioning right ventricle around the deficient LV apex (Figure 2).

The stack of the axial view using SSFP sequences showed a small cavity indicating contractile myocardial out pouching located in the mid-posterolateral LV wall and containing all three layers of the ventricular wall, which suggested LV diverticulum. Furthermore, LV volumes were enlarged, and the ejection fraction was decreased.

Black-blood T1-weighted sequences with and without fat saturation on short-axis and long-axis views were performed to assess alterations of the myocardial signals (Figure 3). Finally, late gadolinium enhancement MRI (LGE-MRI) was performed by means of magnitude-reconstructed and phase-sensitive inversion recovery prepared using a fast gradient echo sequence. After 10 minutes from the administration of 0.2 mmol/kg of gadoterate meglumine (Dotarem®, Guerbet, France), LGE-MR images were obtained along the same axis plane and with the same slice thickness as in the cine MRI. The acquisition parameters were as follows: TR = 600 ms; TE = 3.4 ms; FA = 25°; acquisition matrix = 156 × 256; FOV = 320 × 400 mm; slice number = 10 slices; and cardiac phase = mid-diastole. There were no signs of fibrosis or necrosis tissue presenting in the circumferential wall of the diverticulum showing by the delayed enhancement images (Figure 4).

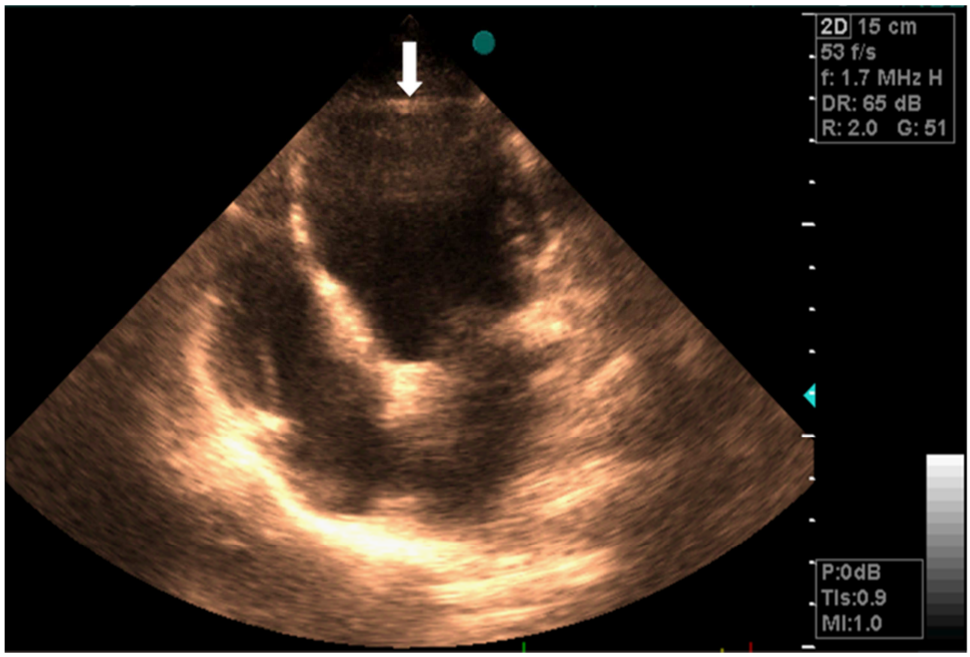

Figure 1. Four-chamber view in a transthoracic echocardiogram showing enlargement of the left ventricle (LV) (The LV apical structure was unclear in this view)

