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ARYA Atherosclerosis

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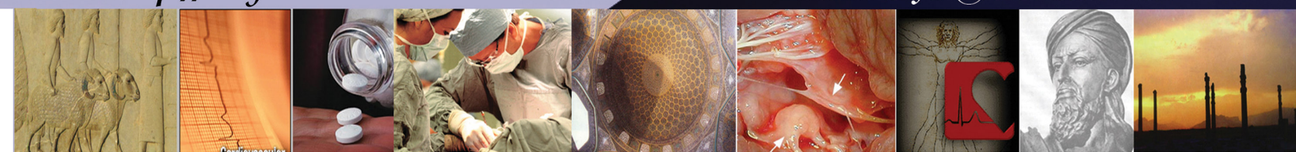

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* All the words of the article containing the references; each table is considered as 300 words.

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Effectiveness of a self-care education program on hypertension management in older adults discharged from cardiac-internal wards

Fatemeh Farahmand[(1)], Parvaneh Khorasani[(2)], Mohsen Shahriari[(3)]

Original Article

Abstract

BACKGROUND: The aim of the present study was to determine the effectiveness of a self-care education (SCE) discharge program with telephone follow-ups in managing hypertension (HTN) in older patients.

METHODS: The study was conducted on 56 older patients with HTN who had recently been discharged from the cardiac wards of hospitals in Isfahan, Iran, in 2017. Participants were randomly allocated to the intervention and control groups. The intervention was a 60-minute SCE discharge program with 4 re-educative telephone follow-ups every 2 weeks based on 4 chapters of the designed SCE program and booklet. After coding the data and entering them into SPSS software, data were analyzed for the comparison of mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) as well as frequency of managed HTN in the intervention and control groups at baseline (before discharge), and 2 and 3 months after discharge.

RESULTS: Statistical tests showed no significant difference in any of the demographic and confounding variables as well as baseline BPs ($P > 0.050$), but at post-intervention follow-ups, after Mauchly's sphericity test, repeated measurements ANOVA showed that the effect of time ($P < 0.001$) and group ($P = 0.043$) on SBP was significant. The effect of time ($P = 0.036$) and group ($P = 0.047$) on DBP was also significant. McNemar's test showed that the frequency of managed HTN (normal BP), 3 months after discharge, was significantly higher in the intervention group compared to the control group [87.5% (n = 21) vs. 23.1% (n = 6), respectively] ($P < 0.001$).

CONCLUSION: SCE discharge program with telephone re-educative follow-ups was effective in reducing mean BP. The use of this program as a discharged plan for older adults with HTN and comparison of readmission rates for a longer period are recommended.

Keywords: Elderly, Discharge Planning, Hypertension, Patient Education, Self-Care, Telenursing

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Introduction

Hypertension (HTN) is one of the most prevalent diseases in older adults,[1,2] with a prevalence rate of 61% in Iran.[3] HTN is one of the preventable risk factors of cardiovascular diseases (CVDs) and cerebral accidents.[4] Unmanaged HTN is accompanied with complications leading to disability in older adults. These complications increase in severity with age in older adults.[5,6] Cardiac failure, one of these complications, alone accounts for 27% of the causes of these patients' hospitalization.[7] Poor blood pressure (BP) management in developing countries, compared to developed countries, explains the high prevalence of such complications, which in turn result in patients' higher re-admission costs in such countries.[2]

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HTN is defined as systolic blood pressure (SBP) ≥ 140 mm Hg and diastolic blood pressure (DBP) ≥ 90 mm Hg,[4] and is accompanied with other unhealthy lifestyle risk factors.[8] In 2010, the ratios of awareness of diagnosis, treatment, and disease control were 43.5%, 33.8%, and 12.3%, respectively.[9]

HTN management is associated with a reduction in complications[10] and refers to controlling of BP (less than 140/90 mmHg). Experts believe that administration of self-care (including lifestyle modification), treatment compliance and regular BP rechecks are essential to achieve chronic diseases management. Lifestyle modification including weight reduction, compliance with Dietary Approaches to Stop Hypertension (DASH), increased physical activity, reduced alcohol consumption, and smoking cessation can somehow result in reinforcement of medical method effect and better BP control.[11,12] Considering the physical and mental limitations of older adults, only self-care education is inadequate in disease management, while continuing regular education along with follow-up for the patients and their families' accompaniment seem to result in self-care improvement.[13,14] It seems the missing ring in disease management in older adults with HTN is lack of re-education and post-discharge follow-ups.[15] Studies show that discharge education planning effects readmission and hospitalization days;[16] therefore, application of self-care education as a component of discharge education planning,[17] together with nurses' guidance and follow-up, can enhance self-care and BP control in older adults.[18] This issue can also be investigated concerning HTN in older adults.

In recent years, telephone follow-up, as one of the tele–nursing methods, compared to the routine care treatment system, bridges the gap between patients' discharge and home visit. It not only reduces patients' treatment referrals, but also improves their quality of life (QOL).[19,20] Therefore, with regard to the increased population of older adults, the importance of HTN managment[2,4] and nurses' role in education and management of chronic non-communicable diseases (NCDs),[21] the present study was conducted to define the quarterly effectiveness of a self-care education program with telephone follow-ups on the management of HTN in older adults who were discharged from hospital.

Materials and Methods

This quasi-experimental study (controlled-trial) was conducted in three-stages in two educational medical centers in Isfahan, Iran.

The participants were 56 older adults (60-79 years old) who were diagnosed with HTN and were being discharged from the internal/cardiac wards of 2 major hospitals in Isfahan. Sample size was calculated as at least 25 subjects in each group (control and intervention) based on the following formula:

$$n = \frac{2(z_1+z_2)^2(2S^2)}{d^2}$$

(80%) $z_2 = 0.84$; $z_1 = 1.96$; d = 0.8 S; n (sample size) = 25 subject in each group

In order to recruit subjects, 28 older adults were selected from the two hospitals (considering 10% drop out). Having obtained their informed consent, the subjects were allocated to intervention or control groups with random number assignment (1 or 2) at discharge.

The inclusion criteria consisted of positive history of HTN (recorded in patients' file) and undergoing treatment with antihypertensive medication at least 1 year prior to the study or at least 2 blood pressures over 140/90 mmHg recorded in the vital signs sheet of the patients by staff nurses, and lack of cognitive impairment. In addition, they needed to have the ability to perform daily living activities independently and no acute HTN complications such as heart failure, stroke, renal failure, and visual impairment at sampling time. The exclusion criteria were unwillingness to cooperate, no telephone follow-ups in 2 weeks, or drop out which resulted from stressful events, or diagnosis of an acute disease by a specialist.

