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ARYA Atherosclerosis

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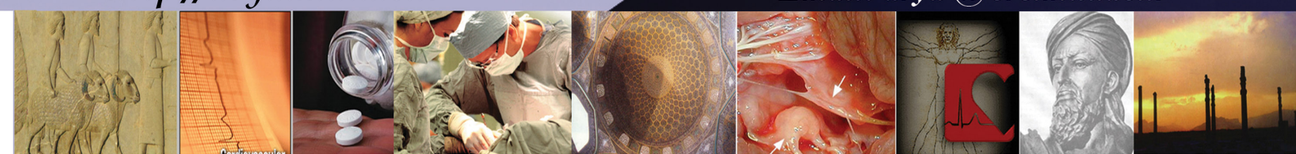

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ORIGINAL RESEARCH

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The effect of aerobic physical rehabilitation on the quality of life in patients with chronic atrial fibrillation; A randomized controlled clinical trial study

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Original Article

Abstract

BACKGROUND: Management of atrial fibrillation (AF), besides prevention of stroke, mainly stresses symptom control and improvement of quality of life (QOL). In patients with permanent AF, exercising may improve QOL, rhythm, and symptoms. The purpose of this study was to determine the impact of aerobic physical rehabilitation on the QOL of patients suffering from AF and admitted to a coronary care unit (CCU).

METHODS: This randomized controlled clinical trial study was conducted on 50 patients who were hospitalized with chronic AF in the CCU of Montazeri Hospital, Najafabad, Iran, and had the inclusion criteria. The participants were selected using convenience sampling method, and were randomly divided into experimental (n = 25) and control (n = 25) groups. The experimental group received a rehabilitation program in the form of an educational package and scheduled physical activity of aerobics for 8 weeks, and the control group received CCU routine care. The researcher measured the patients' QOL before and after the intervention using the 36-Item Short Form Health Survey (SF-36).

RESULTS: There was no significant difference in the mean score of total QOL between the control and experimental groups before the intervention (P > 0.050). However, the comparison of the mean score of total QOL after the intervention showed a significant increase in the experimental group (P < 0.050).

CONCLUSION: Aerobic rehabilitation activities are effective on the QOL of patients with chronic AF.

Keywords: Aerobic Exercise, Rehabilitation, Quality of Life, Atrial Fibrillation, Coronary Care Units

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Introduction

Atrial fibrillation (AF) is the most common form of sustained arrhythmia; this indicates an epidemic and growing disease.[1] It is predicted that its prevalence will reach 12.1 million people in 2030 compared to 5.2 million people in 2010, which is mainly due to aging.[2] Its prevalence is 0.3% per year in the United States, and it is, economically, a costly disease.[3] AF is an arrhythmia often independently connected with increased morbidity and mortality. This disease is associated with complications such as ischemic stroke, systemic thromboembolism, heart failure, and increase in hospitalization. Although AF can occur without symptoms, two-thirds of patients experience its symptoms. Management of AF, besides prevention of stroke, mainly stresses symptom control and improvement of quality of life (QOL). This disease has symptoms such as palpitations, shortness of breath, and fatigue.[4]

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Studies conducted on Health-related Quality of Life (HRQoL) in chronic diseases indicate adverse effects on the physical, psychological, and social performance of the patients. Thus, measuring QOL has become important in the treatment of heart diseases.[5]

Most atherosclerotic cardiovascular disease (ASCVD) factors are also connected with AF. Although most guidelines have confirmed these risk factors, no suggestions have been provided in this regard based on diet, exercise, changes in QOL, and initial and secondary preventions.[6] Based on the international guidelines, many patients with AF are advised to increase their physical activity because of their illness.[7,8] Exercise could be an important supplement and, in some cases, an appropriate substitute for drugs or an invasive technique, and is associated with much fewer risks and complications.[9] As a preventive treatment, exercise should be recommended daily, as is done for a pill. In 2013, the American Heart Association made a scientific statement concerning standards of exercise for testing and education. Sports and physical rehabilitation improve risk factors for ASCVD, and have anti-adrenergic, anti-inflammatory, anti-ischemic, anti-arrhythmic, and anti-thrombosis effects.[10] In patients with permanent AF, QOL, rhythm, and symptoms improved after exercise.[11] Moreover, studies have shown that a moderate level of exercise is useful for patients with AF, and plays a protective role for them.[12,13] Changes in lifestyle and the correction of risk factors reduce AF and its recurrence after lactation, and exercise should be included in the management of AF.[14] Aerobic Interval Training (AIT) is an effective and distinctly controlled method. This method has the potency to be done with higher activity, and induce more biological effects compared to regular exercise.[15,16]

During the years of working in a coronary care unit (CCU), the researcher has seen that patients and their families do not have sufficient information and knowledge on the disease, rehabilitation measures, and cardiac rehabilitation. Moreover, sometimes, due to a misconception of heart problems, they are unable to return to normal work and life. Furthermore, considering the insufficiency of existing knowledge, lack of studies in this field, and the different and contradictory results of various studies on the effect of cardiac rehabilitation on the QOL of patients with AF, the present study was planned and conducted. With the aim to assess the effect of cardiac rehabilitation on the QOL in these patients, we compared the scores of QOL in pre- and post-intervention in both the intervention and control groups, as well as between the groups. Our hypothesis was that cardiac rehabilitation can improve the QOL in these patients.

Materials and Methods

This randomized controlled clinical trial study with parallel design included two groups and was conducted in two stages with a pretest-posttest design.

The population consisted of patients, diagnosed with chronic AF and admitted to the CCU of Shahid Mohammad Montazeri Hospital, Najafabad, affiliated to Isfahan University of Medical Sciences, Iran. The sample size was calculated using the sample size calculation formula based[17] on confidence index (Z_1) of 1.96, test power (Z_2) of 0.84, and the margin of error (d) of 0.8. Subjects were selected through convenience sampling and were assigned to study and control groups based on the random numbers table. That number was chosen by using the random number table by closing the eyes by placing a finger on one of the numbers. The direction of movement was predetermined and horizontally to the right, then upwards, and then to the left of the table; each number in the group A or test group was placed and each pair number was entered in group B or control.

The inclusion criteria of the study were age of 30-75 years, stable physical condition, anticoagulants use, lack of pregnancy and breastfeeding, willingness to participate in the study (patient and his/her family), AF with a ventricular response below 100, and lack of presence of angina and valvular diseases. The exclusion criteria were severe resistant hypertension, severe and moderate lung disease, re-admittance after discharge in the past month, the inability to enforce or comply with the study protocol, AF with a rapid ventricular response above 100, coagulation disorders, and AF with a pacemaker or implantable cardioverter defibrillator (ICD). Patients, who had the study inclusion criteria, participated in the research, and in case of their unwillingness to cooperate at any stage of the research and any change in any of the conditions of inclusion at any stage they were excluded. Finally, the study was conducted on 50 patients admitted to the CCU with a diagnosis of chronic AF.

Data collection methods used were observation (arrhythmia, HR) and interviews, and the tools used were the patients' medical records and a questionnaire. The questionnaire consisted of two parts. The first section included a demographic

questionnaire, which had two parts, namely personal information and health and medical characteristics of patients associated with AF. The second section was the 36-Item Short Form Health Survey (SF-36). The questionnaire was completed before and after the intervention for both groups.

To assess QOL, the SF-36 was used which is a standard questionnaire the reliability of which has been approved by Montazeri et al. (Cronbach's alpha = 0.7).[18] This questionnaire consists of two parts, general physical health and mental health. This questionnaire was developed by Ware and Sherbourne, consists of 36 items, and measures 8 domains.[19] These domains include physical function, physical limitation due to physical problems, emotional limitation due to mental problems, vitality, mental health, social function, body pain, and general health. The total score in this questionnaire ranges from 0 to 100, where higher scores show a better QOL. As it was mentioned before, the questionnaire was completed before the intervention (upon admission to the CCU) and at the end of the intervention by the subjects. The average scores of each individual before and after the intervention were compared.

The study was done from 22.10.2016 to 5.6.2017. In the first stage, the participants became acquainted with the nature and manner of the study and gave their written consent for participation, and then, the pretest was administered by having them answer the SF-36.

The experimental group underwent a rehabilitation program in the form of a training package consisting of the aerobic scheduled physical activity in two four-week periods. Aerobic exercises, designed in consultation with a few trained practitioners in this field, physiotherapist, and patient's physician, were conducted 2 sessions a week with light to moderate intensity based on the decision of cardiologist. Each session lasted 60 minutes and consisted of 10 minutes of warm up, 40 minutes of treadmill movements, and 10 minutes of relaxation and cooling. In first 4-week period, the rehabilitation program consisted of exercises with intensity of 40-50 percent of maximum oxygen consumption or heart rate, and maximum metabolic equivalent (MET) of 3.0-5.9; in second 4-week period, the same program was done with intensity of 70-80 percent of maximum oxygen consumption or heart rate, and maximum MET of 8.9. This aerobic physical rehabilitation program was conducted for patients in groups of 5 to 7 individuals. It is noteworthy that there was no coercion to continue the activity during the sessions, and in the event of fatigue and shortness of breath, according to the Borg Scale, the participant would not continue the training.

For the control group, the routine care program was implemented that describes physical rehabilitation as verbal conversation and is more often the response to the patient's questions about the educational and training pamphlet. During this, the control group subjects did not participate in any organized sports programs. For this group, 3 sessions of training were held at the beginning of the course, and on the fourth and eighth weeks. In both groups, to assess the secondary outcome of the intervention that was the effect of cardiac rehabilitation on ejection fraction (EF) of left ventricle in patients with AF, echocardiography was carried out at the time of admission and after the intervention. After completing the exercises, a posttest was performed through both groups answering the questionnaires. The SF-36 was completed once more.

The Kolmogorov-Smirnov test was used to test the distribution of variables. It showed that the distribution of quantitative variables follows a normal distribution. Between-group comparisons were done by conducting the independent sample t-test (for quantitative variables), and paired t-test was used to compare the mean of each of the quantitative variables between before and after the intervention in each group. Discontinuous variables were analyzed using the chi-square test and Fisher's exact test. Continuous variables were presented as mean ± standard deviation (SD) and categorical variables as number and percentage. T-test was used for continuous data analysis and chi-square test for categorical data analysis. All P values of less than 0.05 were considered statically significant. Data were analyzed using SPSS software (version 18, SPSS Inc., Chicago, IL, USA).

The Ethics Committee of Isfahan University of Medical Sciences approved this study with the code IR.mui.rec.1395.3052. Then, the researcher presented the introduction letter from his university to the study group and the subjects, and received written consent forms from all the subjects of the research community for participation in the study. They were all ensured that all information obtained would be kept confidential, and they would be provided with the research results if they wished to have them. The study was registered in the Iranian Registry of Clinical Trials (IRCT) (IRCT2016122727073N2).

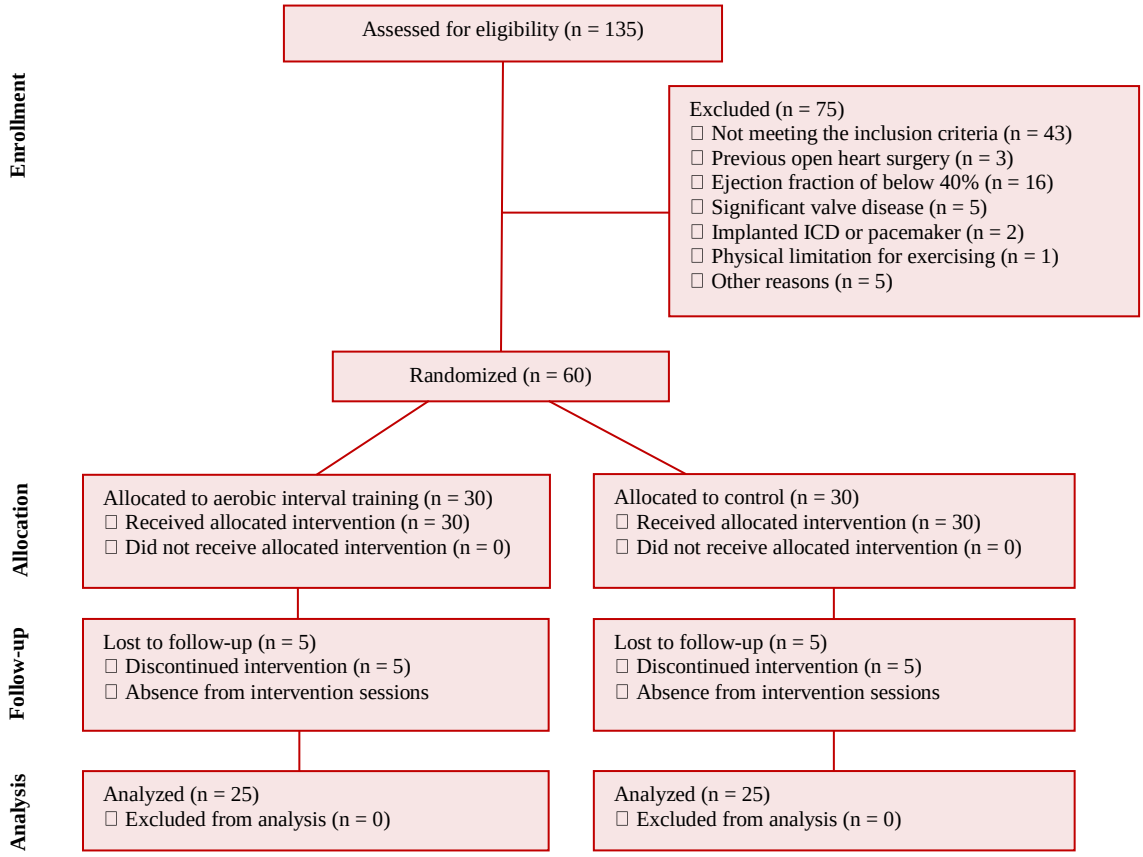

Figure 1. CONSORT diagram of the study

Results

From 135 patients, 60 individuals with inclusion criteria were entered the study.

Of the 60 participants, 50 individuals completed the study; 10 patients (5 from each group) were excluded from the study due to absence in cessions (Figure 1).

The results of this study indicated no significant differences between the control and experimental groups in terms of demographic variables, cardiac risk factors, AF duration, warfarin consumption (mg), signs of AF, quantitative variables of blood pressure, quantitative variables of heart rate, and consumed drugs ($P > 0.050$) (Tables 1 and 2).

The mean score of QOL in the experimental group before the intervention was 53.2 ± 3.2. After the intervention, the overall mean of QOL was 72.62 ± 2.50. Paired t-test showed that in the experimental group, the mean scores of overall QOL and its domains, except mental health, statistically increased after the intervention ($P < 0.050$) (Table 3).