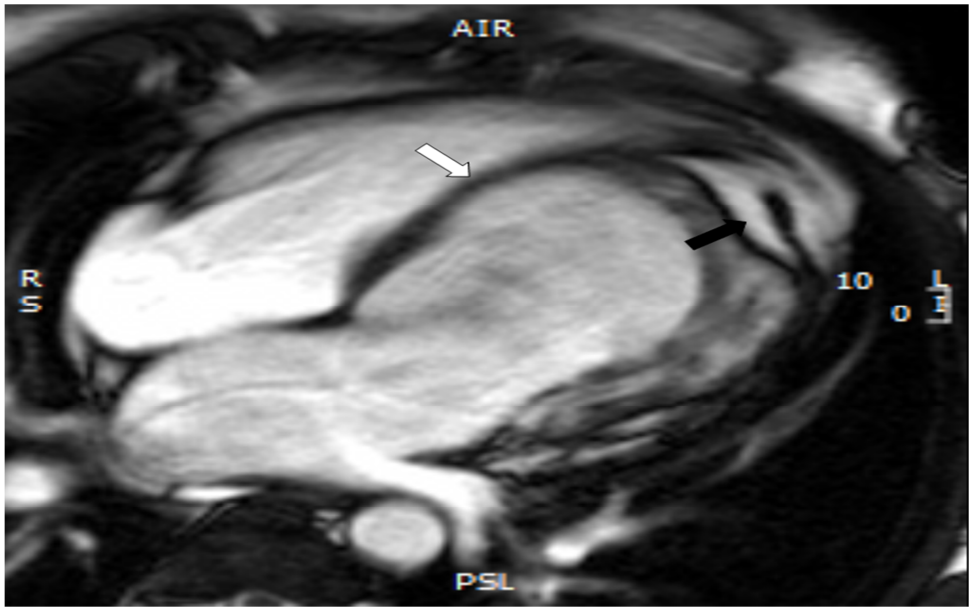

Figure 2. Cine cardiac magnetic resonance imaging (MRI) image in a four-chamber view shows bulging of the interventricular septum (IVS) toward the right ventricle (white arrow) and invagination of fatty material (black arrow)

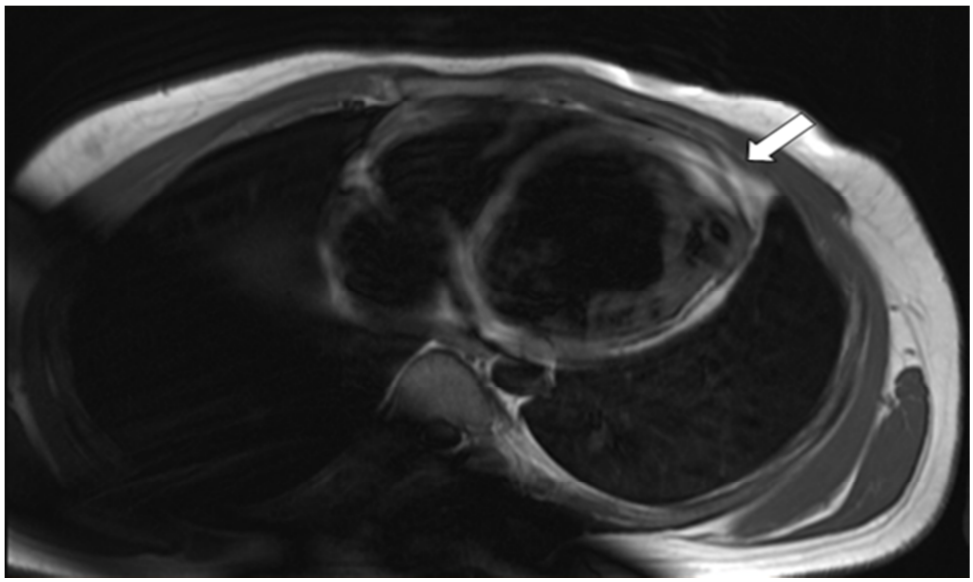

Figure 3. A T1-weighted image shows bright tissue replaced in the left ventricle (LV) apical position (white arrow), which could suggest the presence of fat replacement

Discussion

Previous studies reported a limited number of cases relating to LV apical hypoplasia accompanied by other cardiac diseases.[5-7]

In our case report, the patient had LV diverticulum, mental retardation, and a family history of SCD. To our knowledge, this is the first case of LV apical hypoplasia combined with LV diverticulum. In our patient, although not documented, the family history of SCD may also have raised suspicions of a familial pattern of disease at least in a subset of patients, which necessitated screening of other family members.