First, the researcher extracted the list of hospitalized elders with HTN on consecutive days within 2 weeks. After obtaining informed written consent, according to the study inclusion criteria and using r quota sampling, the patients were assigned to intervention and control groups.

A digital sphygmomanometer (model Alpk2 K2-232, Japan) was used as data collection tool to measure SBP and DBP and a researcher made 16-item questionnaire was used to record the subjects' data in two sections:

A) Demographic characteristics form with 8 questions on age, sex, level of education, occupation, marital status, number of children, residence address, and people they live with.

B) Baseline information form about probable cofounding variables [number of years of HTN history, weight and height to calculate body mass index (BMI), history and dosage of anti-hypertension medications, history of contraceptive consumption (women), history and number of hospitalizations due

to HTN 1 year prior to the study, history and amount of smoking, specific diet, physical activity, and major diseases] with 8 questions and matched in the two groups before analysis of dependent variables.

To confirm face and content validities of the questionnaire, it was reviewed and evaluated by 10 experts in various professions of nursing and medicine. After implementing their modifications, reliability was estimated at 80% correlation of test-retest on 10 subjects with a 3-day interval. To ensure the accuracy of the BP measurement device, it was calibrated using a mercury sphygmomanometer. As BP measurements were all conducted by the researcher, to confirm accuracy (reliability), SBP and DBP measurements were administrated twice with 2-5-minute interval in 10 subjects; a high correlation of 80% was observed in standard conditions. To maintain reliable results during the study, BP measurement was conducted only by the researcher and with a unique sphygmomanometer after confirmation of reliability.

SBP and DBP were measured and recorded for the subjects twice with an interval of 2-5 minutes in standard conditions (sitting position, sphygmomanometer cuff size appropriate to patients' arm circumference, laying arm at the heart level, at least 5 minutes of rest before BP measurement, bladder voiding and no smoking and coffee 30 minutes before measurement, and folding patients' sleeves up to arm).[22]

Primary discharge data form was filled for the patients at the time of discharge in the presence of accompanying persons. Having coordinated with the ward manager, a 60-minute self-care education (SCE) session was held based on the designed education program in the form of a booklet in 2-6 member groups through lecture and Teach Back method (a method of repeated question and answer for providing feedback and deep learning). An educational booklet had been designed prior to the study based on needs assessment conducted among the older adults with HTN[23] with focus on disease control, secondary complications prevention, medicine education, appropriate diet, weight loss, increased physical activity, and smoking secession. This booklet was used as teaching aid not only to enhance their learning but as a source of information in telephone follow-ups. Subjects in the control group and their accompanying persons were recommended to have routine visits in health system. The primary outcomes of this study include:

1-Intergroup and intragroup comparison of mean SBP and DBP in the intervention and control groups before discharge, as well as 2 and 3 months after discharge

2- Intergroup and intragroup comparison of frequencies of managed HTN in the intervention and control groups before discharge, as well as 2 and 3 months after discharge

In addition to the above-mentioned educational intervention, the intervention group participants were followed up at their home by the researcher through phone calls every 2 weeks since the day of discharge. The 25-30-minute phone calls were aimed at reviewing the already presented materials and completing the educational program about HTN management in older adults and were presented based on 4 chapters of the SCE booklet. The SCE program and telephone follow-ups in the intervention group have been presented in table 1. The researcher conducted 4 telephone follow-ups for each older adult in the intervention group for 8 weeks. Then, the follow-ups were discontinued for 1 month and both groups were called back to the relevant center to undergo BP measurement by the researcher 2 and 3 months post discharge (The diagram of the study is showed in figure 1).

After coding the data and entering them into the SPSS software (version 18, SPSS Inc., Chicago, IL, USA). Continuous and categorical variables were reported as mean ± SD and absolute number (percent), respectively. The collected data were analyzed using independent t-test, Mann-Whitney U, chi-square, and repeated measures ANOVA with Mauchly's sphericity test, Cochran's Q, and McNemar's tests. P-values of less than 0.050 were considered as significant.

Results

Statistical tests showed no significant difference in any of the demographic and confounding variables, age (71.5 ± 4.5 and 69 ± 4.9 years, respectively, in the intervention and control groups), history of HTN (9.9 ± 5.9 and 8.8 ± 8.2 years, respectively, in the intervention and control groups), BMI (29.1 ± 4.1 and 28.4 ± 3.1 kg/m^2, respectively, in intervention and control groups), gender, marital, occupational, and life status, level of education, and number of hospitalizations for BP control, in the year prior to the study ($P > 0.050$) (Table 2).

Moreover, the other variables such as history of medication, concurrent diseases (CVDs, diabetes, hyperlipidemia, and renal failure diseases), hormonal contraceptive methods, smoking, any special diets, and level of physical activities were similar in both groups before the study ($P > 0.050$).