Table 1. The mean of some demographic and clinical characteristics variables in the two groups

Variable	Experimental group (n = 25)	Control group (n = 25)	P
	Mean ± SD	Mean ± SD	
Age (year)	57.2 ± 7.4	59.9 ± 7.5	0.200
Weight (kg)	78.1 ± 13.0	75.4 ± 8.3	0.380
Height (cm)	165.9 ± 8.6	165.4 ± 7.9	0.840
Abdominal circumference (cm)	96.7 ± 8.3	95.7 ± 6.3	0.650
BMI (kg/m^2)	28.4 ± 4.6	27.6 ± 2.7	0.440
Atrial fibrillation duration (year)	2.2 ± 1.3	2.6 ± 2.0	0.420
PT	23.0 ± 5.6	24.7 ± 2.7	0.180
INR	1.9 ± 0.5	1.9 ± 0.3	0.630
EF	54.0 ± 6.3	50.9 ± 7.3	0.110

BMI: Body mass index; PT: Prothrombin time; INR: International normalized ratio; EF: Ejection fraction; SD: Standard deviation

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Table 2. Frequency of some clinical characteristics and past medical history variables in the two groups

Variable	Experimental group (n = 25)	Control group (n = 25)	P
	n (%)	n (%)	
Sex (male)	10 (40)	13 (52)	0.400
Medical history			
Hyperlipidemia	5 (20)	8 (32)	0.330
Hypertension	19 (76)	20 (80)	0.730
Diabetes	3 (12)	5 (20)	0.350*
Smoking	2 (8)	4 (16)	0.330*
Overweight*	13 (52)	12 (48)	0.780
Clinical symptoms			
Dyspnea	16 (64)	18 (72)	0.540
Palpitation	16 (84)	20 (80)	0.210
Dizziness	9 (36)	11 (44)	0.560
Weakness	11 (44)	10 (40)	0.770
No symptoms	2 (8)	3 (12)	0.500*
Medication at baseline			
Antiplatelet	12 (48)	8 (32)	0.250
Flecainide	1 (4)	0 (0)	0.500*
Amiodarone	2 (8)	3 (12)	0.500*
Sotalol	0(0)	0 (0)	> 0.990
Digoxin	5 (20)	7 (28)	0.510
Calcium Blocks	7 (28)	3 (12)	0.160
β-Blockers	9 (36)	6 (24)	0.350
ACE I-ARB	14 (56)	16 (64)	0.560
α-Blocking agents	7 (28)	9 (36)	0.540
Statin	7 (28)	9 (36)	0.500
Warfarin	24 (96)	25 (100)	0.500*

Overweight: Body mass index (BMI) > 25 kg/m^2
ACE-Is: Angiotensin converting enzyme inhibitors; ARBs: Angiotensin receptor blockers
* Fisher's exact test; Other items: Chi-square test

The mean score of the QOL in the control group before the intervention was 51.9 ± 2.8. After the study, the overall mean score of QOL was 52.9 ± 2.7. Paired t-test showed that in the control group, the mean score of overall QOL and its domains did not have significant changes after the intervention compared to before it (P > 0.050) (Table 3).

Table 3. The mean of total quality of life score and its domains before and after the intervention in the two groups

Aspects of quality of life	Group	Before the intervention	After the intervention	P*	Mean differences	P**
		Mean ± SD	Mean ± SD		Mean ± SD	
Physical function	Experimental	62.5 ± 4.10	88.9 ± 1.7	< 0.001	26.4 ± 3.1	< 0.001
	Control	61.2 ± 4.30	59.7 ± 4.3	0.450	-1.5 ± 1.9	
Limitation due to physical problems	Experimental	40.4 ± 5.90	66.0 ± 6.3	< 0.001	25.6 ± 3.9	< 0.001
	Control	37.0 ± 6.50	35.0 ± 7.1	0.630	-2.0 ± 4.1	
Limitation due to mental problems	Experimental	39.5 ± 6.60	76.0 ± 7.1	< 0.001	36.5 ± 5.9	< 0.001
	Control	36.0 ± 7.90	36.0 ± 8.1	> 0.990	0 ± 0	
Vitality	Experimental	60.4 ± 3.40	67.4 ± 3.2	0.020	7.0 ± 2.8	0.040
	Control	57.2 ± 3.70	56.4 ± 3.3	0.760	-0.8 ± 2.6	
Mental health	Experimental	58.1 ± 4.70	62.1 ± 4.2	0.340	4.0 ± 1.4	0.490
	Control	57.9 ± 3.90	58.4 ± 3.2	0.870	0.5 ± 2.9	
Social health	Experimental	62.5 ± 4.02	80.5 ± 3.5	< 0.001	18.0 ± 3.2	< 0.001
	Control	60.8 ± 2.90	62.5 ± 3.5	0.580	1.7 ± 3.1	
Body pain	Experimental	62.0 ± 4.40	78.8 ± 2.8	0.001	16.8 ± 4.4	0.008
	Control	60.5 ± 3.70	61.0 ± 3.7	0.900	0.5 ± 3.9	
Overall health	Experimental	43.4 ± 3.80	55.9 ± 4.4	0.006	12.5 ± 4.2	0.010
	Control	44.8 ± 2.90	44.0 ± 2.4	0.780	-0.8 ± 2.8	
Total quality of life score	Experimental	53.2 ± 3.20	72.6 ± 2.5	< 0.001	19.4 ± 1.8	< 0.001
	Control	51.9 ± 2.80	52.2 ± 2.7	0.800	0.3 ± 1.4	

* Paired samples t-test; ** Independent samples t-test; SD: Standard deviation

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The comparison of the mean changes in the overall QOL score and its domains after and before the intervention in the two groups is presented in table 3. Independent t-test showed that after the intervention, the mean total score of QOL and its domains in the experimental group, except mental health, were significantly more compared to control group ($P < 0.050$). However, the mean value of mental health score changes did not differ significantly between the two groups ($P > 0.050$).

Based on our findings, in experimental group, the mean EF was 54.0 ± 6.3 percent before the intervention; which changed to 57.1 ± 5.6 percent after it. Paired t-test showed that EF significantly increased in this group ($P < 0.050$). But in control group, the mean EF was 50.9 ± 7.3 and 50.8 ± 7.5 percent before and after the intervention, respectively, which showed no significant difference ($P > 0.050$). Moreover, the mean EF was not significantly different between the two groups before the intervention ($P < 0.050$).

Discussion

The existence of no differences between demographic variables and QOL before the intervention in the two groups suggests appropriate homogeneity between the groups. A statistically significant difference was not observed in QOL the end of the intervention in the control group. However, in the test group, improvement was evident in all aspects of QOL, excepting mental health. According to the findings, the QOL of patients with AF improved significantly ($P < 0.050$) after rehabilitation, which was consistent with the results of Malmo et al. in Norway.[17] They indicated that aerobics reduces AF load and improves QOL at physical and mental health levels. However, in their study, all aspects of QOL had increased in the experimental group, except for the level of mental health and euphoria that was higher in the control group.[19] Moreover, the result of another review by Santos-Lozano et al. in the United States indicated that sports interventions in patients with AF increase VO_2 peak and QOL in these patients.[20] Another study by Conraads et al. Conducted in Belgium showed that 12 weeks of aerobic exercise had a significant effect on VO_2 peak, QOL, and some of the risk factors for cardiovascular diseases ($P < 0.001$).[21] Moreover, the clinical trial paper by Osbak et al. in Denmark showed that muscle strength, exercise capacity, and QOL increase with exercise in people with AF.[22] In another study in Canada, Giacomantonio et al. showed that moderate physical activity can improve the capacity for daily living activities, and overall QOL in people with AF.[23] Furthermore, in a meta-analysis conducted in Texas in 2016 on atherosclerosis and AF, Mohanty et al. showed that an average amount of physical activity reduced the risk of AF and increased QOL in both women and men.[24]

In this regard, contradictory results have also been reported in studies. An example is a review study conducted by Risom et al. in Denmark on cardiac rehabilitation for adults with AF. Given the small number of patients and the random results, they could not examine the actual impact of exercise-based cardiovascular rehabilitation on mortality or complications and their findings suggested no clinically relevant effect on QOL, but an increase in physical capacity as a result of exercise.[25] This study was inconsistent with the present study findings due to the small number of patients and randomized results. Moreover, Dakei et al. conducted a study in Kermanshah, Iran, entitled "The Effect of Two Resistance and Aerobic Protocols on Performance Capacity and Quality of Life in Male Patients after Myocardial infarction".[26] Their results showed that in terms of QOL, no significant difference existed between the 3 groups of resistance, endurance, and control over time. This may be due to the low volume of samples (24 men in 3 groups of 8 individuals).[26]

The results of most of the above studies are in line with the present study, indicating that aerobic rehabilitation can improve the QOL of patients with AF. The learning of cardiac rehabilitation by nurses is easy as they pass academic education at universities, and the implementation of these activities in the clinic does not have high costs. Thus, training these activities to the nurses working in cardiovascular departments can improve the QOL of patients and their physical and mental health indices. Moreover, it is possible to improve patients' QOL by educating patients about the principles of rehabilitation and the gradual progression of activities. Moreover, by doing so, complications caused by lack of awareness and the patient's non-observance of appropriate activities at the time of recovery can be prevented after discharge, resulting in a reduction in frequent hospitalization and related costs. Nevertheless, performing these rehabilitation activities requires the training of patients and monitoring of the correct functioning of rehabilitation activities.

Of the limitation of this study was the individual differences in patients that could be effective on the

QOL of individuals, which the researcher could not control. In addition, the results are only generalizable to those who refer to the CCU.

Finally, the researchers recommend that a similar study be conducted with more participants and for a longer duration.

Conclusion

The results of this study, as well as other studies conducted in the field of rehabilitation of patients with AF, suggest the improvement of QOL through the performance of cardiac rehabilitation intervention. Thus, given the increase in the aging population, the increase in the rate of AF, and the role of nurses in promoting health and empowerment of patients with the help of these programs, it is necessary to pay more attention to the rehabilitation of these patients.

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Conflict of Interests

Authors have no conflict of interests.

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The association of anthropometric indices and cardiac function in healthy adults

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Original Article

Abstract

BACKGROUND: Obesity is a major risk factor for many diseases including cardiovascular diseases (CVDs). Recently, it has been shown that upper body obesity can predict CVDs per se. In this study, we aimed to determine the association between indicators of upper body obesity and echocardiographic indices.

METHODS: In this cross-sectional study conducted in Hajar Hospital in Shahrekord, Iran, from March to August 2014, 80 healthy adults were included. Participants' neck circumference (NC), waist circumference (WC), body mass index (BMI), and blood pressure were measured. Echocardiography was performed for all participants, and echocardiographic indices such as early (E') and late (A') diastolic tissue velocity, early (E) and late (A) transmitral flow velocity, E/E' ratio, pulmonary arterial pressure (PAP), and left atrial volume (LAV) were recorded. The association between these indices were investigated using bivariate Pearson correlation coefficient.

RESULTS: For men, NC had a significant correlation with LAV, systolic blood pressure (SBP), diastolic blood pressure (DBP), PAP, and A', and a negative correlation with E′. WC had a significant correlation with LAV, SBP, and PAP, and a negative correlation with E′, while BMI had a significant correlation with LAV, PAP, SBP, A, and A'. For women, NC had a significant positive correlation with LAV, A, ejection fraction (EF), SBP, PAP, and A', and a negative correlation with E′ and E/E′. WC had a significant positive correlation with LAV, DBP, PAP, A, A', and a negative correlation with E′, while BMI had a significant correlation with LAV, EF, SBP, PAP, E', A, and A'.

CONCLUSION: The positive correlation of NC with SBP, A, and A', as well as NC, WC, and BMI with LAV and PAP in both sexes, and the negative correlation of NC with E′ show the importance of these measures in estimation of metabolic and cardiovascular risk factors.

Keywords: Obesity, Risk Factors, Cardiovascular Diseases

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Introduction

Insight into echocardiographic parameters in the general population may facilitate early recognition of ventricular dysfunction, and reducing the population's morbidity and mortality due to heart failure.[1] Echocardiographic parameters can predict cardiovascular events in several clinical settings.[2] For decades, metabolic syndrome including obesity has been a major risk factor for cardiovascular diseases (CVDs).[3] Recently, the results of observational studies have stated that upper body obesity has a significant association with CVD, hyperinsulinemia, diabetes mellitus (DM), and hypertriglyceridemia independently.[4-7] It has been shown that upper body obesity is correlated with CVDs and metabolic syndrome more than general obesity and body mass index (BMI).[8]

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There are many different ways to assess upper body obesity. Although imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT), and double X-ray are known as the best methods for estimation of upper body obesity, the excessive costs and adverse effects of radiation has disabled using them as appropriate screening methods. Thus, anthropometric measurements, such as measuring waist circumference (WC), waist to hip ratio, waist to height ratio, and neck circumference (NC), have been suggested as commonly-used simple and non-invasive methods for estimation of upper body obesity.[9-13] Evidence suggests NC as an independent indicator of upper body obesity, associated with metabolic syndrome factors and CVDs.[14] As some studies have shown the variation of upper body obesity based on the population's ethnicity and race for predicting DM and CVD,[4] and this association has not been studied in Iranian population, in this study, we aimed to determine the association between upper body anthropometric measurements and cardiac diastolic dysfunction in people with normal ejection fraction (EF).

Materials and Methods

This cross-sectional study was performed in Hajar Hospital, Shahrekord, Iran, from March to August 2014. Eighty participants were selected from those who referred to the cardiovascular clinics, only to accompany a patient. The participants' age ranged from 35 to 50 years, and all were invited to the study after reading and signing the written informed consent form. Any patient with any of the following criteria was excluded from the study: sleep apnea, DM, neck deformity, lymphadenopathy, thyroiditis, thyromegaly, hypertension, left ventricular hypertrophy, EF < 50%, and valvular heart diseases.

The participants' demographic characteristics were recorded on the study checklist, including positive family history of cardiac disorders and risk factors (like DM, smoking, and hypertension). Participants' height and weight were measured by the researcher with precision of 1 mm and 100 grams, respectively, while the person was wearing light clothing and no shoes; BMI was calculated by dividing weight (in kilograms) by squared height (in meters). The participants were asked to stand straight with their head positioning in Frankfort horizontal level, and a tape measure was placed right under laryngeal prominence around the neck in order to measure the NC. WC was measured while the participants stood up with no clothes, and a tape measure was placed between the last rib and the iliac crest. Systolic (SBP) and diastolic (DBP) blood pressures were measured using an oscillometric approach, and an appropriate cuff was used based on the participants' right arm circumflex. Before measuring BP, all participants relaxed for at least 10 minutes, and BP was measured only once.

Echocardiography was performed using a Vivid 3 Ultrasound Machine (cardiac ultrasound images). Cardiac function parameters such as EF, early diastolic mitral annular (E'), and late diastolic (A') velocities were measured by Doppler Tissue Imaging (DTI), and the E/E' ratio was computed. Recorded mitral inflow measurements included early mitral filling (E) and late (A) velocities, E/A ratio, deceleration time of E velocity, and duration of A.[15] Left atrial volume (LAV) was also measured using prolate ellipse method ($D_1 \times D_2 \times D_3 \times 0.523$).[16] Systolic pulmonary artery pressure (SPAP) was measured using tricuspid regurgitation and Bernoulli formula.[16] All the measurements were performed by a single investigator and echocardiography assessments were carried out by a fixed individual cardiologist.

All data were analyzed using SPSS software (version 20.0, IBM Corporation, Armonk, NY, USA). Numerical measurements were normally distributed and reported as mean ± standard deviation (SD). Two samples t test was used to compare mean differences of cardiac function parameters between men and women participants. Pearson correlation coefficient was calculated to evaluate association between anthropometric measures (NC and WC) and cardiac function parameters. To avoid multiplicity problem, Bonferroni correction was applied. P-values of less than 0.050 were considered statistically significant.

Results

Eighty subjects (54 women and 26 men) with mean (± SD) age of 40.0 (± 8.1) years participated in this study. None of the participants were a known case of CVDs or DM. The mean values of BMI, NC, WC, and BP are presented in table 1. Independent t test showed that the difference between the mean age and BMI of the women and men were not statistically significant (P > 0.050). But, there were significant differences between men and women in terms of other variables such as height and weight, NC, and WC (P < 0.050 for all).

The correlation of NC, WC, and BMI with echocardiographic variables and BP was tested for men and women, and the results of which are shown in tables 2 and 3, respectively.