Although the exact mechanism is unclear, it is believed that deficient partitioning of both ventricles during embryonic life may lead to a spherical LV with an elongated right ventricular covering around its truncated apex. Furthermore, the finding of LV diverticula may be a physiological consequence of the severity of the dysplasia, which makes the LV wall weak and leads to the formation

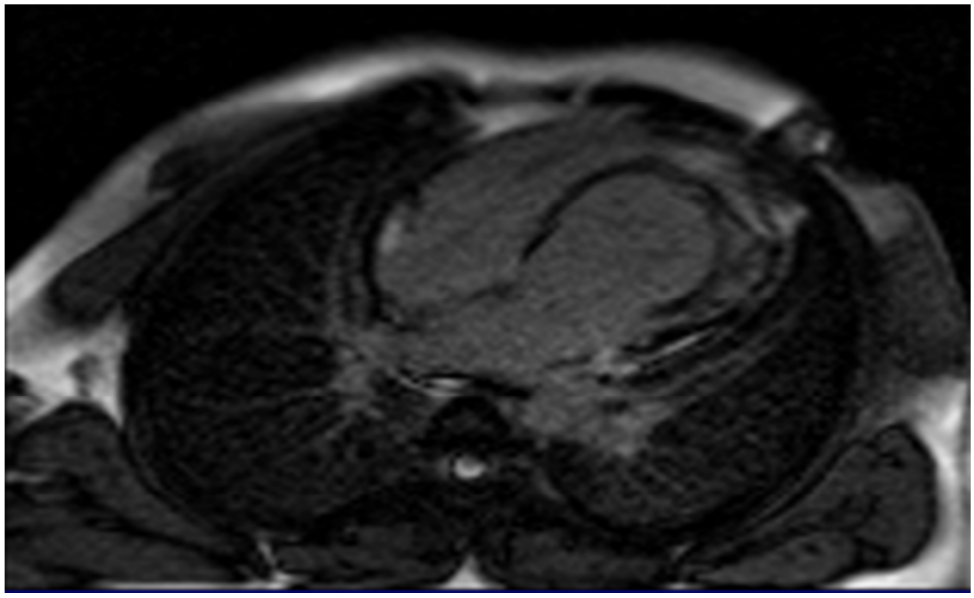

Figure 4. A late gadolinium enhancement (LGE) image performed 10 minutes after the contrast media injection showed no intramyocardial hyperenhancement area but indicated the presence of myocardial tissue in the out pouching; this confirmed the congenital nature of the diverticulum

of diverticula. The main manifestation relates to an indication of four definitive components of isolated left ventricular apical hypoplasia on MRI, including: (1) left ventricular truncation with systolic dysfunction; (2) substitution of the left ventricular apex with fat tissue; (3) papillary muscles originating from the anteroapical region; and (4) the wrapping of the right ventricle around the LV.[3,4,8,9-13] We also demonstrate the novel finding of LV diverticulum.

In spite of scarce knowledge, the presented cases depict a spectrum from no symptoms or non-specific symptoms, mainly during childhood, to systolic or diastolic dysfunction of the congestive heart failure, or even malignant tachyarrhythmia, usually in adulthood. The hemodynamic condition of the anomaly described in our report looked like restrictive cardiomyopathy manifested by left ventricular dysfunction[7] or by a reduced left ventricular ejection fraction.[3,5,13,14] Although there is little documentation on this phenomenon, a close follow-up of patients is recommended if only for the purpose of evaluating the signs and symptoms of pulmonary hypertension, heart failure, and potentially malignant tachyarrhythmia.[11,13] Furthermore, screening of other family members if there is a suspicious family history may be valuable.

Conclusion

In this case report, we presented a teenage patient with combined LV apical hypoplasia, LV diverticulum, and a suspicious family history. A study of other living family members using echocardiography was negative. Our patient is still undergoing intensive treatment with standard drugs for systolic heart failure and is also under close observation for the occurrence of an arrhythmia and ventricular dysfunction.