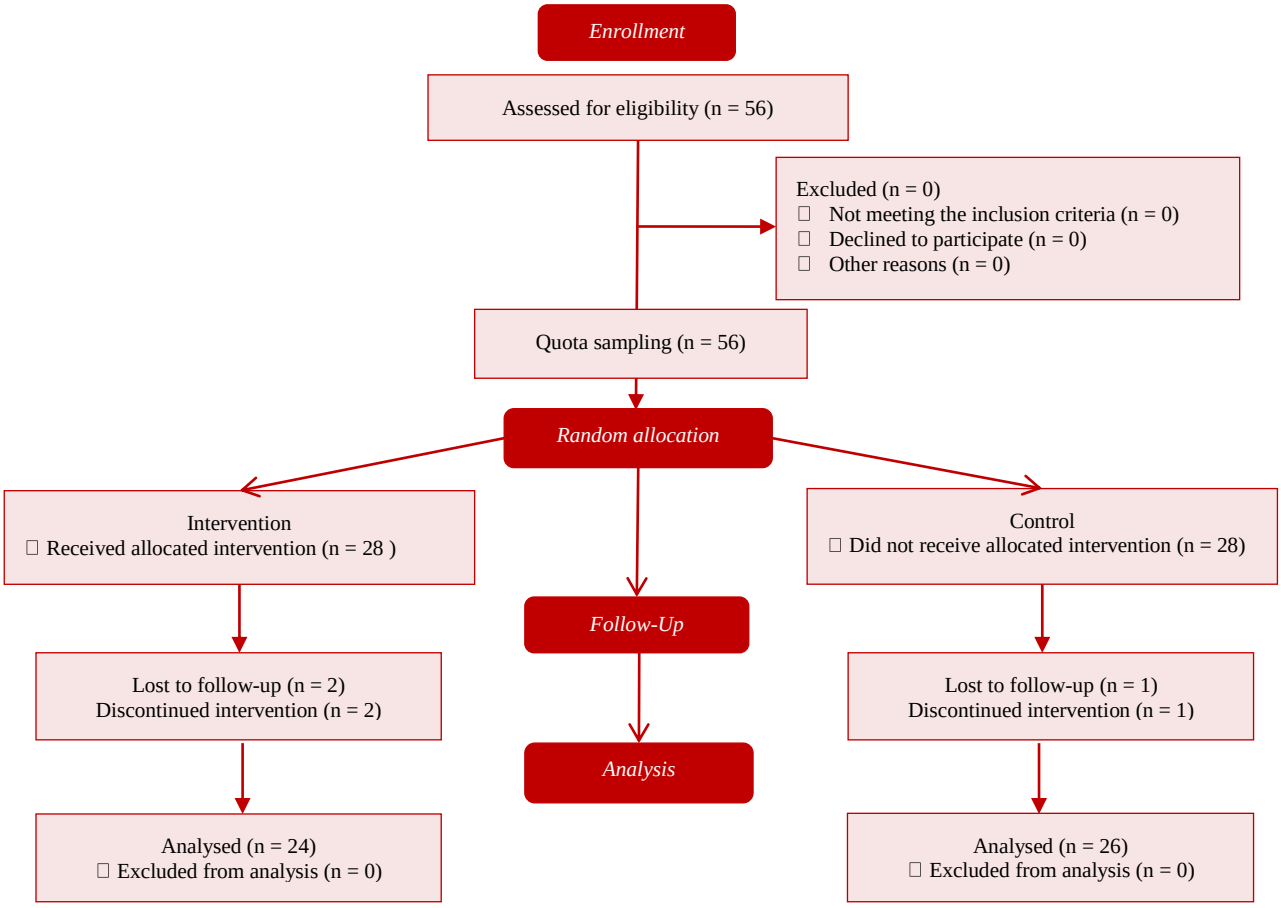

Figure 1. Diagram of the study

From among 56 subjects, 4 subjects in the intervention group and 2 subjects in the control group were excluded from the study due to the exclusion criteria (lack of response to the telephone follow-ups twice consecutively and lack of referral for BP measurement in the third run).

After Mauchly's sphericity test, repeated measurements ANOVA showed that the effect of time ($P < 0.001$) and group ($P = 0.043$) on SBP was significant. The effect of time ($P = 0.036$) and group ($P = 0.047$) on DBP was also significant (Table 3).

Frequency of normal range BP (managed HTN) before discharge was 33.3% (n = 8) and 30.8% (n = 8) in the intervention and control groups, respectively ($P = 0.760$). HTN crisis occurred in one subject in the control group who was excluded from the study because of lack of response in follow-ups. The frequency of managed HTN was 41.7% (n = 10) and 26.9% (n = 7) in the intervention and control groups, respectively, 2 months after discharge; this differences was not significant ($P = 0.270$). Furthermore, the frequency of managed HTN, 3 months after discharge, was significantly higher in the intervention group compared to the control group [87.5% (n = 21) vs. 23.1% (n = 6)] ($P < 0.001$). In addition, Cochran's Q test showed that the frequency of managed HTN in the intervention group was significantly different between the three times ($P < 0.001$); however, in the control group, there was no significant difference between the three times ($P = 0.470$). McNemar test showed that the frequency of managed HTN in the intervention group did not differ significantly before discharge and 2 months after discharge ($P = 0.620$); however, 3 months after discharge, it was significantly higher than before discharge ($P < 0.001$) and 2 months after discharge ($P = 0.001$) (Table 4).

Discussion

Considering the decreased SBP in the intervention group 2 months after discharge and reduced mean SBP and DBP 3 months after discharge compared to the previous measurements in this group, and the increase in mean SBP and DBP in the control group during the same time interval, the SCE program together with telephone follow-ups was found to be effective.

Table 1. Self-care education program and telephone follow-ups in the intervention group

Educational subject	Summary of conversations and the outcome of the initial and final evaluation of the meeting Compliance with self-care recommendations related to in-person education at discharge
First telephone call: familiarity with medications The content: greeting -Review previous session results; -Review goals: 1. Identifying and prescribing antihypertensive medications 2. Reporting the amount, frequency, time, and method of taking antihypertensive medication correctly in accordance with the latest prescription Time: …./…./2017 . . : . . am/pm	Help questions: 1. What have you changed in your diet? Evaluation: Patient can explain three changes in his/her diet that are related to blood pressure control. Result:□ No change (totally inappropriate) □ No change (relatively inappropriate) □ Change (proper proportion) □ Change (complete) 2. Explain the amount of salt intake during the last week. Evaluation: Patient describes the amount of salt consumed by referring to the relevant principles in the previous class. Result:□ No change (totally inappropriate) □ No change (relatively inappropriate) □ Change (proper proportion) □ Change (complete) Recommendation / Referral / Consultant / Additional guidance:
Second telephone call: Appropriate diet The content: greeting -Review previous session results; -Review goals: 1. Explaining at least three of the principles of appropriate diet in hypertension by simple and complete words 2. Identifying the four main food groups in the hypertension diet Time: …./…./2017 . . : . . am/pm	Help questions: 1. Explain the amount, timing, and frequency of taking two consumable medicines. Evaluation: Patient can explain the amount, timing, and frequency of taking two consumable medicines referring to the relevant principles in the previous call. Result:□ No change (totally inappropriate) □ No change (relatively inappropriate) □ Change (proper proportion) □ Change (complete) 2. Explain the relationship between the hypertensive medication and its three side effects experienced by the patient. Evaluation: Patient can relate medicinal side effects to the type of hypertensive medication consumed. Result:□ No change (totally inappropriate) □ No change (relatively inappropriate) □ Change (proper proportion) □ Change (complete) Recommendation / Referral / Consultant / Additional guidance:
Third telephone call: Physical activity and weight loss The content: greeting -Review previous session results; -Review of goals: 1. Explaining the type and required duration of physical activity to reduce blood pressure 2. Explaining the importance of having physical activity regularly and its relationship with weight loss and blood pressure reduction in their own words Time: …./…./2017 . . : . . am/pm	Summary of conversations on how to comply with relevant self-care recommendations Help questions: 1. Explain at least three main principles of appropriate diet in hypertension by using own words. Evaluation: Patient can explain three main principles of appropriate diet in hypertension referring to the relevant principles in the previous call. Result:□ No change (totally inappropriate) □ No change (relatively inappropriate) □ Change (proper proportion) □ Change (complete) 2. Describe the maximum amount of salt consumed. Evaluation: Patient can describe the maximum amount of salt consumed referring to the relevant principles in the previous call. Result:□ No change (totally inappropriate) □ No change (relatively inappropriate) □ Change (proper proportion) □ Change (complete) Recommendation / Referral / Consultant / Additional guidance:

Table 1. Self-care education program and telephone follow-ups in the intervention group (Continue)

Educational subject	Summary of conversations and the outcome of the initial and final evaluation of the meeting Compliance with self-care recommendations related to in-person education at discharge
Forth telephone call: Familiarity with hypertension symptoms and complications: The content: greeting -Review previous session results; -Review goals: 1. Explaining at least three symptoms of increased blood pressure in its self 2. Explaining at least three symptoms of decreased blood pressure in its self Time: …./…./2017 . . : . . am/pm	Summary of conversations on how to comply with relevant self-care recommendations Help question: 1. Explain the type and required duration of physical activity for blood pressure reduction. Evaluation: Patient can explain the type and required duration of physical activity for blood pressure reduction referring to the relevant principles in the previous call. Result:□ No change (totally inappropriate) □ No change (relatively inappropriate) □ Change (proper proportion) □ Change (complete) 2. Explain the importance of having physical activity regularly in reduced blood pressure in their own words. Evaluation: Patient can explain the importance of having physical activity regularly in reduced blood pressure referring to the relevant principles in the previous call. Result:□ No change (totally inappropriate) □ No change (relatively inappropriate) □ Change (proper proportion) □ Change (complete) Recommendation / Referral / Consultant / Additional guidance:

Table 2. Demographic and confounding variables in the intervention and control groups at baseline

Variable		Group		P
		Intervention group (n = 28)	Control group (n = 28)	
		Mean ± SD	Mean± SD	
Age (year)		71.5 ± 5.4	69.03 ± 4.9	$P^1 = 0.100$
History of hypertension (year)		9.9 ± 5.9	8.80 ± 8.2	$P^1 = 0.570$
Body Mass Index		29.1 ± 4.1	28.40 ± 3.1	$P^1 = 0.540$
		n (%)	n (%)	
Gender	Female	10 (41.7)	12 (46.2)	$P^2 = 0.750$
	Male	14 (58.3)	14 (53.8)	
Marital status	Married	17 (70.8)	20 (76.9)	$P^2 = 0.610$
	Widowed	7 (29.2)	6 (23.1)	
Occupational status	Employed	2 (8.3)	4 (15.4)	$P^2 = 0.860$
	Retired	8 (33.3)	9 (34.6)	
	Insurance Recipient	5 (20.8)	4 (15.4)	
	Housekeeper	9 (37.6)	9 (34.6)	
Living status	Alone	3 (12.5)	3 (11.5)	$P^2 = 0.650$
	With wife	16 (66.7)	20 (77.0)	
	With children	5 (20.8)	3 (11.5)	
Level of Education	Illiterate	3 (12.5)	6 (23.1)	$P^3 = 0.920$
	pre-high school diploma	15 (62.5)	11 (42.3)	
	High school diploma	6 (25.0)	8 (30.8)	
	Academic education	0 (0)	1 (3.8)	
Hospitalization for HTN in the past year	less than once	16 (66.7)	20 (76.9)	$P^3 = 0.460$
	one to two times	6 (25.0)	4 (15.4)	
	more than twice	2 (8.3)	2 (7.7)	

SD: Standard deviation; P^1: Independent t-test; P^2: Chi-Square test; P^3: Mann-Whitney U test

Table 3. Blood pressure status for intervention and control groups at three stages of the study

Variable	Group	Time			P[1]	P[2]
		Baseline (before discharge)	2 months after discharge	3 months after discharge		
		Mean ± SD	Mean ± SD	Mean ± SD		
SBP	Intervention group (n = 24)	153.4 ± 13.7	145.7 ± 11.3	137.2 ± 9.0	0.043*	< 0.001*
	Control group (n = 26)	150.5 ± 15.6	151.3 ± 14.0	153.3 ± 13.7		
DBP	Intervention group (n = 24)	87.6 ± 9.3	85.7 ± 8.9	84.1 ± 8.3	0.047*	0.036*
	Control group (n = 26)	88.5 ± 10.5	89.4 ± 9.5	90.0 ± 7.9		

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; SD: Standard deviation
P[1]: Effect of group; P[2]: Effect of time; * P-value of less than 0.050 was considered as significant.

Findings showed the effect of the intervention on the reduction of SBP and DBP in the intervention group at the end of the study compared to before the intervention. During the same time interval (i.e., before discharge until the end of the study), mean SBP and DBP showed an increase in the control group. Similarly, Chiu and Wong reported that mean SBP and DBP were significantly lower in their intervention group after educational session and counseling by phone calls for 8 weeks in older adults (mean age of 54 years) with HTN compared to the control group who only received nursing counseling at the clinic.[24] Furthermore, Park et al. obtained similar results in older adults with HTN residing in nursing homes after SCE with 8-week follow-ups.[10] Their results showed that SCE, especially with follow-ups and counseling, reduced BP of older adults with HTN. Their research was different from the present study in terms of the discharge planning protocol and administration of regular self-care education, which can lead to effectiveness of education and a behavior change in self-care by reinforcing follow-ups. In some other studies, the effectiveness of counseling and telephone follow-ups on self-care behaviors of patients with HTN has been evaluated differently. For example, Faraji showed that the intervention had a consistent positive effect on the patients' SBP control after 8 weeks (P = 0.030), but it could not improve the patients' adherence to treatment and lifestyle modification (P > 0.050).[25] Researchers emphasized the necessity of long-term and regular follow-up to enhance the patients' self-care behaviors in chronic conditions. The difference in the results of the above-mentioned research and the present study could be due to difference in the participants' age group (18-65 vs. 60+ years).