Table 1. The demographic characteristics of participants

Variable	Men (n = 26)	Women (n = 54)	Total (n = 80)	P
Age (year)	41.5 ± 7.3	39.2 ± 8.3	40.0 ± 8.1	0.227
Height (cm)	171.8 ± 9.7	160.3 ± 6.1	40.0 ± 8.1	0.003
Weight (kg)	82.3 ± 15.1	71.2 ± 12.7	40.0 ± 8.1	0.001
NC (cm)	40.1 ± 3.4	35.6 ± 3.1	37.1 ± 3.8	0.023
WC (cm)	94.9 ± 12.5	83.5 ± 11.5	87.2 ± 12.9	0.008
SBP (mmHg)	120.9 ± 6.6	114.3 ± 7.5	116.5 ± 7.8	0.040
DBP (mmHg)	80.7 ± 5.9	76.2 ± 5.5	77.7 ± 6.0	0.001
BMI (kg/m^2)	27.8 ± 4.4	27.7 ± 4.8	27.7 ± 4.6	0.879

Data are reported as mean ± standard deviation (SD).
NC: Neck circumference; WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index

According to table 2, for men, NC had a positive correlation with LAV, SBP, pulmonary arterial pressure (PAP), A', and DBP, and a negative correlation with E'. WC had a significantly positive correlation with LAV, SBP, and PAP, but a negative correlation with E'. BMI had a significantly positive correlation with LAV, PAP, SBP, A, and A'.

According to table 3, for women, NC had a positive correlation with LAV, A, EF, SBP, PAP and A' and a negative correlation with E' and E/E'. WC had a significant correlation with LAV, DBP, PAP, A, and A' and a negative correlation with E'. BMI had a significant positive correlation with PAP, E', LAV, EF, SBP, A, and A'.

Discussion

The results of this study indicated that NC was significantly correlated with LAV, SBP, DBP, and PAP, which shows that all of them can be used as predictors of probable myocardial diastolic dysfunction. WC and BMI were also correlated with parameters, predicting the probability of myocardial dysfunction, but they both had a rather weaker correlation, compared to NC. Preis et al. showed that NC could be a marker of fat deposit, associated with great potential risk of CVDs.[8] Ben-Noun and Laor also recognized the positive association between NC and some features of metabolic syndrome, predicting the risk of CVDs.[14] The results of both studies are in line with that of ours.

In our study, NC was associated with SBP and DBP. In previous studies, the relationship between NC and BMI or WC has been addressed in order to show the relation between NC and metabolic syndrome.[4-8] Our study is in line with these statements, but adds the correlation of NC, another item of the metabolic syndrome, with SBP and DBP. This indicates that NC can be a potent criterion in metabolic syndrome and probable CVDs, which could be associated with the aforementioned matters. In our study, there was a strong negative correlation between NC and E', and a weak negative correlation between E' with WC and BMI, which shows that E' can be a better predictor for cardiac diastolic dysfunction than BMI and WC.

Table 2. The correlation of neck circumference (NC), waist circumference (WC), and body mass index (BMI) with echocardiographic parameters in men

Variable	NC (cm)		WC (cm)		BMI (kg/m^2)	
	R	P	R	P	R	P
LAV (ml)	0.968	< 0.001	0.668	< 0.001	0.641	< 0.001
EF (%)	0.060	0.298	-0.124	0.137	0.103	0.365
SBP (mmHg)	0.442	< 0.001	0.387	< 0.001	0.291	0.009
DBP (mmHg)	0.239	0.030	0.143	0.200	0.133	0.239
PAP (mmHg)	0.777	< 0.001	0.679	< 0.001	0.500	< 0.001
A (cm/s)	0.469	0.008	0.084	0.342	0.337	0.046
A' (cm/s)	0.612	< 0.001	0.185	0.182	0.379	0.029
E' (cm/s)	-0.410	< 0.001	-0.383	< 0.001	-0.269	0.008
E/E'	-0.015	0.447	-0.024	0.416	0.088	0.437

P-values of less than 0.050 were considered as statistically significant.
NC: Neck circumference; WC: Waist circumference; BMI: Body mass index; LAV: Left atrial volume; EF: Ejection fraction; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PAP: Pulmonary arterial pressure; A: Peak velocity of mitral inflow during atrial contraction, A′: Late diastolic mitral annular velocity, E: Peak velocity of mitral inflow during early filling phase; E′: Early diastolic mitral annular velocity

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Table 3. The correlation of neck circumference (NC), waist circumference (WC), and body mass index (BMI) with echocardiographic parameters in women

Variable	NC (cm)		WC (cm)		BMI (kg/m^2)	
	R	P	R	P	R	P
LAV (ml)	0.935	< 0.001	0.541	0.008	0.722	0.030
EF (%)	0.270	0.024	-0.120	0.465	0.277	0.021
SBP (mmHg)	0.290	0.017	0.182	0.094	0.354	0.004
DBP (mmHg)	0.134	0.167	0.143	0.024	0.136	0.164
PAP (mmHg)	0.289	0.017	0.693	0.003	0.596	< 0.001
A (cm/s)	0.555	< 0.001	0.446	0.002	0.472	0.002
A' (cm/s)	0.589	0.030	0.489	0.003	0.372	0.003
E' (cm/s)	-0.382	< 0.001	-0.234	0.038	0.399	< 0.001
E/E'	-0.123	0.002	-0.075	0.294	0.207	0.067

P-values of less than 0.050 were considered as statistically significant.
NC: Neck circumference; WC: Waist circumference; BMI: Body mass index; LAV: Left atrial volume; EF: Ejection fraction; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PAP: Pulmonary arterial pressure; A: Peak velocity of mitral inflow during atrial contraction, A′: Late diastolic mitral annular velocity, E: Peak velocity of mitral inflow during early filling phase; E′: Early diastolic mitral annular velocity

For many years, BMI has been used to evaluate obesity, as a risk factor of CVDs. Also many studies have considered central obesity and WC as important markers for predicting CVDs.[17-20] Similarly, the results of our study confirmed the association between WC with different echocardiographic parameters and SBP.

Looking to the whole picture reveals a stronger association between NC and echocardiographic parameters, compared to general obesity and WC. This is in line with studies that present upper body fat deposit as a better predictor of CVDs.[6-22]

In our study, there was no significant correlation between NC and EF in neither sexes. This finding may be due to including only participants with EF of more than 50%. Thus, further studies are needed to evaluate the relation between NC and EF in participants with a wide range of EFs. Similarly, there was no significant correlation between NC and E/E' in men. The inclusion of participants with EF of more than 50% could be the reason for this finding; as E/E' is mainly impaired in advanced diastolic dysfunction, whereas in this study all cases were healthy, and no abnormality in E/E' ratio was expected.

The cross-sectional study design is main drawback of our findings, as it is not possible to discuss the causal relationship between anthropometric indices and cardiac function. Furthermore, the fact that the studied participants came from a healthy population, could be either considered as a positive point or a limitation. Many patients with CVDs suffer from obesity and metabolic syndrome concurrently, and we excluded patients with CVD or DM to decrease the risk of bias in our study. On the other hand, such an inclusion criteria could be a limitation for studying the association between NC and some pathological features such as EF and E/E'.

Conclusion

In this study, it was observed that NC, WC, and BMI had a significant correlation with LAV and PAP, both in men and women. NC had a significant correlation with SBP in men and women, and also BMI had significant correlation with A in both sexes. These findings imply that these measures may help refine evaluations of metabolic and cardiovascular risk factors. Accordingly, regular NC, WC, and BMI screening is recommended as an easy and effective way of assessing body weight for prevention of weight-related diseases in men and women.

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Conflict of Interests

Authors have no conflict of interests.

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Comparison of the incidence and severity of delirium and biochemical factors after coronary artery bypass grafting with dexmedetomidine: A randomized double-blind placebo-controlled clinical trial study

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Original Article

Abstract

BACKGROUND: One of the most common postoperative problems, such as open heart surgery, is delirium, which is responsible for increased mortality and morbidity. Therefore, it is necessary to find a way to cure this disease. The purpose of this study was to assess the effect of dexmedetomidine administration on the prevention of delirium after coronary artery bypass grafting (CABG) surgery.

METHODS: This randomized double-blind placebo-controlled clinical trial was performed on 88 patients (44 in the intervention group and 44 in the control group) undertaking CABG surgery. The intervention group was subcutaneously treated with doses of 1 µg/kg of dexmedetomidine for 10 minutes, and 0.2-0.7 µg/kg in hour infusion was applied. The control group underwent normal saline infusion as a placebo. Chi-square and analysis of variance (ANOVA) tests were used to compare the data.

RESULTS: Administration of dexmedetomidine in intervention group significantly decreased delirium (P = 0.040) and delirium intensity (P = 0.001). Moreover, patients treated with dexmedetomidine had more stability in laboratory variables and vital signs, and also the duration of hospitalization in these patients was significantly lower than control group (P = 0.002).

CONCLUSION: Considering the efficacy of dexmedetomidine on preventing the incidence and severity of delirium and reducing mortality and morbidity, it is recommended that another study with the larger sample size, with different doses and different prescribing methods be conducted to better understand the effect of this drug and achieve a safe dose with maximum efficacy.

Keywords: Delirium, Coronary Artery Bypass Grafting, Dexmedetomidine

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Introduction

One of the most common problems after surgery including open heart surgery is delirium, which causes increased mortality and morbidity.[1-4] Delirium is a cognitive-behavioral disorder and its causes after surgery include change in the normal nervous activity, secondary to systemic disorders including impaired cholinergic system. Although postoperative delirium may occur in all individuals, however, some people are at high risk including older people (> 70 years of age), those with diabetes, smoking and narcotics, lung surgery, history of high blood pressure, pulmonary disease, atrial fibrillation (AF), and electrolyte disturbances including sodium and hypoglycemia.[5,6]

According to researches, the prevention and treatment of fast-acting delirium after surgery can reduce mortality and morbidity.[7] Several drugs have been designed for delirium after heart surgery including endonestrone, haloperidol, ketamine, rivastigmine and dexmedetomidine, midazolam, and morphine.

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The purpose of the prescribing drugs is sedation, prevention, and treatment of delirium, blood pressure control, rapid patient extubation, reduction of cognitive impairment, and consequently reduced mortality and morbidity.

Selective treatment of delirium after surgery is haloperidol.[1] However, a specific drug is not a selective drug for the prevention of delirium, and many studies have been conducted on various drugs to evaluate the effectiveness of the treatment of delirium after surgery. The purpose of this research is to find a more effective drug with less complication. Haloperidol and dexmedetomidine are two of the most effective drugs in the prevention of delirium that have been studied in the studies. One of the studies in this field was conducted by Reade et al., comparing dexmedetomidine and haloperidol, which showed that intensive care unit (ICU) duration and delirium induced by dexmedetomidine administration was less than haloperidol.[7] In a study by Urden et al., comparing dexmedetomidine and haloperidol, the duration of hospitalization in the ICU with dexmedetomidine was lower than haloperidol, but there was no difference in the incidence of delirium[8]

Considering the high prevalence of delirium after surgery including cardiac surgery and the preventive effect of dexmedetomidine on mortality and morbidity, and according to research conducted in comparison it with other drugs and the contradictory results of the studies, the aim of this study is to assess the efficacy of dexmedetomidine in preventing and controlling delirium after cardiac surgery.

Materials and Methods

This was a randomized double-blind clinical trial. In order to prevent possible errors and biases during data collection and evaluation, clinical and analytic caregivers were unaware of the assignment of the study group. Subjects of this study included all patients undergoing coronary artery bypass grafting (CABG) surgery who referred to Shahid Chamran Hospital in Isfahan, Iran, in 2016-2017. The sample size of this study was calculated using the sample size estimation formula for outbreak studies. The 95% confidence interval (CI) level was considered, the prevalence of agitation after CABG surgery was considered to be 0.5, which included 44 persons (in each group). The probability of loss of subjects in each group would be 50 people. Sampling was done in a non-probable and randomized manner (Figure 1).

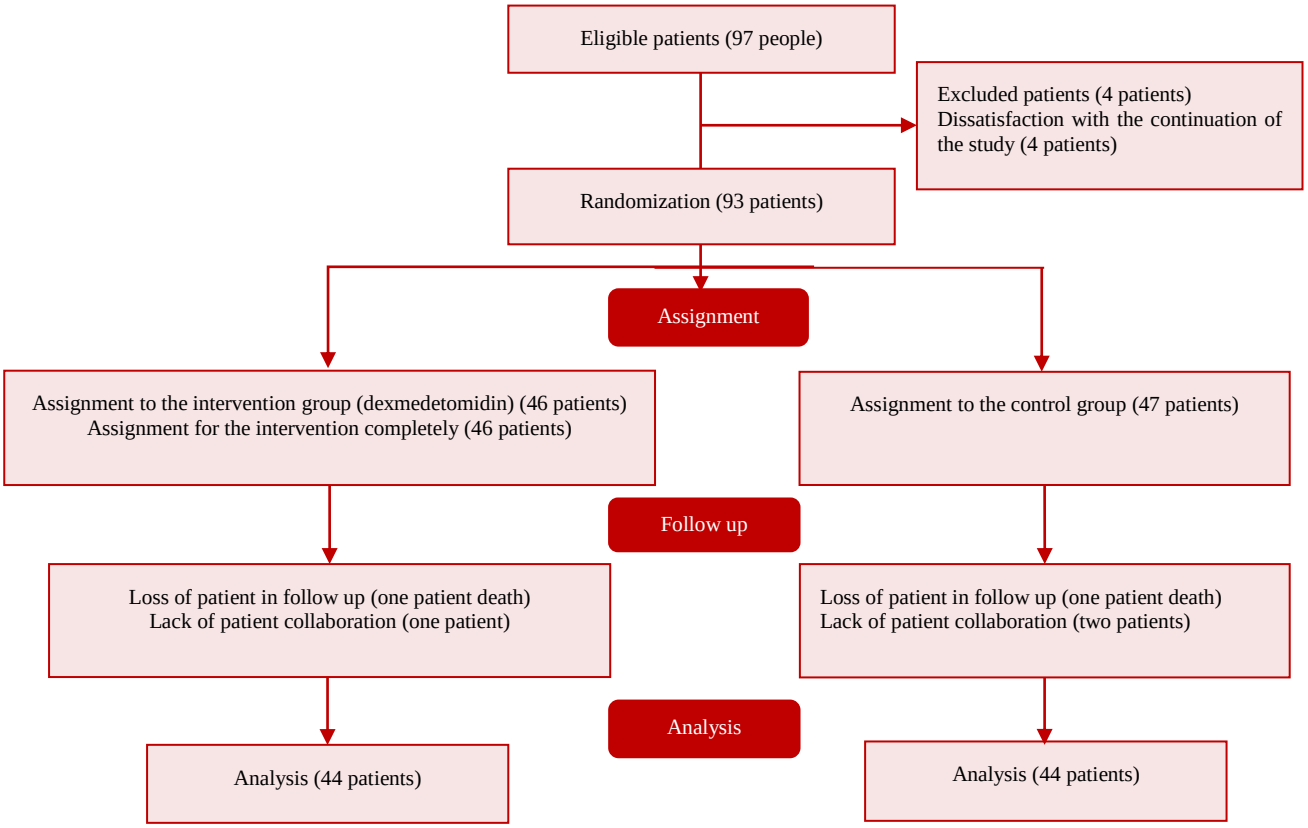

Figure 1. Study flowchart (CONSORT format)

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The inclusion criteria included living patients aged 40-80 years who were candidates for CABG surgery and approved to participate in the study and had no history of mental illness and dementia. Exclusion criteria included a person's lack of cooperation, defect in the examined data, the need for re-operation due to hemorrhage after entering ICU, excessive sensitivity to haloperidol and phenothiazines, having Parkinson's disease (resting shaking) and weakness in the central nervous system (CNS), glaucoma, history of seizure, and receiving anti-seizure, anti-Parkinson, or lithium medication.