Acknowledgments

None.

Conflict of Interests

Authors have no conflict of interests.

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Dolichoectasia in vertebrobasilar arteries presented as transient ischemic attacks: A case report

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Images in Clinical Medicine

Abstract

BACKGROUND: Vertebrobasilar dolichoectasia (VBD) is a rare vasculopathy. The etiology of this disease is unknown. Transient ischemic attacks (TIAs) of vertebrobasilar system refer to a transient (< 24 hours) lowering of blood flow in the posterior circulation of the brain. We present a case of dolichoectasia in the vertebrobasilar artery that presented with TIAs.

CASE REPORT: A hypertensive 54-year-old man with true vertigo, nausea, imbalance, dysarthria, dysmetria, horizontal nystagmus, and gait ataxia was referred to Alzahra Hospital, Isfahan, Iran. The symptoms improved in the 1st day, but recurred in the 2nd day, lasting for 6-7 hours. According to clinical manifestations, a diagnosis of TIAs in the vertebrobasilar circulation was made. Imaging studies showed vascular anomaly. The vascular anomaly was considered as the cause of the patient's symptoms. A medical management was started using antiplatelet and antihypertensive drugs. The patient was referred for a more evaluation for other vascular anomalies.

CONCLUSION: Dolichoectasia usually affects vertebral and basilar arteries and simultaneous involvement of carotid arteries is rare seen in only 0.5% of these patients. The usual symptom of dolichoectasia is ischemia and rarely hemorrhages. The most common type of ischemic stroke is lacunar type. Ischemia evolves from embolic that originate from thrombi or plaques in the walls of the ectatic artery. While hemodynamic effects are the most common cause of the presenting signs and symptoms of the anomaly. We report a case of dolichoectasia that presented with TIAs of the verterbrobasilar artery. VBD is a distinct arteriopathy known as stroke risk.

Keywords: Vertebrobasilar Dolichoectasia; Transient Ischemic Attacks; Vasculopathy

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Introduction

Vertebrobasilar dolichoectasia (VBD) is a rare vasculopathy. The etiology of this disease is unknown. Arterial wall of vertebral and/or basilar arteries are affected by VBD. VBD cause elongation, torsion, and enlargement of arteries that followed by hemodynamic and hemostatic changes. Finally, these changes cause thrombosis, microembolization, and brainstem compression, with or without aneurysm formation.[1] Its prevalence has been reported to vary from 0.06 to 5.8% according to different studies.[2]

Transient ischemic attacks (TIAs) of vertebrobasilar system refer to a transient (< 24 h) lowering of blood flow in the posterior circulation of the brain.[3]

The presentation of dolichoectasia is usually due to hemodynamic disturbances and sometimes due to compressive effects. There are different clinical syndromes that are in association with ectatic vertebrobasilar arteries.[2] It may present with a headache, vertigo, sudden deafness, trigeminal neuralgia, facial spasm or palsy and basilar-type migraine.[4,5] Rare presentations such as hydrocephalus have also been reported with bilateral obstruction of Monro foramina by posterior cerebral arteries.[6]

The pathophysiology of dolichoectasia seems to have association with hypertension, atherosclerosis,

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and destruction of the internal elastic membrane.[7] The anomalous arteries usually have degeneration and gaps in the internal elastic lamina, thinning of media due to the reduction of reticular fibers and atrophy of smooth muscle cells.[5] It is associated with Marfan, Ehlers-Danlos, and tuberous sclerosis.[1] Furthermore, dolichoectasia is in association with increasing age, male sex, hypertension and previous myocardial infarction.[8]

In this study, a case of dolichoectasia in the vertebrobasilar artery that presented with TIAs has been discussed.

Case Report

A hypertensive 54-year-old man referred to Alzahra Hospital, Isfahan, Iran, with true vertigo, nausea, and imbalance from the previous night.

In the neurologic physical examination, the patient had dysarthria, dysmetria, horizontal nystagmus and gait ataxia. The strength of the extremities was symmetric. The symptoms improved in the 1st day, but recurred in the 2nd day, lasting for 6-7 hours.