Moreover, the frequency of managed HTN at the end of the study was significantly higher in the intervention group compared to the control group. This variable was a little higher in the intervention group 2 months after discharge with no significant difference (P > 0.050). Furthermore, controlled HTN distribution was significantly higher in the intervention group compared to the control group 3 months after discharge (P < 0.050). These results are consistent with those of Park et al. who reported a significant increase in the percentages of managed HTN in the intervention group compared with the control group (P = 0.03).[10] Mohammadi et al. also reported a significant increase in the level of managed SBP (P < 0.001) and DBP (P < 0.004) in the intervention group after 3 months of follow-ups compared to the control group.[26] Comparison of the aforementioned results show the importance of follow-up along with SCE in the reduction of the percentage of unmanaged HTN which is one of the main factors for readmission among older adults with HTN.

Table 4. Frequency of managed hypertension (normal blood pressure) for the intervention and control groups at three stages of the study

Group	Time			P[2]
	Baseline (before discharge)	2 months after discharge	3 months after discharge	
	Frequency (%)	Frequency (%)	Frequency (%)	
Intervention group (n = 24)	8 (30.8)	7 (26.9)	6 (23.1)	< 0.001*
Control group (n = 26)	8 (33.3)	10 (41.7)	21 (87.5)	0.470
P[1]	0.76	0.27	< 0.001*	

P[1]: McNemar's test; P[2]: Cochran's Q test; * P-value of less than 0.050 was considered as significant.

Conclusion

This program was designed with a holistic approach towards the educational needs of older adults considering their specific barriers of learning such as their physical and functional restrictions. Therefore, the positive changes observed in SBP and DBP and the increase in the percentage of controlled HTN seem to result directly from this program. Designing a discharge program for older adults with HTN and the holistic approach towards their educational needs and self-care behaviors along with telephone follow-ups aimed at providing continuous training are the outstanding points of the present study compared to previous research.

Research Constraints: Regarding the chronicity of the process of HTN management and the importance of long-term follow-up in these cases, the short duration of the study was one of the limitations of this research (because of the limitation of thesis protocols in MSc degrees). In addition, polypharmacy, comorbidities, and lack of permanent access to these patients or their relatives for telephone follow-up limited the obtaining of valuable information.

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Conflict of Interests

Authors have no conflict of interests.

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CASCADE screening and registry of familial hypercholesterolemia in Iran: Rationale and design

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Original Article

Abstract

BACKGROUND: Familial hypercholesterolemia (FH) is one of the most common genetic disorders, which leads to premature coronary artery disease (CAD). It has been suggested that heterozygous FH affects around 1:250 to 1:500 in the general population or even more than this, and homozygous FH affects 1:1000000 of the population. If patients with FH are not diagnosed and treated early in life, many of them will develop premature CAD event. As most of the patients with FH are undiagnosed, it is recommended that the general population be screened for high risks of the events since early treatments can reduce the risk of premature CADs. The clinical diagnostic criteria for FH consist of increased plasma low-density lipoprotein cholesterol (LDL-C), clinical features and family history of CAD. However, deoxyribonucleic acid (DNA)-based detection of FH mutation has high diagnostic values. As there was no screening for FH in Iran up until now, we have started screening and registering patients with FH using the CASCADE method.

METHODS: We detected FH subjects in the general population by screening laboratories according to their high LDL-C levels (more than 190 mg/dl or 150 mg/dl if receiving treatments), while our second approach was hospital-based in which one screens hospitalized patients with premature CAD events.

RESULTS: We intended to screen families of indexed patients to provide standard care and therapy in order to optimize their LDL-C.

CONCLUSION: This article provides detailed information on the rationale and design of this screening and registry in Iran.

Keywords: Screening, Registries, Familial Hypercholesterolemia, Iran

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Introduction

Familial hypercholesterolemia (FH), an autosomal dominant disorder, is a common genetic condition affecting low-density lipoprotein cholesterol (LDL-C) metabolism with mutations in LDL receptor *(LDL-R)* gene, apolipoprotein B (APOB), a gene encoding the protein constituent of LDL-C, or proprotein convertase subtilsin-kexin type 9 (PCSK9*)*

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a gene encoding a protease that degrades LDL-C receptors. It is estimated that heterozygous FH exists 1 out of 500 to 1 out of 250 and in some areas could be up to 1 out of 100 in the general population which is more common than cystic fibrosis (CF), diabetes mellitus (DM), or neonatal hypothyroidism. These figures are even much higher in certain populations such as the French Canadians or Christian Lebanese.[1,2] FH is characterized by LDL-C level above 190 mg/dl, and in some patients it is characterized with the presence of xanthelasma palpebrarum (XP), corneal arcus, as well as the presence of xanthoma on the tendons of hands, elbows, knees, feet, and particularly the Achilles tendon.[3]

Because of a lifelong burden of high LDL-C levels, individuals with FH have a > 20-fold increased risk of premature coronary artery disease (CAD) compared with the general population.[4] Untreated men have a 50% risk of a coronary event by the age of 50, while untreated women have a 30% risk by the age of 60.[5] If the treatment is initiated in young adulthood, patients with FH will have nearly the same risk of CAD compared to their healthy counterparts. They demand lifelong pharmacotherapy with different lipid-lowering medications, dietary management, and modification of other risk factors to prevent cardiac diseases. Unfortunately, physicians are either unaware of the importance of early FH diagnosis or its prevalence or incidence in different countries. FH is a significant global public health concern; patients are often asymptomatic. As a result, an appropriate method to improve detection, management, and treatment of FH in order to decrease premature CAD events and its related death tolls are required among different populations. Previous studies showed that the prevalence of definite FH in premature CAD was about 5-10 percent based on the clinical phenotype.[6,7] However, the true prevalence would be much higher.

Due to the fact that the premature CAD events and its death tolls can be significantly decreased by early diagnosis and proper treatments and also based on our estimates that FH is underdiagnosed and undertreated in Iran,[8] we decided to perform FH screening and registry in the general population and in premature cardiac patients using the CASCADE screening method.[9]

The CASCADE screening method provides a cost-effective way of identifying new cases of FH. Using this method, a person diagnosed with FH and referred to as the indexed case, becomes the starting point for treatment among his or her family members among which a systemic screening of the close relatives is implemented.