After obtaining permission from the Medical Ethics Committee of Isfahan University of Medical Sciences, Isfahan City, and the registration of the trial with IRCT20171104037209N1 code number at the Iranian Center for Clinical Trials and performing the necessary coordination, candidates for CABG surgery referring to Shahid Chamran Hospital were selected. After obtaining their informed consent to participate in the study, their demographic information including age, sex, weight, level of education, history of diabetes [diagnosed by a medical history and taking diabetic drugs or high blood glucose (≥ 126)], hypertension disease (diagnosed by a medical history and taking blood pressure drugs), addiction to cigarette, narcotics and alcohol, history of using psychiatric drugs, and the personality type [that is divided into two categories A and B which having personality type A was considered as a risk factor for cardiovascular disease (CVD) due to being aggressive, impatient, and competitive; this variable is evaluated by a completed questionnaire Ganji[9] was prepared and recorded in a data collection form. Additionally, the newest amount of laboratory variables including hemoglobin (Hb) (g/dl), white blood cell (WBC) (/mm^3), blood urea nitrogen (BUN) (mg/dl), creatinine (mg/dl), sodium (mg/l), and potassium (mg/l) (measured with kits of Parsa and ParsAzmun and electrolyte analyzer device) before surgery was extracted from the case and recorded. Patients were assigned in two groups of intervention and control using random allocation software. The intervention group received 1 µg/kg doses of dexmedetomidine immediately within 10 minutes and the infusion of 0.2-0.7 µg/kg/h of dexmedetomidine in a volume equivalent to 50cc by the syringe pump, and the control group underwent infusion of normal saline with the same volume by the syringe pump as placebo. In the event of agitation, both control and intervention groups received haloperidol (0.5 mg intramuscular) and in the intervention group, the administration of dexmedetomidine continued until that the conditions for separating the patients from the ventilator were obtained.

The patients were followed up to 72 hours after the operation and the daily amounts of Hb (g/dl), WBC (/mm3), BUN (mg/dl), creatinine (mg/dl), sodium (mg/l), and potassium (mg/l) up to 72 hours after surgery were recorded. The incidence of delirium, delirium intensity, prescription dose, duration of administration, side effects, duration of hospitalization in ICU, sedation rate, and duration of intubation was extracted and recorded in each patient's profile.

The frequency of occurrence of post-operative agitation was determined using the Richmond Agitation-Sedation Scale (RASS) and patient's review every 24 hours for up to 72 hours. A RASS questionnaire consists of 10 levels, which according to a researcher's clinical evaluation categorizes patients from aggressive to unresponsive to stimuli levels. Then, patients were divided into two groups of A and B (aggression and non-aggression) based on this criterion. The validity and reliability of the questionnaire was confirmed,[10,11] and the percentage of delirium occurrence was determined by treatment group. Based on the RASS criteria, the score more than +2 was considered as post-operative incidence of agitation in the patient.

The Confusion Assessment Method for ICU (CAM-ICU) was also studied in this study. This tool was introduced by Inouye et al.[12] and Thomason et al.,[13] and has been proven to be effective in detecting confusion and monitoring of delirium in ICU patients. Moreover, the validity of the Persian version of this tool with a specificity of 99.1% and sensitivity of 66.7% was confirmed.[14]

All patients' information including demographic factors and laboratory findings were recorded in a checklist made by the registrar and entered into SPSS software (version 18, SPSS Inc., Chicago, IL, USA). To compare the mean of quantitative variables [the normal distribution of them investigated by the Kolmogorov-Smirnov test (K-S test)] independent t-test was used and to compare the frequency distribution of nominal qualitative variables, chi-square test and if necessary, Fisher's exact test were used. Moreover, to compare the frequency distribution of ordinal qualitative variables the Mann-Whitney U test was used.

Results

Among 88 patients who were candidates for open heart surgery, 72 (81.8%) were men and 16 (18.2%)

were women, the mean age of the subjects was 61.55 ± 4.80 years. In our study, it was found that the overall prevalence of delirium in patients undergoing open heart surgery was 13 patients (14.77%).

Independent t-test revealed that there was no significant difference in mean age (P = 0.810) and ejection fraction (EF) percent (P = 0.340) between the two groups. The Mann-Whitney test showed that there was no significant difference in the level of education between the two groups (P = 0.490). Also, chi-square test showed that there was no significant difference in the distribution of personality type between two groups (P = 0.590). Chi-square test showed that there was no significant difference between the two groups in high blood pressure (P = 0.520), smoking (P = 0.370), alcohol consumption (P = 0.250), and narcotics use (P = 0.190) (Table 1).

Fisher's exact test showed that there was no significant difference in incidence of arrhythmias between the two groups before ICU (P = 0.340) and after ICU (P = 0.330).

There was no significant difference between the mean pH before of the pump until the first day of the ICU between the two groups (P > 0.050), but in the second day (P = 0.002) and third day (P = 0.020) of the ICU, it was significantly higher in the control group than the dexmedetomidine group.

The mean O_2 after the pump (P = 0.030) in the dexmedetomidine group and in the first day of ICU (P = 0.001) in the control group was significantly higher than the other group; but in other times, there was no significant difference between the two groups (P > 0.050). The mean of CO_2 during the pump (P = 0.007), the first day (P = 0.010), and the second day (P = 0.020) of the ICU in the dexmedetomidine group was significantly higher than the control group but at other times there was no significant difference between the two groups (P > 0.050). The mean HCO_3 before the pump (P = 0.030) in the control group and at the first day of the ICU (P = 0.010) in the dexmedetomidine group was significantly higher than the other group, but it did not differ significantly between the two groups at other times (P > 0.050). The mean base excess (BE) before the pump (P = 0.005) and on the second day (P = 0.004) and the third day (P = 0.030) of the ICU in the control group was significantly higher than dexmedetomidine group, but at other times no significant difference was observed between the two groups (P > 0.050).

After Bartlett's test of sphericity, the repeated measures test showed that the effect of time on pH, O_2, CO_2, HCO_3, and BE was significant (P < 0.001). But the effect of the group has only been significant on pH (P = 0.010), CO_2 (P = 0.020), and BE (P = 0.020).

Table 1. Frequency distribution of demographic factors and risk factors in the two groups of dexmedetomidine and control

Variable	Control group (n = 44)	Dexmedetomidine group (n = 44)	P
	Mean ± SD	Mean ± SD	
Age (year)*	61.30 ± 8.90	61.80 ± 7.90	0.810
EF percent*	49.10 ± 8.20	50.80 ± 8.10	0.340
	n (%)	n (%)	
Diabetes**	21 (47.7)	21 (47.7)	> 0.990
Hypertension**	17 (38.6)	20 (45.5)	0.520
Smoking**	13 (29.5)	17 (38.6)	0.370
Alcohol consumption	0 (0)	2 (4.5)	0.250
Narcotics use**	7 (15.9)	12 (27.3)	0.190
Level of education***			0.490
Illiterate	28 (63.6)	32 (72.8)	
Under diploma	9 (20.5)	4 (9.1)	
Diploma	5 (11.4)	6 (13.6)	
Above diploma	2 (4.5)	2 (4.5)	
Personality type**,£			0.590
A	28 (64.0)	30 (68.0)	
B	16 (36.0)	14 (32.0)	

* T-test; ** Chi-square test; *** Mann-Whitney test; £ The personality type is divided into two categories A and B, having personality type A is a risk factor for cardiovascular disease (CVD) due to being aggressive, impatient, and competitive. This variable is evaluated by a completed questionnaire.
SD: Standard deviation; EF: Ejection fraction

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Table 2. Distribution of the need for blood and its products in two groups of dexmedmotidine and control before entering the intensive care unit (ICU) and in the ICU

Variable	Time	Control group (n = 44)	Dexmedetomidine group (n = 44)	P
		n (%)	n (%)	
Packed* cell	During surgery	22 (50.0)	13 (29.5)	0.048
	In the ICU	29 (65.9)	22 (50.0)	0.130
FFP*	During surgery	3 (6.8)	3 (6.8)	> 0.990
	In the ICU	13 (29.5)	15 (34.1)	0.650
Cryo**	During surgery	1 (2.3)	0 (0)	0.500
	In the ICU	3 (6.8)	5 (11.4)	0.360
Platlet**	During surgery	1 (2.3)	1 (2.3)	> 0.990
	In the ICU	3 (6.8)	1 (2.3)	0.310

* Chi-square test; ** Fisher's exact test
FFP: Fresh frozen plasma; Cryo: Cryoprecipitate; ICU: Intensive care unit

Chi-square test showed that the frequency of the need for packed cell before entering ICU was significantly higher in control group than the dexmedetomidine group (P = 0.048), but there was no significant difference in ICU between the two groups (P = 0.130) (Table 2).

Independent t-test showed that there was no significant difference between the mean of BUN before entering ICU (P = 0.25) and in the first day of ICU (P = 0.86) between the two groups, but in the second day (P = 0.007) and the third day (P = 0.001) of ICU, it was significantly higher in the control group than in the dexmedetomidine group. There was no significant difference in the pre-operative sodium level in the second day of ICU between the two groups (P > 0.050), but on the third day of ICU, it was significantly higher in the control group than the dexmedetomidine group (P = 0.003). The mean of potassium before entering the ICU was completely identical in both groups, but after the first day of ICU in the control group, it was significantly higher than the dexmedetomidine group (P < 0.050). After Bartlett's test of sphericity, the repeated measures test showed that the effect of time on Bun, creatinine, Hb, sodium, and potassium was significant (P < 0.001). But the effect of the group has only been significant on Bun (P = 0.030), sodium (P = 0.004), and potassium (P = 0.002) (Table 3).

Independent t-test showed that the mean duration of hospitalization in ICU (P = 0.002) and pump (P = 0.030) in control group was significantly higher than the dexmedetomidine group.

Chi-square test showed that the delirium frequency in the ICU was significantly higher in the control group than in the dexmedotine group (P = 0.040). The Mann-Whitney test showed that the severity of delirium in the ICU was significantly higher in the control group than the dexmedetomidine group (P < 0.001) (Table 4).

Our results verified that there was no significant difference between two groups before ICU and after separation from the pump in receipt of inotropic drugs (P > 0.050).

The mean of arterial blood pressure before surgery (P = 0.500) and in the third day of ICU (P = 0.530) did not show significant difference between the two groups, but in the first day (P = 0.002) and the second day (P < 0.001) of the ICU, it was significantly lower in the control group than in the dexmedetomidine group. There was no significant difference in mean heart rate at any time between two groups (P > 0.050).

Discussion

The results of our study revealed that the administration of dexmedetomidine significantly reduced the delirium and also the severity of delirium in the affected patients. On the other hand, our study showed that patients receiving dexmedetomidine had more stability in laboratory variables [sodium, potassium, and arterial blood gases (ABGs)] and the vital signs including blood pressure, and the duration of hospitalization in these patients was significantly lower. Therefore, based on the results of our study, it can be concluded that dexmedetomidine significantly reduces delirium and increases the stability of vital signs in patients.

A study by Thomason et al. revealed that delirium after using dexmedetomidine was less than haloperidol use (54% vs. 76%, P < 0.001).[13] The results of this study are consistent with findings of our study.

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Table 3. Evaluation of some laboratory variables in patients in both dexmedetomidine and control groups

Variable	Time	Control group (n = 44)	Dexmedetomidine group (n = 44)	P	P effect of time	P effect of group
		Mean ± SD	Mean ± SD			
Bun*	Before entering ICU	34.80 ± 11.30	32.40 ± 8.03	0.250	< 0.001	0.030
	First day in ICU	28.90 ± 8.10	29.20 ± 9.70	0.860		
	Second day in ICU	37.10 ± 10.50	31.60 ± 8.10	0.007		
	Third day in ICU	43.20 ± 11.70	34.80 ± 11.40	0.001		
Creatinine*	Before entering ICU	1.04 ± 0.20	1.02 ± 0.19	0.590	< 0.001	0.390
	First day in ICU	1.03 ± 0.19	1.05 ± 0.21	0.530		
	Second day in ICU	1.15 ± 0.31	1.11 ± 0.16	0.470		
	Third day in ICU	1.10 ± 0.24	1.01 ± 0.14	0.020		
Hb*	Before entering ICU	13.90 ± 2.30	13.70 ± 1.80	0.610	< 0.001	0.380
	Before the pump	12.20 ± 2.30	12.90 ± 2.20	0.140		
	During the pump	8.30 ± 1.40	9.40 ± 1.40	0.360		
	After the pump	9.50 ± 1.60	10.02 ± 1.10	0.080		
	First day in ICU	10.60 ± 1.50	10.20 ± 1.30	0.130		
	Second day in ICU	10.30 ± 1.10	10.40 ± 1.10	0.650		
	Third day in ICU	10.30 ± 0.90	10.60 ± 0.90	0.150		
Sodium*	Before entering ICU	140.80 ± 3.90	138.40 ± 3.80	0.150	< 0.001	0.004
	Before the pump	138.80 ± 5.10	138.60 ± 2.50	0.820		
	During the pump	133.70 ± 5.50	131.80 ± 3.60	0.260		
	After the pump	134.70 ± 4.20	134.20 ± 3.20	0.510		
	First day in ICU	140.90 ± 4.20	140.50 ± 3.20	0.650		
	Second day in ICU	141.02 ± 4.50	140.30 ± 2.90	0.360		
	Third day in ICU	141.02 ± 3.70	137.70 ± 4.40	0.300		
Potassium*	Before entering ICU	4.40 ± 0.50	4.40 ± 0.40	> 0.999	< 0.001	0.002
	Before the pump	4.10 ± 0.90	3.70 ± 0.40	0.004		
	During the pump	5.10 ± 0.90	4.80 ± 0.70	0.045		
	After the pump	5.50 ± 0.90	4.90 ± 0.70	0.001		
	First day in ICU	4.70 ± 0.80	4.40 ± 0.50	0.030		
	Second day in ICU	4.40 ± 0.50	4.30 ± 0.50	0.370		
	Third day in ICU	4.10 ± 0.50	4.20 ± 0.40	0.640		

* T-test and repeated measures test

BUN: Blood urea nitrogen; Hb: Hemoglobin; ICU: Intensive care unit; SD: Standard deviation

In a study by Tan and Ho comparing dexmedetomidine and haloperidol, the duration of hospitalization in the ICU with dexmedetomidine was lower than haloperidol, but no difference was observed in the delirium incidence.[10]

Table 4. Evaluation of the conditions of operation, incidence and severity of delirium, and the administration of haloperidol in the event of delirium in patients of both dexmedetomidine and control groups

Variable		Group		P
		Control group (n = 44)	Dexmedetomidine group (n = 44)	
		Mean ± SD	Mean ± SD	
Clamp time (minute)*		60.20 ± 16.80	55.20 ± 21.70	0.230
Pump time (minute)*		100.90 ± 25.80	89.10 ± 31.50	0.030
Duration of surgery (hour)*		4.70 ± 0.60	4.80 ± 1.00	0.730
Mechanical respiration duration (hour)*		10.50 ± 4.04	10.50 ± 3.40	> 0.990
Duration of admission to ICU (day)*		2.70 ± 0.70	2.30 ± 0.60	0.002
The onset of a diet (day)*		11.40 ± 4.20	10.70 ± 3.00	0.480
		n (%)	n (%)	
Delirium occurrence**	No	35 (79.5)	40 (90.9)	0.040
	Yes	9 (20.5)	4(9.1)	
CAM-ICU (delirium intensity)***	Step 1	2 (4.5)	16 (36.4)	0.001
	Step 2	33 (75.0)	25 (56.8)	
	Step 3	4 (9.1)	2 (4.5)	
	Step 4	5 (11.4)	1 (2.3)	
Receiving haloperidol in the event of delirium		9 (20.5)	2 (4.5)	0.020

* T-test; ** Chi-square test; *** Mann-Whitney test

SD: Standard deviation; ICU: Intensive care unit; CAM-ICU: Confusion assessment method for intensive care unit

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Study results concerning the reduction of hospital stay in the ICU is consistent with our findings, but the lack of superiority to dexmedetomidine contradicts our study results. The reason for the difference in the results of our study and the mentioned study may be due to the difference in the sample size, the demographic characteristics, the type of disease, and the applied dose of drugs. But in a study by Girard et al. dexmedetomidine, comparing with other drugs, was highly effective in reducing the incidence of delirium.[1] The results of this study are consistent with findings of our study.[1]

In 2010, Yapici et al. suggested that dexmedetomidine was a selective drug in treating delirium after cardiac surgery because of side effects of other drugs including haloperidol.[15]

Although Hipp and Ely introduced haloperidol as the preferred drug for treating delirium, they reported that dexmedetomidine was safer and also depletion of delirium and more effective treatment of delirium with the administration of dexmedetomidine were reported.[16] The results of these studies are consistent with the findings of our study. Siobal et al. stated that dexmedetomidine was less complicated and the incidence of delirium decreased with the administration of dexmedetomidine.[17] The results of this study are consistent with the findings of our study.