According to clinical manifestations, a diagnosis of TIAs in the vertebrobasilar circulation was made and the patient underwent imaging studies. Brain computed tomography scan (CT scan) showed hyperdense lesion in the brain stem and cerebellum (Figure 1).

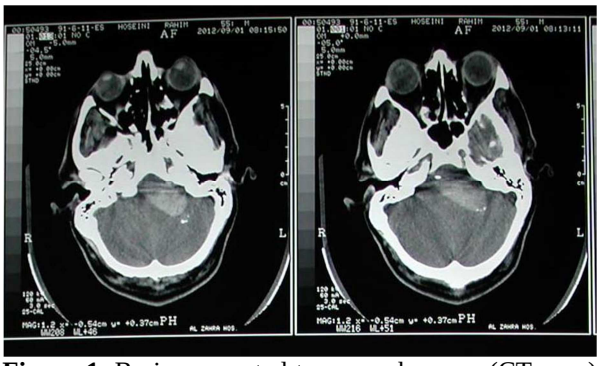

Figure 1. Brain computed tomography scan (CT scan) showing a hyperdense lesion in the brain stem and cerebellum

Brain magnetic resonance imaging (MRI) in both axial and sagittal views showed fusiform dilatation of an intracranial segment of internal carotid artery (ICA) as well as basilar artery, with extrinsic pressure over both sides of the medulla, pons and anterior aspect of left cerebellar hemisphere. Moreover, there was a marked compression and a displacement of the left pons and lower mesencephalic by the basilar artery (Figure 2). Brain MRI showed long segment dilatation and severe tortuosity of basilar artery, as well as long segment slight dilated ICA proximal to bifurcation (Figure 3). MR angiography (MRA) of cerebral arteries showed fusiform dilatation of left vertebral artery and proximal two-thirds of basilar artery (dolichoectasia), with similar changes in supraclinoid portion of both internal carotid arteries as well as (Figure 4).

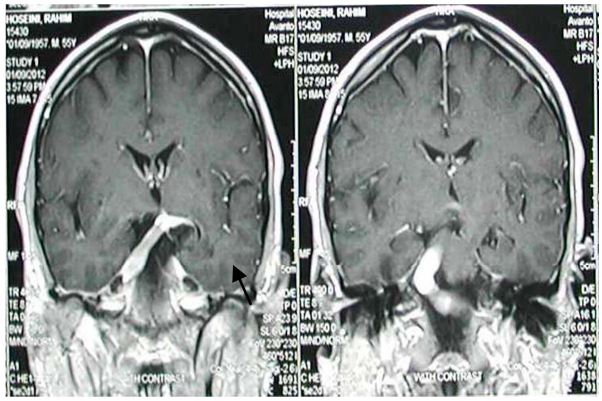

Figure 2. Brain magnetic resonance imaging (MRI), with contrast showing dilatation of intracranial segment of basilar artery, with extrinsic pressure over both sides of medulla

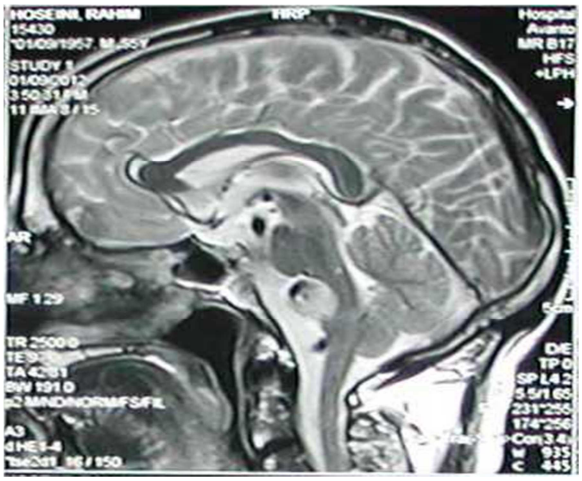

Figure 3. Brain magnetic resonance imaging (MRI) sagittal view showing dilatation of intracranial segment of basilar artery, with extrinsic pressure over both sides of medulla

The vascular anomaly was considered as the cause of the patient's symptoms. Medical management was started using antiplatelet and antihypertensive drugs. The patient was referred for more evaluation for other vascular anomalies in the setting of a systemic condition (especially cardiovascular systems) involving large to medium size arteries and for vascular intervention.