We believe that this FH registry will be a powerful tool for monitoring the patients and their families. Using this method provides the health decision makers with pivotal information that can be used in promoting our clinical practice. In addition, we will study other CAD risk factors, identify family members with existing or new FH diagnosis, and develop a bio-bank of deoxyribonucleic acid (DNA) and other biomaterials of patients with FH and their close relatives for future genetic and epigenetic studies. We intend to screen the suspected FH cases by using two approaches. The first approach deals with detecting our cases in the general population by screening their LDL-C levels whereas the second approach was a hospital-based one aimed to screen patients who have been hospitalized due to premature CAD events. This article provides detailed and precise information on the rationale and design of the above-mentioned approaches in Iran.

Materials and Methods

The enrollment framework in these approaches was based on first investigating laboratories for contacting patients with high LDL-C to enroll them in our study (National Clinical Trial No.2865694). All individuals aged above 2 years, irrespective of their sex with LDL-C of more than 150 mg/dl (LDL-C > 190 mg/dl or LDL-C > 150 mg/dl but under pharmacological treatments were considered eligible) were contacted by phone to come to our clinic for further evaluation. We used the Dutch Lipid Clinic Network Score (DLCNS) which was based on the clinical symptoms of FH and family history[9] (Table 1).

Our patient screening was based on young patients with CAD (men less than 55 years old and women less than 60 years) who were hospitalized for percutaneous coronary interventions (PCI) in hospitals with specialized cardiology facilities (National Clinical Trial No.02870660) in Isfahan, Iran.

Our key exclusion criteria were those suffering from genetically hyperlipidemia (secondary hyperlipidemia), patients with chest pain and CADs along with concomitant serious diseases, and those who were previously screened.

All subjects were referred to our FH clinic to be registered. Then they were asked to complete a questionnaire which included demographic characteristics such as physical examination looking

for tendon xanthomas and corneal arcus, the history of CAD and other diseases in the patients or their families, and the medications being used, especially anti-lipid drugs and other medications. In order to be able to follow them for a year, their addresses and phone numbers were collected.

We performed our clinical examination with emphasis on the presence of tendon xanthoma, xanthelasma, or corneal arcus. Finally, the total Dutch criteria score indicates the probability of having or not having FH. Accordingly, people are divided into 4 categories: those whose scores are below 3 are very unlikely to have FH and those whose scores are above 8 are definitely affected by FH. People with scores between 3 and 8 have moderate and high risks of having FH; therefore, those whose scores are more than 8 definitely suffer FH, those whose scores are between 6–8 probably suffer from FH, and those whose scores are between 3–5 possibly suffer from FH[10] (Table1).

All participants underwent a complete blood test consisting of high-density lipoprotein cholesterol (HDL-C), LDL-C, triglyceride (TG), fasting blood sugar (FBS), and other blood indices such as red blood cells (RBC), white blood cells (WBC), platelet count, red cell distribution width (RDW), platelet distribution width (PDW), hematocrit (HCT), and hemoglobin (Hb). The patients' DNA was extracted and frozen for further genetic evaluation.

Management and CASCADE testing: This method has also been used in other countries that have performed FH registry including the Netherlands and Canada. The CASCADE FH Registry is a national, multicenter initiative that tracks FH therapy, family screening, clinical outcomes, and patient-reported outcomes longitudinally.[11] The CASCADE FH Registry represents collaboration among the FH registry team, lipid specialists, cardiologists, primary care providers, and subjects with FH.[12] Our FH registry team implemented a recruitment design to maximize the participation of confirmed and suspected patients with FH. Figure 1 shows the algorithm of our study design.

Results

Upon the approval of probable or definite FH diagnosis, patients would be managed by a specialist if necessary. Patients' lipid levels and cholesterol-lowering medication would be monitored every 3 months along with other lifestyle factors. Our team was responsible for the CASCADE testing of FH relatives. It was expected that up to 50% of first relatives would be diagnosed with FH; however, it was acknowledged that not all relatives would be followed up as they might decline the follow-up.[12]

Data were stored in a password-protected database on a secure server. Only specified research personnel were permitted to have access to the data.

Analyses were conducted using Stata software (version 13, Stata Corporation, College Station, TX, USA). Descriptive statistics were used to outline the number of patients at each point of the study (screened, at risk, followed up, and clinically diagnosed with FH).

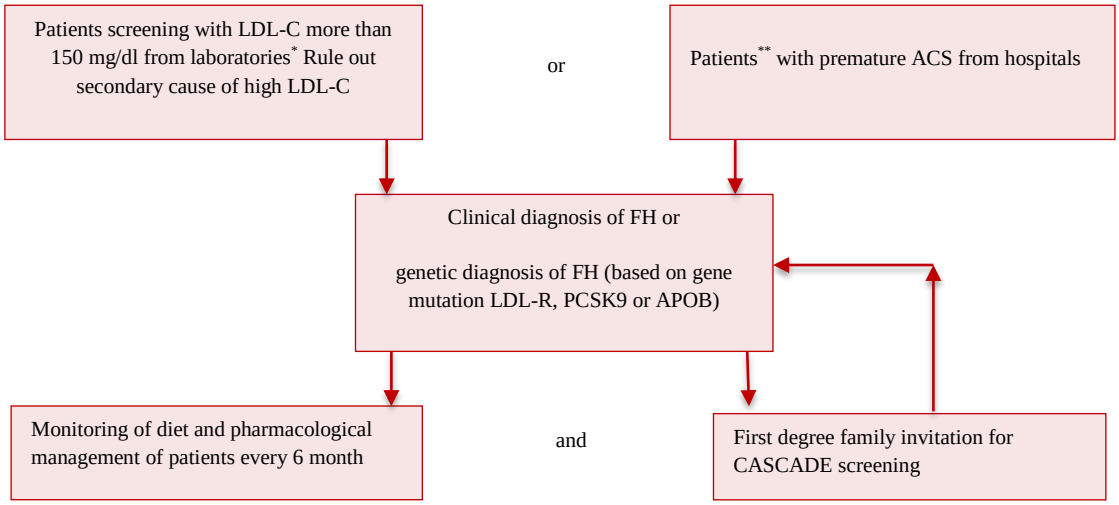

Figure 1. Schematic representation of the patient screening process for registry enrollment
* Rule out secondary cause of high LDL-C
** Age > 65 or > 55 for women and men, respectively
LDL-C: Low-density lipoprotein cholesterol; ACS: Acute coronary syndrome; FH: Familial hypercholesterolemia; LDL-R: Low-density lipoprotein receptor; PCSK9: Proprotein convertase subtilsin-kexin type 9;APOB: Apolipoprotein B