Conclusion

The results of our study showed that the administration of dexmedetomidine significantly reduced the delirium and also the severity of delirium in the affected patients. On the other hand, our study showed that patients receiving dexmedetomidine had more stability in laboratory variables and vital signs including blood pressure. On the other hand, the duration of hospitalization was significantly lower in these patients. Due to the high incidence of delirium after surgery, the diagnosis, screening, and successful treatment of this disease by dexmedetomidine with the least complication after open heart surgery is very important.

Study limitations: One of the limitations of the study was the impossibility of using different doses and different methods of administering dexmedetomidine in the studied patients, which was due to the lack of sample size at the time of the study. Therefore, considering the efficacy of dexmedetomidine, another study with the larger sample size and with different doses and different prescribing methods can be used to better understand the effect of this drug and achieve a safe dose with maximum efficacy. Also, in our study, the long pump and the need for packed cell more in the haloperidol group are two confounding factors. Therefore, another study with a larger sample size is recommended to overcome these two confounding factors.

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Conflict of Interests

Authors have no conflict of interests.

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Association between sleep duration and hypertension: Isfahan Healthy Heart Program, Iran

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Original Article

Abstract

BACKGROUND: Hypertension (HTN) is an important risk factor for atherosclerotic and non-atherosclerotic cardiovascular disease (CVD). HTN increases risk of stroke and diabetes complications and at the end stage renal disease. Sleep disorders including short sleep duration are involved in pathogenesis of HTN. This study aimed to examine the association between self-reported sleep duration and HTN in a group of adult population in Isfahan City, Iran.

METHODS: This cross-sectional survey was performed as part of the Isfahan Healthy Heart Program (IHHP). A total of 12492 individuals aged over 19 years (6110 men and 6382 women) entered the study. Sleep duration was recorded according to subjects' self-report. HTN was defined as a systolic blood pressure (SBP) of ≥ 140 mmHg, a diastolic blood pressure (DBP) of ≥ 90 mmHg, or use of antihypertensive medication. The relation between sleep hours and HTN was examined using multiple logistic regression in three models, unadjusted, adjusted according to age and sex, and adjusted according to age, sex, body mass index (BMI), and waist circumference (WC).

RESULTS: Sleeping time less than 5 hours, in comparison to sleep duration of 7-8 hours per night,was associated with a higher risk of HTN [odds ratio (OR) = 2.52, 95% confidence interval (CI): 2.17-2.93]. This association remained significant even after adjustment for age, sex, BMI, and WC (OR = 1.38, 95% CI: 1.16-1.64). Sleep duration over 9 hours had a negative association with risk of HTN among those under 60 years old (OR = 0.63, 95% CI: 0.47-0.86).

CONCLUSION: Sleep duration less than 5 hours is positively associated with HTN. It seems that sleep duration might affect HTN and atherosclerotic CVD.

Keywords: Sleep Duration, Hypertension, Cardiovascular Diseases

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Introduction

Several basic research studies have demonstrated the impact of sleep disorders in the occurrence or development of common diseases such as obesity, diabetes, or hypertension (HTN). More recent epidemiological surveys seem to confirm this association in Iranian population.[1,2] These studies have observed that a total sleep time under 6 hours is associated with an increased body mass index (BMI) and a higher occurrence of diabetes and HTN.[3] In longitudinal analysis of the first National Health And Nutrition Examination Survey (NHANES I), American adults aged 32 to 59 years with sleep duration of ≤ 5 hours per night had a 60% higher risk of incidental HTN.[4]

Sleep Heart Health Study (SHHS) with a cross-sectional design showed a significant higher prevalence of HTN in persons with sleep duration above or below the median of 7 to 8 hours per night. This association was stronger in those persons with short sleep duration (6 hours per night), with a 66% higher risk of HTN.[5]

Prevalence of HTN in Iran is 25%.[4] Age, male gender, obesity, central obesity, hypercholesterolemia, and diabetes have been known as determinants of HTN among Iranians.[6]

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However, little is known about usual sleep duration among Iranian subjects and whether it has any association with high blood pressure (BP).

This study aimed to assess the association of HTN with sleep duration in a sample of Iranian adult population. Moreover, it is the first report of daily sleep duration among Iranian subjects.

Materials and Methods

This cross-sectional study was conducted in 2000-2001 as a part of Isfahan Healthy Heart Program (IHHP) in Isfahan, Iran. IHHP is a six-year comprehensive integrated community-based program for cardiovascular disease (CVD) prevention and control via reducing CVD risk factors and improvement of cardiovascular healthy behaviors.[7]

Participants were 12492 individuals aged over 19 years. 6110 men and 6382 women entered the study. Sociodemographic characteristics such as age, sex, marital status, occupation, education, and income were recorded. Sleep time was obtained by the question "how many hours of sleep do you usually get?".[8]

Height, weight, waist circumference (WC), and BP were measured by trained health professionals. Weight was measured with calibrated scale, with patient in the standing position with light clothes. Height was measured in the standing position with the patient barefoot. BMI was calculated as weight/height^2 (kg/m^2). WC was measured at the part of the trunk located midway between the lower costal margin (bottom of lower rib) and the iliac crest (top of pelvic bone) while the person was standing, with feet about 25-30 cm apart. BP was measured twice on the right arm, in sitting position and after 15-minute rest. The mean of two recordings was reported. The first and fifth Korotkoff sounds were considered as systolic BP (SBP) and diastolic BP (DBP), respectively. HTN was defined as a SBP of 140 mmHg or more, a DBP of 90 mmHg or more, or use of antihypertensive medication.[9]

Baseline characteristic data of patients were presented as mean ± standard deviation (SD) for quantitative variables and frequencies and percentages for multiple variables. Differences between groups for continuous variables was analyzed by one-way analysis of variance (ANOVA) and for multiple variables was assessed by chi-square test. The relation between sleep time and HTN was examined using binary logistic regression in three models, unadjusted, adjusted according to age and sex, and adjusted according to age, sex, BMI, and WC. P-values of 0.050 or less were considered statistically significant.

The analysis was performed using SPSS statistical software (version 15, SPSS Inc., Chicago, IL, USA).

Results

The study population included 12492 persons, 6110 (49.9%) men and 6382 (51.1%) women with a mean age of 38.89 ± 14.93 years. 1911 (15.3%) participants were hypertensive. Of all the participants, 7622 (61%) reported sleeping 7-8 hours per night, 3783 (30.3%) reported sleeping 6 hours or less, and 1087 (8.7%) reported sleeping 9 hours or more (Table 1).

Considering sleep duration of 7-8 hours per night as reference category, multiple logistic regression showed that sleep duration less than 5 hours was associated with a higher risk for HTN [odds ratio (OR) = 2.52, 95% confidence interval (CI): 2.17-2.93]. The association remained significant even after adjustment for age, sex, BMI, and WC (OR = 1.38, 95% CI: 1.16-1.64). However, among subjects with sleep duration of 9 hours or more, a reveres association with HTN was found (OR = 0.71, 95% CI: 0.56-0.89) (Table 2).

Table 1. Characteristics of the study participants

Sleep duration (hour)	Reported usual sleep time per night					P
	≤ 5	5-6	7-8	≥ 9	Total	
Number of subjects [n (%)]	1447 (11.6)	2336 (18.7)	7622 (61.0)	1087 (8.7)	12492	-
Female sex [n (%)]*	725 (50.1)	1109 (47.5)	3894 (51.1)	652 (60.0)	6380 (51.1)	< 0.010
BP [n (%)]						< 0.010
HTN	379 (26.2)	378 (16.2)	1030 (13.5)	124 (11.3)	1911 (15.3)	
Normal	535 (37.0)	1042 (44.6)	3658 (48.0)	572 (52.6)	5789 (46.5)	
Age (year) (mean ± SD)**	47.35 ± 16.19	40.52 ± 14.36	37.26 ± 14.08	35.49 ± 15.81	38.89 ± 14.93	< 0.010
BMI (mean ± SD)**	26.21 ± 5.12	26.00 ± 4.68	25.32 ± 4.68	25.02 ± 5.08	25.52 ± 4.78	< 0.010
WC (mean ± SD)**	93.30 ± 13.57	92.23 ± 13.48	89.86 ± 13.13	88.40 ± 13.63	90.57 ± 13.37	< 0.010

* Chi-square test; ** ANAOVA test

BMI: Body mass index; WC: Waist circumference; BP: Blood pressure; HTN: Hypertension; SD: Standard deviation

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Table 2. Data for hypertension (HTN) and pre HTN by reported usual time in subjects

Usual sleep time/night	Model						
	1		2		3		4
	HTN	Pre HTN	HTN	Pre HTN	HTN	Pre HTN	HTN Pre-HTN
≤ 5	2.52 (2.17,2.93)	1.24 (1.09,1.41)	1.58 (1.33,1.86)	1.15 (1.01,1.31)	1.38 (1.16,1.64)	1.06 (0.93,1.22)	0.99 (0.82,1.19) 0.98 (0.86,1.12)
6	1.30 (1.13,1.49)	1.09 (0.99,1.21)	1.21 (1.04,1.40)	1.07 (0.97,1.18)	1.06 (0.91,1.23)	0.99 (0.89,1.10)	0.86 (0.73,1.02) 0.96 (0.87,1.07)
≥ 9	0.77 (0.63,0.95)	0.85 (0.74,0.98)	0.66 (0.53,0.83)	0.86 (0.75,0.98)	0.71 (0.56,0.89)	0.90 (0.79,1.04)	0.79 (0.61,1.02) 0.93 (0.81,1.08)

HTN: Hypertension

Data are given as odds ratio (OR) and 95% confidence interval (CI) for the presence of HTN and pre HTN relative to normal blood pressure, from categorical logistic regression models using 7-8 hours of sleep per night as the reference category. Model; 1: Was unadjusted, 2: Adjusted for age and sex, 3: Adjusted for age, sex, waist circumference (WC), and body mass index (BMI), and 4: Adjusted for age, sex, WC, BMI, and physical activity.

When adjusted for age and sex, this relation was true for subjects aged under 60 years. Sleeping less than 5 hours (OR = 1.67, 95% CI: 1.29-2.16) or 6-8 hours (OR = 1.28, 95% CI: 1.02-1.59) was associated with higher odds for HTN among women under 60 years (Table 3).

Discussion

In this study, sleep duration under 5 hours was positively associated with HTN. This was independent of age, sex, BMI, and abdominal obesity. Sleep duration more than 9 hours was negatively associated with HTN only in subjects under 60 years old. The mean age of subjects in our study was 38.89 ± 14.93 years, so majority of them were middle-aged.

Other studies have reported inconsistent results regarding association of HTN and sleep duration. Vgontzas et al. evaluated the combined effect of insomnia and short sleep duration on HTN risk. They found an increased risk of HTN in persons who had insomnia and short sleep duration; this risk was comparable to that of other common sleep disorders such as sleep apnea. They examined the joint effect of insomnia and objective short sleep duration on HTN risk and found that insomnia with short sleep duration was associated with increased risk of HTN, to a degree comparable to that of other common sleep disorders such as sleep apnea.[10] In the NHANES I after an 8- to 10-year follow-up, incidence of HTN was higher in participants aged 32 to 59 years who slept 5 hours or less, compared to those sleeping 7 to 8 hours.[4] In the Whitehall II Study, prevalence of HTN was higher in women with short sleep duration (< 5 hours).[11] On the other hand, Lopez-Garcia et al. studied 3600 individuals over 60 years old and concluded that self-reported sleep duration was not associated with HTN in older adults.[12] Moreover, in NHANES I or in older adults in the Rotterdam Study, no association was observed between sleep duration and HTN in subjects aged 59 years and older.[13] In addition, one meta-analysis of 17 cohort studies reported that short sleep duration was related to increased HTN risk.[14] Conversely, some cross-sectional, but not longitudinal studies revealed that long sleep duration was associated with prevalence of HTN.[15,16]

Table 3. Odds ratio (OR) of hypertension (HTN) in relation to sleep duration adjusted for age and sex (logistic regression models using 7-8 hours of sleep per night as reference category)

Variable	Number	Reported usual sleep time per night				P
		< 5	5-7	7-8	≥ 8	
		HTN [OR (95% CI)]				
Sex						
Male	3494	1.11 (0.84,1.47)	0.83 (0.65,1.06)	ref	0.62 (0.42,0.930)	0.030
Female	4139	1.67 (1.29,2.16)	1.28 (1.02,1.59)	ref	0.73 (0.53,1.002)	0.001
Age (year)						
< 60	6525	1.48 (1.19,1.84)	1.08 (0.90,1.29)	ref	0.63 (0.47,0.860)	0.001
≥ 60	1108	1.13 (0.79,1.59)	0.89 (0.61,1.29)	ref	0.78 (0.48,1.270)	0.510

HTN: Hypertension; OR: Odds ratio; CI: Confidence interval

It has been shown that decreased sleep duration and sleep deprivation are associated with higher activity of autonomic sympathetic system and increased activity of hypothalamic-pituitary-adrenal axis (HPA axis). Sleep deprivation may also increase the activity of these systems by its effect on other body stressors.[17] Acute sleep deprivation increases sympathetic and decreases parasympathetic cardiovascular modulation and baroreflex sensitivity (BRS).[18]

Sleep duration under 5 hours may induce small autonomic imbalance that is not significant immediately, but in long time, will increase BP.[18] Short sleep duration also increases cardiovascular events in patients with HTN independently, and according to recent studies, it also increases mortality from heart disease.[19,20]

The mechanism of the effect of short sleep duration on HTN may be different in the elderly.[13] Sympathetic tone decreases with age,[21] so the effect of short sleeping hour is not significant in the elderly. This may explain why some studies found no relation between sleep duration under 5 hours and HTN in those over 60 years old.[4,13]

In our study, sleep duration over 9 hours in those under 60 years old, was negatively associated with HTN. In the SHHS, sleep duration was associated with increased prevalence of HTN.[5] This difference may be explained by different level of daily stress in different societies. It means that in a society with a high level of daily stress, increased sleep duration means lower level of waking-time stresses and lower sympathetic tone, and this means decreased prevalence of HTN. Consequently, a recent review has concluded that enough duration of sleep has several advantages and few complications; however, it is required to prioritize proper time for rest.[22]

Our findings were based on subjects' self-report of the duration of their sleep. We did not also check quality of sleep or sleep disorders in our sample.

Conclusion

Sleep duration under 5 hours is associated with HTN. Although a casual relation can not be inferred from this cross-sectional study, it may influence patients with CVD. Further studies are needed to characterize any causal relationship and find whether short sleep duration might be considered as a risk factor or at least as a health problem in preventive cardiology.

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Conflict of Interests

Authors have no conflict of interests.