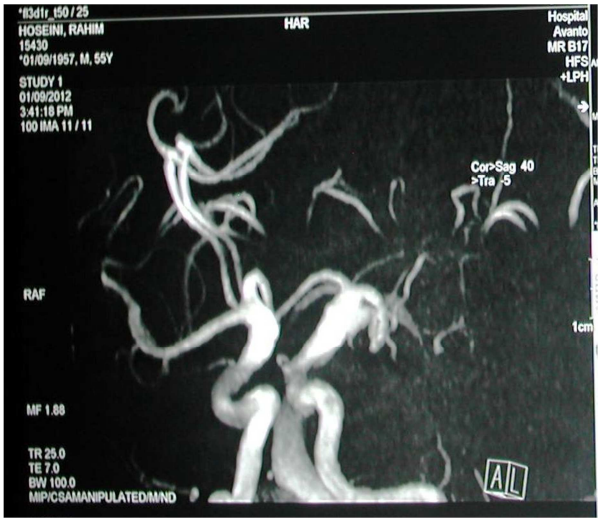

Figure 4. Magnetic resonance angiography of brain showing fusiform dilation of basilar artery and the segment of bilateral internal carotid arteries

Discussion

We presented very rare condition, TIAs of posterior circulation due to dolichoectasia,[9] a case of vertebrobasilar and carotid dolichoectasia. There are some studies reported the relationship between cerebrovascular events and VBD in occasional cases and in a few patient series.[10] It is usually presented as ischemia and sometimes with hemorrhage.[4]

Dolichoectasia usually affects vertebral and basilar arteries, and simultaneous involvement of carotid arteries is rare seen in only 0.5% of this patients.[11] The ICA is also at high risk to be affected. Our patient had this rare entity.

The usual symptom of dolichoectasia is ischemia and rarely hemorrhages. The most common type of ischemic stroke is the lacunar type.[8] Ischemia evolves from embolic that originate from thrombi or plaques in the walls of the ectatic artery. While hemodynamic effects are the most common cause of the presenting signs and symptoms of the anomaly.[4] VBD was defined as the diameter of the basilar artery ≥ 4.5 mm and the diameter of the intracranial vertebral artery ≥ 4.0 mm on MRA.[12] Although MRA showing ICA involvement, the manifestations were limited to posterior circulation, brain MRI showed fusiform dilatation of intracranial segment of ICA as well as basilar artery, with extrinsic pressure over both sides of medulla, pons and anterior aspect of left cerebellar hemisphere. Our patient showed some compressive effects of the dolichoectasia on the medulla, pons and anterior aspect of left cerebellar hemisphere. Moreover, this case presented with TIA in the vertebrobasilar field which is a less frequent presentation.

A study estimated the prevalence of dolichoectasia in stroke patients to be about 3.1%. Age, sex, hypertension, diabetes and previous history of TIA did not seem to have statistically significant difference between patients with dolichoectasia and without it. Patients with dolichoectasia had better survival but higher recurrence rate of stroke.[4] There are studies which have been reported a higher rate of hypertension among patients with dolichoectasia.[7] In another study, patients had a 60.0% survival rate after 3 years follow-up independent of the type of symptoms is ischemic versus compressive.[12] According to a cohort study dolichoectasia may be considered a risk factor for stroke and was associated with higher mortality in a 4-7 year period.[13] Stroke event in VBD patients could be achieved by intensive management of these clinicoradiological factors.

We report a case of dolichoectasia that presented with TIAs of the verterbrobasilar artery. VBD is a distinct arteriopathy known as stroke risk.

Acknowledgments

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Conflict of Interests

Authors have no conflict of interests.

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