Table 1. Dutch lipid clinic network score (DLCNS) for diagnosis of familial hypercholesterolemia (FH)

Criteria	Score
Family history	
First-degree relative with known premature coronary and vascular disease	1
OR	
First-degree relative with known LDL-C level above the 95th percentile	2
Clinical history	
Patient with premature CAD	2
Patient with premature cerebral or peripheral vascular disease	1
Physical examination	
Tendinous xanthomata	6
Corneal arcus prior to 45 years of age	4
LDL-C levels (mg/dl, mmol/l)	
≥ 330, ≥ 8.5	8
250–329, 6.5–8.4	5
190–249, 5.0–6.4	3
155–189, 4.0–4.9	1
DNA analysis	
Functional mutation in the LDL-R, APOB, or PCSK9 genes	8
Diagnosis (based on the total number of points obtained)	
Definite FH	> 8
Probable FH	6-8
Possible FH	3-5
Unlikely FH	< 3

LDL-C: Low-density lipoprotein cholesterol; CAD: Coronary artery disease; DNA: Deoxyribonucleic acid; LDL-R: Low-density lipoprotein receptor; APOB: Apolipoprotein B; PCSK9: Proprotein convertase subtilsin-kexin type 9; FH: Familial hypercholesterolemia

At 12 months, the number of new index cases and the number of new family cases that have been detected would be reported. Changes in LDL-C level would be examined using a multilevel mixed-effects modelling. LDL-C level at 12 months would be the dependent variable. Random effects included: authorized medical staff (cluster effects) and time (repeated observations on the same individual). Analysis would also be adjusted for sex and age.

Discussion

Isfahan FH registry as the first FH registry in Iran will provide important evidence on the detection, prevalence, and management of patients with FH. It is well-known that registries are helpful in rapid and efficient collection of data that can be useful for further research, clinical practice, and health policy making. Many researchers prefer using registries' data as they allow the analysis of a disease in real-life conditions. Data obtained from registries provide a perspective of a problem in the community and allow for comparison of the results with large reference populations. This can stimulate improvements in quality and consistency of the practice.[13]

FH registries and screening methods are either general population or selective screening which is based on specific criteria. The selective screening methods can be classified into different categories such as: 1) collective lipid and genetic screening, 2) genetic CASCADE screening, 3) lipid CASCADE screening, 4) family CASCADE screening, and 5) based on a family history of dyslipidemia or coronary or CVD risk factors in the screened person.[14,15]

Isfahan FH registry can increase our knowledge on the burden of FH in Iran. Its results will enable comparisons of the attitudes and practices held in different disciplines including cardiology, internal medicine, and endocrinology. However, the calculation of FH prevalence may be difficult. In this study, we used the CASCADE method to detect patients with FH for both of our approaches. Our criterion for recruitment was high LDL-C level which was above 150 mg/dl (190 mg/dl if subjects did not receive treatments). Subjects were recruited from laboratories and invited to visit our FH clinic to undergo genotyping too. It became an integral part of clinical practice for FH, so all patients underwent genetic tests.

The Dutch criteria for the diagnosis of FH are a modification of the Simon-Broome criteria.[9] The principal reason for developing the Dutch criteria is that the Simon-Broome criteria diagnoses FH based

on personal and family history, physical examination, and laboratory findings. To address this shortcoming, the Dutch criteria introduce a point system and take the molecular defect of FH into consideration. Therefore, we studied our FH participants and classified them to different categories. Accordingly, they were defined as definite, probable, or possible.[3,14]

The advantages of our work are using an internationally well-known method, using two approaches at the population and premature CAD patients' levels, face-to-face examination of the participants, looking for examining the presence of tendon xanthomata and corneal arcus in addition to developing a bio bank of future genetic and other studies.

Our limitation is not performing genetic study simultaneously to conform the final Dutch criteria score at this stage.

Conclusion

Isfahan FH registry is the first FH registry in Iran which will generate valuable evidence regarding the diagnosis and management of these patients in this country. This will fill the gap in preventive care and establish the effective treatments of FH. While the implementation has been initiated in Isfahan, the scale-up pilot study at the national level will be started which may improve the quality and consistency of clinical practice and lead to the establishment of a national policy for the diagnosis and treatment of patients with FH. These data would be a source for local and international research.

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Conflict of Interests

Authors have no conflict of interests.

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Behavioral beliefs of reducing salt intake from the perspective of people at risk of hypertension: An exploratory study

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Original Article

Abstract

BACKGROUND: The average salt intake in Iran is 12 g per day and it is reported to be about 10 g per day in Yazd City, Iran. This study was conducted to explain the behavioral beliefs toward salt intake reduction in people at risk of hypertension (HTN) based on Theory of Planned Behavior (TPB) guideline.

METHODS: This study was a TPB-based exploratory research. The participants were 25 married individuals at risk of developing HTN, with a mean age of 42.9 ± 7.2 years. They were selected by purposive maximum variation sampling continued until data saturation. The data collection method was a semi-structured interview. Study lasted from January 2017 to April 2017.

RESULTS: Concerning the advantages and disadvantages of reducing daily salt intake, data analysis yielded 52 primary codes, 19 subcategories, and 5 categories. Advantages in two categories included disease prevention and misconceptions about the benefits, and disadvantages in three categories included physical health disorder, difficulty following a low-salt diet, and false beliefs about the disadvantages of salt intake reduction.

CONCLUSION: According to the findings of this study, prevention of high blood pressure and cardiovascular diseases (CVDs) was among the most important advantages of reducing salt intake, and undesirable taste of low-salt foods and family members' disagreement were among the most important disadvantages of reducing salt intake. The misconceptions of our participants included blood lipids reduction and creation of difficulty contracting the muscles. It is recommended to correct misconceptions and strengthen behavioral beliefs to promote salt intake reduction behavior in educational interventions.