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The efficacy and safety of using amplatzer for transcatheter closure of atrial septal defect in small children with less than 10 kg

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Original Article

Abstract

BACKGROUND: Atrial septal defect (ASD) accounts for about 10% of congenital heart diseases (CHDs). Self-closure of these defects in patients with defects less than 8 mm has been reported in several studies. In children, transcatheter closure of the ASD is suggested for asymptomatic patients older than two years and with weight > 15 kg. The purpose of this study was to show that transcatheter closure of ASD in small children with body weight less than 10 kg is an effective and safe method.

METHODS: Between July 2016 and September 2018, 35 children with body weight less than 10 kg underwent percutaneous closure of ASD using amplatzer. All patients had minimum defect size of 6 mm, pulmonary blood flow (Qp) to systemic blood flow (Qs) ratio above 1.5, right atrial and ventricular dilation, symptoms of delayed growth, and recurrent respiratory infections in their evaluation and had acceptable rims for intervention. Follow-up evaluations were done 1 day, 1 week, 1 month, 6 months, and yearly after discharge with transthoracic echocardiography (TTE) and electrocardiography (ECG).

RESULTS: The mean age of patients at procedure was 12.06 ± 4.47 months (range: 6 to 14 months), mean weight was 8.32 ± 0.72 kg (range: 7.5 to 9.8 kg). The mean defect size was 10.00 ± 2.32 mm (range: 6-13 mm). The mean device size used was 10.57 ± 2.57 mm (range: 7.5 to 15 mm). Mean duration of follow-up was 16.66 ± 6.93 months (range: 1-29 months). Respiratory rate, heart rate, pulmonary stenosis (PS), and Qp to Qs ratio had significant difference before and after procedure during the follow up (P < 0.001).

CONCLUSION: Transcatheter closure of ASD with amplatzer in symptomatic small children and infants is a safe and effective treatment associated with excellent success, but long-term follow-up in a large number of patients would be warranted.

Keywords: Atrial Septal Defect, Devices, Septal Occluder

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Introduction

Atrial septal defect (ASD) is one of the most common congenital heart diseases (CHDs) and accounts for about 10% of CHDs, which is regarded as the third common CHD in the world.[1] There are various types of this malformation, which cause blood shunt between the systemic and respiratory blood stream. The majority of these atrial defects can be observed in the central area of atrial septum and fossa ovalis, size of which can vary from a small hole to extremely large defects which involve almost the entire atrial septum.

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Presentation of the disease is more marked during adulthood and is diagnosed with heart failure (HF) or cardiac dysrhythmia during the third or fourth decade of life. In infants, this disease could be manifested by recurrent respiratory infections, delayed growth, reduced activity tolerance, and HF, even at an early age. Self-closure of these defects in patients with an ASD of less than 8 mm has been reported in several studies.[2,3]

Hemodynamically, it is suggested that these defects must be closed in patients with the ratio of pulmonary blood flow to systemic blood flow (Qp/Qs) of above 1.5 and/or a dilated right atrium and ventricle. Surgical treatment of these patients has been initiated since the 1960s, which has had positive results and is performed before the age of 25 years. Studies have indicated that surgical closing of ASD can significantly improve the function and morphology of the right ventricle. Interventional closure of this atrial defect was reported and has had significant advances during the past years. Compared to other surgical techniques, this method is associated with shorter hospital stay and fewer complications.[4] In children, closure of the defect is suggested for asymptomatic patients older than 2 years and with weight > 15 kg.[5,6] Symptomatic patients who suffer from recurrent respiratory diseases or lack of sufficient growth and require respiratory support, might benefit from the correction of this defect at an earlier age. Closure of ASD at earlier ages requires more experience in this area, and there is a limited number of reports in this regard.[1,2,7-16]

This research aimed to evaluate the reliability, safety, and effectiveness of percutaneous ASD closure in patients with body weight less than 10 kg.

Materials and Methods

This observentional prospective study was approved by the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.MED.REC.1398.067) and written informed consent was obtained from the parents befor the procedures. All patients with ASD and body weight less than 10 kg who were hospitalized in Chamran Hospital affiliate to Isfahan University of Medical Sciences during July 2016 to September 2018 and underwent intervention procedures for ASD closure entered the research.

Inclusion criteria were body weight less than 10 kg, minimum ASD size of 6 mm and more, having Qp/Qs above 1.5 in echocardiography evaluations, having right atrial and ventricular dilatation, having the symptoms of delayed growth, and having recurrent respiratory infections.

Exclusion criteria were: patients with other complex heart diseases who required corrective surgery, patients with body weight more than 10 kg, and patients with no acceptable rims for ASD closure according to echocardiography evaluations.

At first, patients underwent echocardiography which was performed by a pediatric cardiologist in children heart clinic, and were hospitalized in the center for intervention after proving the presence of ASD and the existence of reliable rims and rulling out the existence of partial anomalous pulmonary venous connection (PAPVC). Echocardiography was performed using Samsung MEDISON EKO 7 Ultrasound Machine (Samsung Co., Seoul, South Korea), and all necessary information was recorded in medical files of the patients. Two-dimensional (2D) transthoracic echocardiography (TTE) was performed in standard apical four chamber, subcostal four chamber, and subcostal bicaval views for accurate calculation of ASD size. Signs of increased volume overload in the right side of the heart, along with the increased size of right heart side were observed in all patients. In addition, all of the patients underwent anesthesia with midazolam and ketamine in catheterization room. In the beginning of angiography, patients were injected with 50 units/kg of heparin, followed by the administration of the next doses of heparin for patients with activated clotting time (ACT) values above 200 seconds. During the process, patients received a dose of cefazolin, which continued for 24 hours. Angiography was performed according to standard protocols, and patients were evaluated during the process for pulmonary artery pressure (PAP).

Angiography was performed in the pulmonary artery and right upper pulmonary vein (RUPV) for more accurate assessment of the absence of PV anomalies. Closure of ASD was performed under fluoroscopy and angiography and by controlling the process by TTE. However, no balloon sizing was used, and size of ASD was measured by echocardiography. In ASDs below 10 mm, an amplatzer was designated based on ASD size and in sizes above 10 mm the device was selected 1-2 mm more than echocardiographic size. The selected device was entered into the left atrium by the delivery system that was suitable for selected device and had the smallest size because of low weight of patients. Left disc of device was opened at the beginning of the left upper PV (LUPV), followed by the opening of the right disc in the right atrium and

testing of accurate placement and strength of amplatzer on septum with "Minnesota wiggle" maneuver. If the guiding of the device toward the LUPV was difficult in a patient, the RUPV would be used as opening of amplatzer (Figure 1). At the end of the procedure and before releasing the device, echocardiography, contrast echo, and injection of contrast agent in left atrium were performed to ensure the lack of presence of any residue, followed by the release of the device. At the end, the open disc measurement was performed at the best possible angle which showed the exact size, and the result was compared with the echo size.

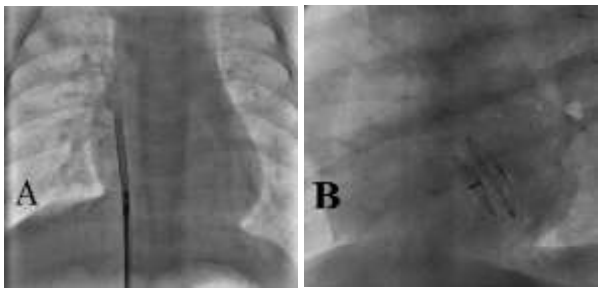

Figure 1. Implantation of atrial septal defect (ASD) device occluder in right upper pulmonary vein (RUPV) approach during (A) and at the end of procedure (B)

Patients received heparin for 24 hours and 3-5 mg/kg of aspirin for six months on a daily basis. Moreover, echocardiography was performed on patients 1 day and 1, 3, and 6 months after the procedure and then annually. Serial electrocardiography (ECG) analysis was carried out for all patients in the next follow-ups to evaluate delayed arrhythmias. Patients were discharged from the hospital after 24 hours and received outpatient follow-up in the next appointments.

Quantitative and categorical data were expressed as mean ± standard deviation (SD) (minimum–maximum) and frequency and percentage, respectively. Within-group comparisons based on quantitative data were conducted using paired samples t-test. Analyses were performed by SPSS software (version 19, SPSS Inc., Chicago, IL, USA). Statistical significance was defined as a P-value < 0.050.

Results

In this study, 35 patients were entered, 16 of them were male and 19 were female. Mean age, weight, and height of patients were 12.06 ± 4.47 months (range: 6-14 months), 8.32 ± 0.72 kg (range: 7.5-9.8 kg), and 64.40 ± 5.20 cm (range: 59-71 cm), respectively. In addition, mean sizes of ASD and the selected device were 10.00 ± 2.32 mm (range: 6-13 mm) and 10.57 ± 2.57 mm (range: 7.5-15 mm), respectively. Table 1 shows demographic and characteristic data of the patients.

Furthermore, there was a left to right shunt in all patients. According to the results, closure of ASD was successfully performed for all patients.

Mean weight (kg) to device size (mm) ratio was 0.85 ± 0.16, which varied from 0.57 to 1.12. In addition, the mean duration of fluoroscopy was 5.4 ± 3.7 minutes (range: 3.7-11.5 minutes) and mean total duration of the procedure was 33.8 ± 10.3 minutes (range: 25-60 minutes). Respiratory rate, heart rate, pulmonary stenosis (PS), and Qp/Qs had significant difference before and after procedure during the follow-up (P < 0.001). Blood pressure (systolic and diastolic) and ejection fraction (EF) did not have significant difference before and after procedure (Table 2).

Furthermore, no immediate shunt was observed in 27 patients (77%). In 5 of the patients, no shunt was seen two days after angiography, and no shunt was found in the remaining 3 patients until one month (100%).

Table 1. Basic demographic and characteristic data of the patients

Variant	Total (n = 35) (mean ± SD) (minimum-maximum)	Male (n = 16) (mean ± SD)	Female (n = 19) (mean ± SD)
Age (month)	12.06 ± 4.47 (6.0-14.0)	11.10 ± 4.20	13.40 ± 4.00
Weight (kg)	8.32 ± 0.72 (7.5-9.8)	8.80 ± 1.40	8.10 ± 0.20
Height (cm)	64.40 ± 5.20 (59.0-71.0)	67.58 ± 7.20	61.33 ± 2.70
ASD size (mm)	10.00 ± 2.32 (6.0-13.0)	10.40 ± 1.50	10.00 ± 1.20
PAP (mmHg)			
Systolic	22.90 ± 7.20 (15.0-30.0)	23.20 ± 7.10	20.20 ± 6.10
Diastolic	12.70 ± 6.10 (8.0-19.0)	14.10 ± 4.90	12.10 ± 3.80
Mean PAP (mmHg)	17.70 ± 4.20 (12.0-23.0)	18.20 ± 4.80	16.10 ± 4.50
Fluoroscopy time (minute)	5.40 ± 3.70 (3.7-11.5)	4.90 ± 2.10	5.90 ± 2.70
Total angiography time (minute)	33.80 ± 10.30 (25.0-60.0)	31.50 ± 11.60	33.90 ± 12.90
Size of amplatzer (mm)	10.57 ± 2.57 (7.5-15.0)	10.60 ± 3.10	11.40 ± 2.90

ASD: Atrial septal defect; PAP: Pulmonary artery pressure; SD: Standard deviation

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Table 2. Mean of study variables before and after procedure

Variable	Before procedure (mean ± SD)	After procedure (mean ± SD)	P
Blood pressure (mmHg)			
Systolic	92.50 ± 5.40	94.60 ± 6.10	0.350*
Diastolic	72.40 ± 4.90	75.50 ± 5.10	0.360*
Respiratory rate	38.56 ± 1.12	28.90 ± 2.18	< 0.001*
Heart rate	112.90 ± 10.38	92.80 ± 8.30	< 0.001*
PS (mmHg)	25.20 ± 5.26	12.30 ± 2.40	< 0.001*
EF (%)	65.24 ± 8.25	67.36 ± 7.31	0.510*
Qp/Qs	2.52 ± 0.80	1.10 ± 0.10	< 0.001*

* Based on t-test; PS: Pulmonary stenosis; EF: Ejection fraction; Qp: Pulmonary blood flow; Qs: Systemic blood flow; SD: Standard deviation

Mean duration of follow-up was 16.66 ± 6.93 months (range: 1-29 months) for the patients, during which the growth curve of the patients improved and their weight increased about 10%. None of the patients required hospital readmission, and no delayed bleeding was reported. In 32 patients, delivery system was guided toward LUPV. In 3 patients, the mentioned process was difficult; therefore, delivery system was guided toward RUPV, and the left disc was opened in this PV. During the procedure, 2 patients suffered paroxysmal supraventricular tachycardia (PSVT) attack, which immediately improved without treatment. None of the patients had bleeding and showed signs of hematoma before hospital discharge. Moreover, no acute complications, such as the need for blood transfusion, was observed in the patients, and no femoral vein thrombosis was seen in the patients. One of the patients had seizure about 8 hours after the procedure, which was followed by immediate computed tomography (CT)-scan and magnetic resonance imaging (MRI), showing cerebral thrombosis. Right side hemiparesis was happened in this patient after the seizure and treatment was immediately initiated for the mentioned patient, and the symptoms of the patient were corrected in the next follow-ups. It should be noted that the size of ASD in the patient was large and duration of the procedure was longer, compared to the other patients.

At the beginning of the procedure, one patient had respiratory apnea and bradycardia immediately after receiving anesthesia, which led to postponing of the procedure to the next visit. After two months, the patient underwent angiography one more time and ASD was closed successfully. Device embolism was observed in none of the patients, and there was no sign of delayed arrhythmias or atrioventricular (AV) block in the participants.

Discussion

Patients with ASD may be asymptomatic in their early years, and the smaller the size of the defect, the more common it is to experience no symptoms. In patients with larger defects, this disease can be manifested by symptoms, such as HF, recurrent respiratory infections, and/or delayed growth.[17-19] One of the problems of these patients is lack of symptoms of the disease, which leads to the diagnosis of the illness at older ages. Therefore, there would be no long follow-ups before surgical procedures or interventions for these patients. In this regard, the main question is about the speed of increasing of ASD size and the best time to perform therapeutic measures. In a research by McMahon et al., it was reported that the size of ASD increased in 2/3 of patients, which was up to 50% of the primary size in some of the patients.[3] As reported by McMahon et al., the size of the defect increased about 0.8 mm in some patients every year. According to the mentioned researchers, the greater the size of the defect, the higher the increase of its size.[3] Increased age of patients might lead to increased size of the defect, in a way that performing interventional treatments could be difficult. The majority of centers believe that treatment of patients without a sign must be delayed until the age of 4-6 years.[20] However, increased experience of various centers has led to the performing of the relevant procedures at earlier ages. Various reports have been made on ASD closure at ages below 4 years or weights less than 15 kg.[16,21] In a report by Thomas et al., this interventional procedure was performed in children aged below one year. According to the mentioned research, this procedure could be performed in younger patients, in whom increased pulmonary flow would cause pulmonary symptoms and HF.[22] There is a limited number of articles and evaluations on ASD closure at earlier ages and lower weights. In this regard, there is an insufficient experience since arteries and veins are small in these patients and there might be complications during the procedure. In addition, it is still not clear whether this treatment

is necessary and can be beneficial for children or not. While this was our first experience with this type of disease, the present research is of paramount importance due to insufficient experience in this regard. In the current research, we aimed to electively close ASD in patients with body weight less than 10 kg and we had good results in our study and had no major complications.

According to previous studies in which the enlargement of the defect was reported in some of the patients, the mentioned procedure was performed on patients with defects larger than 6 mm and completely sharp defect edges and no flap in the defect, as well as patients with delayed growth and recurrent respiratory infections. Increased age of patients and enlargement of defects in a number of patients could result in the lack of sufficient strength in defect edges to maintain the device, which might be another cause of performing this procedure at earlier ages. We believe that closing of these defects at earlier ages could lead to the use of smaller devices, which can be beneficial for the patient in long term. In addition, the size of the device to septum ratio could be decreased during growth of the patients. Surgical procedures have long-term follow-ups, while non-surgical procedures have no long-term follow-up. In large defects, we have to use a great device, and in the future, these devices may create different problems for our patients; thus we suggest earlier closure of these defects and during the time decreasing of device to septum ratio and complications. Nevertheless, the experience of individuals in performing this procedure is extremely important, and the level of benefits of this process by patients must be taken into consideration.

In our patients, the respiratory rate and heart rate had significant difference before and after the procedure that could decrease patient's energy consumption and help patient's growth increase. It seems that closing of this defect can affect the improved growth of patients and decreased respiratory infections. Due to lack of effect of ASD on the left ventricle, EF had not significant difference during the study.

One important complication was occurrence of cerebral symptoms in a patient, which was improved with treatment. This complication was either due to our procedure or due to the fact that since the patient had a large defect and the right side of the patient was dilated, previous thrombosis on the right side of the heart might have caused embolism and complications.

Limitations: In the current research, the duration of follow-up was short, which must be improved in the following studies especially on growth of patients. In addition, the volume of study was low in the present research. Therefore, the future studies must be carried out in multiple centers and on larger patient volumes to more accurately evaluate the related complications and benefits of this technique. Furthermore, there was no time to evaluate the ratio of the size of the device to the septum during the follow-up, which should be taken into consideration in following studies. We had limitation for three-dimensional (3D) echo and in future studies, echo indexes, especially 3D, can be reviewed and reported in the results.

Conclusion

ASD closure is beneficial for patients with defects larger than 6 mm and with symptoms of delayed growth or recurrent respiratory infections, where there is no hope for self-closure according to clinical evaluations and echocardiography. However, this procedure must be carried out by individuals with sufficient experience in this area.

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Conflict of Interests

Authors have no conflict of interests.

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A rare case of takotsubo syndrome led to intra-myocardial dissection and left ventricular apical aneurysm

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Case Report

Abstract

BACKGROUND: Takotsubo syndrome (TS) is a reversible left ventricular (LV) systolic dysfunction occurred mostly in post-menopausal women after an emotional or physical stress. The exact mechanism has yet to be found. In clinical settings, TS should be differentiated from myocardial infarction (MI) due to totally different management protocols. Several diagnostic criteria are available, but mayo clinic criteria is the most widely used. Prognosis of TS is favorable and the recurrence and mortality rates are low. Treatment is mostly supportive and after a few weeks, most of patients' electrocardiography (ECG) and echocardiographic findings will be normalized, though to its benign course, TS can cause some complications. Intra-myocardial dissection and LV apical aneurysm, as a complication of TS has never been reported yet and was just announced in rare cases of MI.

CASE REPORT: Our patient was a 32-year-old aphasic woman referring with palpitation and chest discomfort. Further examinations after exclusion of MI revealed TS leading to LV apical aneurysm and intra-myocardial dissection.

CONCLUSION: Intra-myocardial dissection should be considered as one of the rarest TS complications. Several studies are necessary for defining the exact pathophysiological mechanisms.

Keywords: Takotsubo Cardiomyopathy, Dissection, Cardiac Aneurysm

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Introduction

Takotsubo syndrome (TS), apical ballooning syndrome, broken heart syndrome, and stress-related cardiomyopathy are synonyms for an acute severe reversible left ventricular (LV) systolic dysfunction which was first reported by Sato et al. in 1990.[1-5] The word takotsubo refers to an instrument used to catch octopus in Japan.[3,4] From 20th century, the number of articles about takotsubo was increased and some forms like right ventricle (RV) involvement and apical sparing syndrome were also reported as variants of this disease.[6]

The mean age of takotsubo is 62-75 years and is mostly seen in post-menopausal women.[5] Despite the unknown mechanism, several theories have been postulated for the pathophysiology of the disease such as catecholamine-induced myocardial stunning, coronary artery spasm, and coronary microvascular dysfunction (CMD).[1,3,4] Most of the patients first experienced an emotional or physical stress before the onset of symptoms like dyspnea or chest discomfort.[1,5,6]

Till now, there is no acceptable criteria for diagnosing TS and due to its similarity in symptoms and electrocardiography (ECG) and laboratory findings to myocardial infarction (MI), differentiation is crucial because of different management strategies.[1,3,7]

Patients with TS have good prognosis and LV systolic function of 96% of them will be normalized completely after some weeks to months and in-hospital mortality prevalence is 1%-2%.[3,7]

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Despite its good prognosis, some complications had been reported among which heart failure (HF) with or without pulmonary edema was the most common.[6,7] One of the rarest complications in this regard mostly seen in MI is dissection which the intra-myocardial one is more prevalent and the only dissection type which has been reported in literature for TS is spontaneous coronary artery dissection (SCAD).[8-10] However, other rare complication in this context in LV aneurysm leading to intra-myocardial dissection and LV apical aneurysm has never been reported yet.

In this article, we described a rare case of TS which led to intra-myocardial dissection and LV apical aneurysm.

Case Report

The patient was a 32-year-old aphasic woman who came to our emergency department with a history of gradual palpitation and chest discomfort in her left hemithorax.

She had no family history of cardiac diseases. Her past medical history was unremarkable except for two episodes of embolic cerebrovascular accidents (CVAs) eight and six years ago, respectively.

Her first attack happened following physical stress of moving furniture which caused left hemiplegia. Due to probable chance of MI, she underwent angiography in which findings included normal coronary arteries and large aneurysms in anteroapical and posterolateral LV region with ejection fraction (EF) of 40%. Thereafter, she was treated with warfarin.

Her hemiplegia resolved in the next two years after the prior event; then, she discontinued warfarin by herself and she experienced another attack with the occurrence of aphasia. Another angiography results showed several aneurysms in lateral LV wall and EF of 40%. Again, medical treatment was initiated.

At the time of present admission, her vital signs were normal. The patient was aphasic. In her heart auscultation, late systolic murmur was heard in apical region. Other physical examinations did not reveal any positive findings. All laboratory data were in normal ranges. In her requested chest X-ray (CXR), cardio-thoracic ratio (CTR) was normal, but the left upper border of the heart was straight (Figure 1).

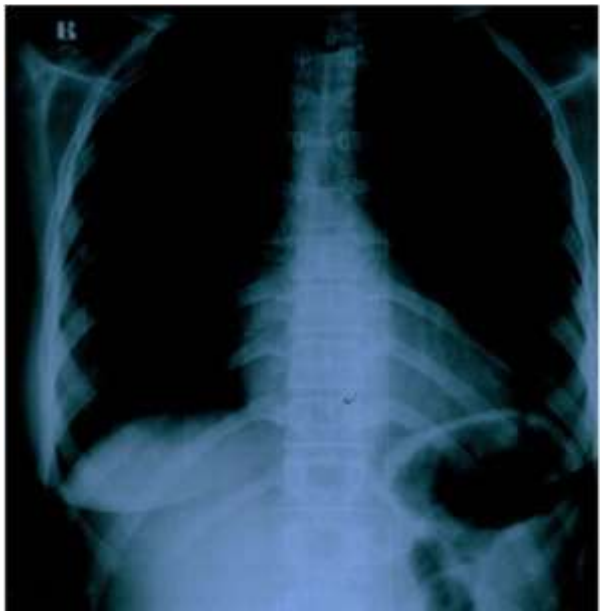

Figure 1. Straight left upper border of heart

Inverted T waves were recorded in the precordial leads (Figure 2).

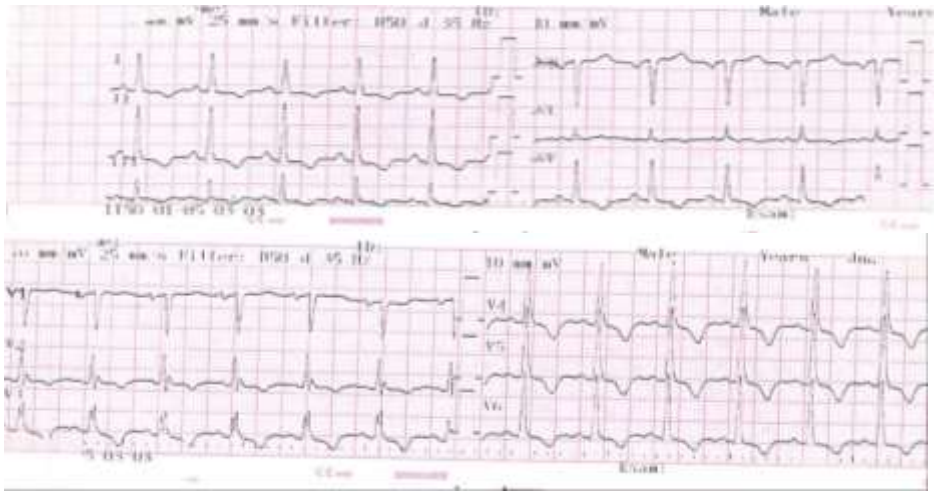

Figure 2. Inverted T waves in precordial leads

Due to possibility of MI, she went under angiography and the result revealed patent coronary arteries. Based on initial signs and symptoms, possible diagnosis of TS was made. Transesophageal echocardiography (TEE) showed moderate LV enlargement with moderate systolic dysfunction (EF = 40%), mild to moderate mitral regurgitation (MR), mild tricuspid regurgitation (TR),[11] and normal RV size. Her pulmonary artery pressure (PAP) was 34 mmHg. Her diastolic function was normal, but there was a pulsatile mass with intra-myocardial dissection to its pericardium in apico-lateral region. In her cardiovascular magnetic resonance (CMR) imaging the followings were reported (Figure 3): disrupted LV myocardial continuity close to apical segments with a large LV apical dyskinetic outpouching which was covered by a thin layer of subepicardial myocytes and pericardium connected directly to apico-lateral LV segment (maximum width: 42 mm, maximum depth: 32 mm, neck: 14 mm). The early gadolinium enhancement (EGE) images did not show any evidence of intra or paracardiac thrombus, but in late gadolinium enhancement (LGE) images, a thin layer of fibrosis around the outpouching and inferolateral apical LV segment was seen. All the results were in favor of a LV apico-lateral pseudo aneurysm without thrombosis. The patient went under surgery due to possibility of sudden aneurysm rupture. An intra-operative finding was moderate true aneurysm in apico-lateral and posterior region of LV segment and therefore aneurysmectomy was performed for her. All the findings revealed a probable old TS leading intra-myocardial dissection and LV apical aneurysm.

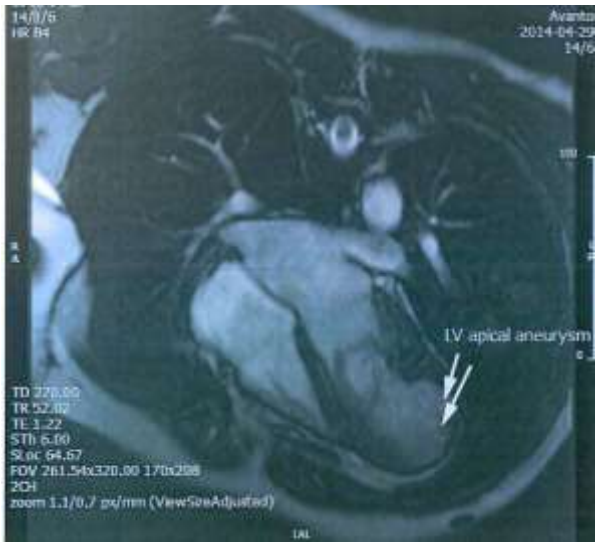

Figure 3. Left ventricular (LV) apical aneurysm

The patient was discharged with warfarin and in acceptable general condition. Her routine follow ups after surgery were normal and did not show any abnormalities.

Discussion

TS became popular in literature during the past 25 years and thousands of articles were published about it and led it to be categorized as one of the topics in cardiomyopathy groups.[1,3,4] This reversible LV dysfunction has several pathophysiologic hypotheses which several other studies must have been done to define the exact mechanism. Three possibilities available are catecholamine-induced myocardial stunning, CMD, and coronary artery spasm which the first two of them are more acceptable worldwide.[3-5,7]

This disease has a classic form in which LV apex is being affected, but there are other forms like inverted takotsubo (artichoke heart) and midventricular (hawk's beak) or isolated RV involvement.[6,7]

Although classic TS is more prevalent in post-menopausal women which could be due to hormonal effects or early dying of men even before diagnosis, younger premenopausal women contain most number of atypical TS.[7] There are some risk factors reported for TS which some of them include estrogen lacking or genetic factors.[3,4] Unlike typical cases, our patient was a young woman with regular menstruation.

TS prevalence was estimated to be between 1.5% and 2.2%.[2] Although it is rare, recurrence could occur 3 months to 13 years thereafter,[7] and the exact recurrence rate has yet to be defined, but ranges from 0%-15% reported in different studies.[5,6,12]

Till today, there is not a comprehensive diagnostic criterion for TS. Although Abe and Kondo, Prasad, Segovia Cubero and Peraira Moral,[13] and Kawai mayo clinic criteria are all used worldwide, the latter is more acceptable among authors.[1,5,7] Chest pain and dyspnea are the most common chief complaints in patients referring to emergency departments, but the spectrum of symptoms would be from an asymptomatic one to cardiogenic shock or arrest.[2,3,5,7] The most similar disease in clinical manifestations to it is MI, but other differential diagnosis should be kept in mind which includes the followings: LV apical aneurysm, aortic dissection, pneumothorax, pulmonary embolism and edema, gastrointestinal (GI) problems like gastroesophageal reflux disease (GERD), esophageal spasm, spontaneous esophageal rupture (Boerhaave syndrome), and myocarditis.[3] Stress, either emotional

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or physical, is often present in past histories of patients which men mostly experience a physical rather than emotional one, but other rare triggers such as natural disasters or snake bite could also cause TS.[6,14,15]

Five percent of patients had no elevation in cardiac biomarkers during TS; but in majority of them, creatine kinase-MB (CK-MB) and troponin levels would be raised in the acute setting.[7] Our patient had a normal range of troponin level during admission. As today, there is not a definite cut-off point to distinguish TS from MI. In a study done by Apple et al., CK-MB and troponin I greater than 10.5 U/l and 4.5 ng/ml, respectively, could be suggestive of ischemia.[11] Like other cardiac diseases, TS has some ECG findings as follows: ST segment elevations especially in anterior leads, inverted T waves, QT_c prolongation, and pathological Q waves. T-wave inversion may be with a poorer prognosis.[3,6,7] Although several efforts had been done for finding a way to distinguish TS just on the basis of ECG changes, it was not being successful yet. Some authors observed that ST elevation less than 1.75 mm or 2.5 mm in leads V2 and V3, respectively, has higher specificity for TS. ECG of patients with TS has few pathological Q waves, less ST depression, and longer QT_c segment. V4-V6/V1-V3 ratio of greater than 1 is highly sensitive and suggestive for TS. All of these ECG alterations usually will be normalized in duration from three weeks to one year after the attack.[6,7,13,16]

Among different imaging techniques, echocardiography is a convenient choice. Typical findings which are almost always present in classic TS are reduced EF and apical akinesia or hypokinesia concurrent with hyperkinesia of basal region, but it will be different in atypical forms due to its specific segment of involvement. Functional valve disturbances like TR, aortic insufficiency (AI), or MR can also occur, but generally all these findings return back to normal ranges during the first one year after TS.[3,4,7] For differentiating TS from MI or even myocarditis, CMR is one of the best tools. Absence of LGE is seen in 95% of patients with TS, while CMR of patients suffering from MI or myocarditis showed LGE.[3,7] If TS is recognized correctly, unlike its resemblance to MI, it will have almost a favorable prognosis. 96% of patients will recover completely during the first weeks or months after the onset.[3] There is not an appropriate guideline for either short or long-term TS treatment. Supportive therapy is the treatment of choice in acute phase and especially in stable patients.[1,3,4,6] Other therapies like β-blocker or α-adrenergic drugs had controversial results and complementary studies must have been done to proof them, but the most important point in treatment of patients is individualization of therapy according to their conditions.[4,6]

HF is one of the most common complications which could occur in TS. Other ones, although rare, like ventricular fibrillation (VF), septal perforation, and ventricle or papillary muscle rupture were also reported. Hayashi et al.[17] reported the first LV aneurysm due to TS in presence of ventricular wall thickening.[7] Dissection is less reported as a TS complication and almost all cases were SCADs, but intra-myocardial dissection due to TS is never reported as mostly found as a major complication in patients with MI.[8,9] Due to similar clinical presentations and gender preference with TS, some authors considered them as a single disease; however, others believe the reverse. For instance, Hassan et al. announced a 54-year-old woman with simultaneous SCAD and TS in different cardiac locations.[10] In contrast, Bakhit and Bin Abdulhak reported a 30-year-old woman presented with probable signs and symptoms of acute coronary syndrome (ACS) which after normal cardiac angiography results, TS was diagnosed and she was discharged. Several days later, she returned back with similar presentations. Further evaluations showed mid to distal coronary left anterior descending (LAD) dissection misdiagnosed as TS in previous admission.[18] TS leading to intra-myocardial dissection and LV apical aneurysm has never been reported and perhaps it is the first case in the literature.

In conclusion, TS is a reversible benign LV systolic dysfunction with favorable prognosis and less significant complications. Intra-myocardial dissection must be categorized as one of rarest TS complication beside LV apical aneurysm and rupture. Further studies are required in order to define the exact etiology and pathophysiological mechanisms.

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None.

Conflict of Interests

Authors have no conflict of interests.

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Adherence of cardiologist physicians to the American Heart Association guideline in approach to risk factors of cardiovascular diseases: An experience from a teaching hospital

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Short Communication

Abstract

BACKGROUND: Cardiovascular disease (CVD) is the leading cause of death globally and has enormous costs for healthcare systems. This disease has a strong association with lifestyle behaviors. Therefore, applying reliable and effective strategies for prevention and treatment of CVD is important. In this study, we aimed to evaluate the adherence of cardiologist physicians to the American Heart Association (AHA) guideline for prevention of CVD.

METHODS: Using a cross-sectional study, data were gathered for 208 patients using their medical records in the cardiology ward of a general teaching hospital. A physician systematically reviewed the medical records and completed the checklist in each domain. Adherence to the AHA guideline was evaluated in treating physician's choices and recommendations regarding these eight variables: hypertension (HTN), dietary intake, weight management, diabetes management, physical activity, blood lipid management, smoking, and aspirin prescription.

RESULTS: Medical records of 208 patients (109 men and 99 women) with the mean age of 62 ± 14 years were reviewed. The frequency of CVDs was 5.3% for coronary heart failure (HF) and 67.8% for the acute coronary syndrome (ACS). Cardiovascular risk factors of patients were HTN (53.8%), diabetes (34.6%), hyperlipidemia (17.3%), smoking (17.8%), and obesity (31.7%). We found a proportion of 59%, 15%, and 26% for high, moderate, and low adherence to AHA guideline, respectively.

CONCLUSION: Our study showed almost 60% high adherence to the AHA guideline by physicians in a teaching hospital. The most and the least adherence to the AHA guideline were for obesity and diabetes recommendations, respectively. More studies are needed to evaluate preventive guideline adherence in Iran. Establishing national preventive and therapeutic guidelines may increase the physicians' adherence to them.

Keywords: American Heart Association, Cardiovascular Diseases, Cardiologists, Guideline, Guideline Adherence

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Introduction

Cardiovascular disease (CVD) is the leading cause of death globally and has huge costs for health care systems in many countries.[1] CVD, particularly coronary artery disease (CAD), is one of the most preventable non-communicable disorders that can be reduced by modifying behavioral risks.[2]

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CVD causes 38% of all deaths in Iran annually, and about 3 million people aged 40 and above die every year from ischemic heart diseases (IHDs) in Iran.[2]

The evidence suggests disturbing increase in the prevalence of CVD risk factors such as diabetes, obesity, and the metabolic syndrome.[3-5] High-risk behaviors such as cigarette smoking, unhealthy dietary habits, physical inactivity, and psychosocial factors have a strong association with CVD.[6] Furthermore, hypertension (HTN), diabetes, and dyslipidemia are under the influence of the unhealthy lifestyle.[7] World Health Organization (WHO) has announced that lifestyle modification can prevent 75% of CVDs.[2]

Recommendations of international guidelines are the most effective way of ensuring that patients receive optimal care.[8] Physician adherence to cardiovascular preventive care guidelines is one of the critical steps to improve the outcomes of patients. Moreover, using guidelines can improve clinical practice.[9] Another study showed that use of guideline-based therapies was associated with significant reduction in mortality and other major adverse outcomes.[10]

For prevention and management of CVD, the American College of Cardiology (ACC) and the American Heart Association (AHA) develop guidelines, standards, and policies to promote optimal patient care and cardiovascular health.[11] The proposed guideline is one of the most reliable guides that are widely used in CVD prevention. It consists of recommendations for the control of blood glucose, lipids, weight, and blood pressure, encouragement of physical activity, safe diet, and also aspirin usage.[11] According to the importance of CVD in population health and its socio-economic consequences, applying reliable and effective strategies for prevention and treatment of these diseases is important. In this study, we aimed to evaluate the adherence of Iranian physicians to the AHA guideline for CVD prevention.

Materials and Methods

In this cross-sectional study, data about physicians' adherence to the AHA guideline were collected from medical records of patients admitted to the cardiology ward of a general teaching hospital of Iran University of Medical Sciences in Tehran City, Iran. Data collection was conducted from April 4 to July 6, 2015. Eligible patients were those who were admitted to the cardiology ward with one of the following diagnoses: IHD, HTN, heart failure (HF), or stroke. We excluded all records that were incomplete or free of CVD.

A data collection checklist was developed for the evaluation of the adherence to the AHA guideline and was completed for each patient using his/her medical records. The selection of checklist domains was performed by an expert panel consisting of experts in relevant medical specialties including community medicine, cardiology, and endocrinology, and eight risk factors were selected for inclusion in the checklist. Adherence to the AHA guideline was evaluated in treating physicians' choices and recommendations regarding these eight variables: HTN, dietary intake, weight management, diabetes management, physical activity, blood lipid management, smoking, and aspirin prescription.

A physician systematically reviewed the medical records and completed the checklists in each domain.

At first, she examined the number of existing risk-factors for each patient. Then, she compared the physicians' recommendations in each patient's medical record with the AHA guideline to determine the number of well-treated risk factors. The next step was to calculate the adherence to the AHA guideline by dividing the first number by the second. The total adherence to the AHA guideline was illustrated in percentage. Finally, we considered an adherence for less than 50%, 50%-80%, and more than 80% of risk factors as a low, moderate, and high adherence, respectively, according to expert opinions in the hospital.

Treatment goals for each variable were as follows:

- ***HTN:*** the target blood pressure was 130/80 for diabetes and 140/90 for the others. Moreover, prescribing proper antihypertensive medications from different classes in cases of high blood pressure was a desirable goal for HTN.
- ***Dietary intake:*** getting recommendations for an overall healthy eating pattern or following the recommendations by the patients.
- ***Aspirin:*** prescribing a low-dose aspirin for individuals at higher risk of coronary heart disease (CHD), especially those with the 10-year risk of CHD ≥ 10%.
- ***Weight management:*** achieving and maintaining a desirable weight [body mass index (BMI): 18.5–24.9 kg/m^2]. Furthermore, it was a goal that patients received proper recommendations about their weight when their BMI was ≥ 25 kg/m^2 or their waist circumference at iliac crest level was equal or more than 40 inches in men or ≥ 35 inches in women.

• ***Diabetes management:*** reaching normal fasting plasma glucose (110 mg/dl) or near normal hemoglobin A1c (HbA1c) (7%).

• ***Physical activity:*** at least 30 minutes of moderate-intensity physical activity on most/all days of the week or recommending this.

• ***Blood lipid management:*** low-density lipoprotein cholesterol (LDL-C) < 160 mg/dl if at least one risk factor was present. LDL-C < 130 mg/dl if two risk factors were present and the 10-year risk of CHD < 20%. LDL-C < 100 mg/dl if two risk factors were present and the 10-year risk of CHD ≥ 20% or if the patient had diabetes.

• ***Smoking:*** complete cessation and no exposure to environmental tobacco smoke.

All statistical analyses were performed using the SPSS software (version 16, SPSS Inc., Chicago, IL, USA). Categorical variables were described as frequency and percentage. Also, continuous variables were reported by mean ± standard deviation (SD).

For calculating the total adherence to the AHA guideline, we divided the number of the well-treated risk factors (in accordance to the AHA guideline) by a total number of the existing risk factors in the patients. The final results were reported in percentage.

Study protocols and procedures have been approved by the review board of Iran University of Medical Sciences.

Results

208 patients (109 men and 99 women) with mean age of 62 ± 14 years were admitted during the study duration and their medical records were reviewed. Frequency of CVD and risk factors are shown in table 1.

Adherence to the AHA guideline was first evaluated for each risk factor separately, and the results are shown in table 2. These included: HTN, diabetes, obesity, hyperlipidemia, and smoking. Among the studied risk factors, obesity treatment had the highest adherence to the AHA guideline (100%) followed by smoking (86.5%). The least adherence was for diabetes with only 31.9%.

Table 1. Baseline clinical characteristics of the study population

Type of CVD	Women (n)	Men (n)	Total [n (%)]
CHF	9	2	11 (5.3)
ACS	59	82	141 (67.8)
Arrhythmia	6	1	7 (3.4)
Type of cardiovascular risk factor			
HTN	69	43	112 (53.8)
Diabetes	40	32	72 (34.6)
Hyperlipidemia	23	13	36 (17.3)
Smoking	3	34	37 (17.8)
Obesity	39	27	66 (31.7)

CVD: Cardiovascular disease; ACS: Acute coronary syndrome; CHF: Congestive heart failure; HTN: Hypertension

Recommendation of healthy alternatives for lifestyle risk factors according to the AHA guideline was investigated as shown in table 3. These included: healthy diet recommendation, physical activity, and aspirin prescription. The results of adherence to the AHA guideline are shown in table 4.

According to the scoring, 59% of the records indicated a high degree of adherence by physicians in the cardiovascular unit of one teaching hospital; 15% of the files showed a medium adherence, and 26% of them illustrated low adherence by physicians.

Discussion

This study has been done by evaluation of 208 patients' medical records who were admitted to the cardiovascular unit of one general teaching hospital. Adherence to the AHA guideline by the treating cardiovascular specialists was evaluated. Our study showed 59% high, 15% moderate, and 26% low adherence to the guideline by physicians in this teaching hospital.

Table 2. Adherence to the American Heart Association **(**AHA) guideline based on the presence of cardiovascular risk factor in the study population

Risk factor	Patients with the risk-factor (n)	Non-adherence to the AHA guideline recommendation [n (%)]	Full adherence to the AHA guideline recommendation [n (%)]
HTN	112	23 (20.5)	89 (79.5)
Smoking	37	5 (13.5)	32 (86.5)
Hyperlipidemia	36	15 (41.5)	21 (58.5)
Diabetes	72	49 (68.1)	23 (31.9)
Obesity	66	0 (0)	66 (100)

AHA: American heart association; HTN: Hypertension

Table 3. Adherence to preventive measures according to the American Heart association (AHA) guideline

Preventive measure	Non-adherence to the AHA guideline recommendation [n (%)]	Full adherence to the AHA guideline recommendation [n (%)]
Healthy diet recommendation	115 (55.3)	93 (44.7)
Physical activity recommendation	118 (56.7)	90 (43.3)
Aspirin prescription	42 (20.2)	166 (79.8)

AHA: American heart association

Table 4. Adherence to the American Heart Association (AHA) guideline

Adherence	Percentage
High	59
Moderate	15
Low	26

In one study which was done in Shahid Modarres Hospital, Tehran City, 52.9% of physicians did not adhere to ACC/AHA guidelines in patients with unstable angina,[12] which is almost in accordance to our study findings (41%). The increase in our adherence result can be due to the fact that current health system pays more attention to the prevention of chronic CVDs. WHO has mentioned that 3/4 of all cardiovascular-related deaths can be prevented by changing one's lifestyle.[2]

Smoking is one of the most important behavioral risk factors for CVD.[13] In this study, 17.8% of the patients were smoker, and smoking cessation was advised to 68.7% of them. There is a relationship between blood pressure levels and occurrence of CVD even in blood pressures that have been defined as normal. In this study, 53.8% of patients had HTN, among which 79.5% had been followed.

High cholesterol/triglyceride (TG) and low high-density lipoprotein (HDL) levels are associated with the occurrence of CVD.[14] In developed countries, cholesterol level is increasing, which is mostly because of the low level of activity and increased fat consumption. In our 208 patients, 36 had hyperlipidemia, from which 21 received diet recommendations and 15 patients did not receive any recommendation. We know that each 1% decrease in blood cholesterol level can cause a 2%-5% decrease in CVD occurrence.[14] In this study, 79.8% of patients were on aspirin that is an effective way to decrease CVD.

Other recommendations in the AHA guideline which have been used in this study were obesity, diabetes, physical activity, and diet. We found that 44.7% of patients were advised to eat more vegetables and fruits and decrease their dietary salt and fat intake. No dietary recommendation was given to 55.3% of patients.

Changes in diet and lifestyle are vital in preventing CVD and cardiovascular deaths.[15] That's why the change of lifestyle and having a healthy diet are among the most important recommendations of the 2006 AHA guideline. According to our study, less than half of the patients did not receive any lifestyle recommendation, noting an important gap between adherence to the therapeutic recommendations of the guideline and the preventive part of that. In Spain, the researchers studied the percentage of adherence to ACC/AHA guidelines and its effects on changing the survival of patients with atrial fibrillation (AF). They found that using the guideline increased the survival of patients with AF up to 3 years.[16]

A study in Croatia showed that although most specialists believed that guidelines were beneficial, only 56.9% used them.[17] HTN was thought to be the most important risk factor by primary care physicians, but diabetes was thought as the most important risk factor by the cardiologist. As mentioned before, guideline-based treatment for patients can reduce mortality and major adverse outcomes.[10,18] Furthermore, most of the physicians accepted guidelines but only half of them used guidelines, and their knowledge about the guidelines was not satisfactory.[17] Also in a study, physicians' adherence to the guideline was significantly lower in nonteaching clinics.[19] Thus, these reasons as well as the lack of time, resources, and knowledge are most likely the main causes of poor management of the risk factors.[17]

Our study had some limitations such as incomplete records and taking data from medical records of the patients. Conducting study in just one general teaching hospital with the probability of more adherence to the guideline is another limitation and reduces generalizability of findings.

The strength point of the current study was to assess the prevention and risk factors of CVDs besides the treatment approach. Majority of previous studies have just considered the treatment approach to CVDs. We suggest further studies to focus on adherence to especially preventive

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guidelines using prospective studies with more supervision of gathering data.

Conclusion

Our study showed 59% high, 15% moderate, and 26% low adherence to the AHA guideline by physicians in the cardiology ward of one teaching hospital. The most adherence to the AHA guideline was about obesity (100%), smoking (86.5%), aspirin prescription (79.8%), and blood pressure (79.5%), respectively. The less adherence was about diabetes (31.9%).

More studies are needed to evaluate preventive guideline adherence in Iran. Establishing national preventive and therapeutic guidelines may increase the physicians' adherence to them and finally promote the health of people.

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Conflict of Interests

Authors have no conflict of interests.

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