Keywords: Sodium Chloride, Psychological Theory, Behavior, Hypertension

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Introduction

The high intake of salt is associated with hypertension (HTN), stroke, heart diseases, kidney stones, and gastric cancer.[1] Reduced salt intake is associated with reduced blood pressure and thus lower chance for developing cardiovascular diseases (CVDs).[2] The amount of salt intake is more than the World Health Organization (WHO) recommended amounts in the most countries of the world.[3] The average salt intake is 12 g per day in Iran,[4] and it is reported to be 10.1 ± 3.0 g per day in Yazd City, Iran.[5]

One of the theories used to change a person's behavior is the Theory of Planned Behavior (TPB) that can be used to predict and explain a wide range of behaviors. According to the theory, human behavior is guided by three kinds of considerations: behavioral beliefs, normative beliefs, and control beliefs, that are considered as the dominant determinants of an individual's intention and behavior.[6]

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Behavioral beliefs determine attitudes toward behavior.[7] Behavioral beliefs are people's beliefs about the outcomes or benefits of doing the behavior.[8]

Studies have shown that there is a relationship between the belief in dietary intake and the healthy behavior pertaining to it,[9] and beliefs about the status and consequences of the disease contribute to the desire of individuals to do health-promoting behaviors.[10]

Behavioral beliefs about certain behaviors such as exercise,[11] walking,[12] and choosing the method of cesarean delivery[13] have been explained by the TPB.

In the studies on the detection of behavioral beliefs about salt intake in patients with diabetes, the relationship of HTN and stroke with high salt intake[14] and the relationship between high salt intake and CVDs[15] were considered as the most important nutritional factors for the risk of CVD due to HTN by participants.[16,17]

In addition, the results of previous studies have shown that people's knowledge about salt is moderate toward low,[5,17-20] and the only correct belief among most people is that high amounts of salt may cause some health problems.[9,21-23]

Most participants also considered that high salt intake for people with chronic illnesses such as HTN and diabetes mellitus (DM) was harmful, and they did not have enough information about these diseases and mistook them.[24] Despite the importance attached to the salient beliefs in the TPB, little attention has been paid to the exploratory phase in the previous researches.[7]

Given the high salt consumption in Iran, the wide variety of food preferences and cultures in the world and their role in dietary habits, and the few theoretical studies on the behavioral beliefs toward salt, this exploratory study was conducted to explain behavioral beliefs toward salt intake reduction in people at risk of HTN based on the guidelines of TPB.[25]

Materials and Methods

The present study was a TPB-based exploratory research. Participants in the study were 25 individuals[25] at risk of developing HTN aged 20-50 years old. The inclusion criteria were having a risk factor for HTN such as DM according to the participants' report, being overweight or obese, living in Yazd, and willing to participate in the study.

A few participants were selected at first by convenience sampling; then snowball sampling helped us select informative participants and maximum variation sampling continued until data saturation, when new conceptual information could not be obtained.[26]

The data collection was performed using a semi-structured interview.[25] The duration of each interview was 30-40 minutes. During the interview, the advantages and disadvantages of reducing salt intake (consuming 5 g per day equivalent to one teaspoon of salt) were asked from the participants by these two questions:

1) What are the advantages of reducing daily intake of salt according to your opinion?

2) What are the disadvantages of reducing daily intake of salt according to your opinion?

Data were collected using exploratory questions as needed to provide further explanation. The study lasted from January 2017 to April 2017. Interviews were held in 25 sessions conducted in places which were convenient for the participants, like workplace and home.

All interviews were transcribed verbatim and read as soon as possible several times to gain a deep understanding and then were broken into the smallest meaning units (primary open codes). Then, the codes were further compared by their similarities to draw new codes after merging.

In the classification step, the merged codes that were more similar were assigned to the same subcategory and similar subcategories were assigned to the same category, and ultimately the themes were formed based on the constructs of the TPB.

Content analysis began after the first interview and continued until the end of the data collection. For the accuracy and robustness of the data collected, in-depth and prolonged engagement was used. The variety of expertise in the research team increased credibility. Member check was also used. This means that the drawn code was given to the participants to take their comments into account about the accuracy of the analysis.

The maintenance of research documents and the researcher's personal interest in the subject matter also led to data confirmability.[27] For transferability, the maximum variation sampling was considered for age, education, and occupation.

The protocol of the study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran (approval code: IR.SSU.SPH.REC.1395.133).

Before the interview, the purposes of the study were explained to the participants and an informed oral consent for participating in the study was obtained from them. In addition, the participants

were assured that their personal information would be kept confidential. Participants could also withdraw from the study whenever they wished.

Results

In the present study, 25 people at risk of developing HTN, with a mean age of 42.9 ± 7.2 years old, who were all married were enrolled (Table 1).

Table 1. Demographic characteristics of participants in the study

Variable		[n (%)]
Age (year)	< 40	8 (32)
	40-50	17 (68)
Gender	Men	11 (44)
	Women	14 (56)
Education	Under diploma	2 (8)
	Diploma	7 (28)
	College education	16 (64)
Occupation	Housewife	1 (4)
	Employee	21 (84)
	Self-employed	3 (12)

With respect to the advantages and disadvantages of reducing daily salt intake, 52 primary codes were drawn, 21 of which were assigned to 19 subcategories and five categories (advantages in two categories and disadvantages in three categories), and finally, two main themes of the advantages and disadvantages of salt intake reduction were formed (Table 2).

Regarding salt intake reduction, two categories, namely, disease prevention and misconceptions about the advantages were drawn.

Preventing diseases: The first drawn category included the subcategories of positive effects for the heart, effects for the brain, gastrointestinal (GI) effects, renal effects, osteoporosis prevention, vision enhancement, asthma severity reduction, and obesity prevention.

Positive effects for the heart: Participants said that heart disease, heart attacks, and HTN could be prevented by reducing daily salt intake.

One of the participants (a 50-year-old housewife) said: *"Reducing salt intake causes us at least not to develop an illness called HTN, which is the source of dozens of other illnesses such as stroke*".

Positive effects for the brain: Participants said that reducing daily salt intake would prevent stroke.

A participant (a 47-year-old female employee) said: *"When we eat less salt, our blood pressure does not go up, as a result we ['ll] not develop stroke".*

Positive gastrointestinal effects: Participants reported a decrease in gastric ulcer and also in gastric cancer, lack of sour stomach, better nutrition, and prevention of food rotting as beneficial GI effects of salt intake reduction.

A self-employed, 45-year-old man said: *"When we eat less salt, the acidity of the stomach increases, as a result, the consumed food will not rot and will be prepared for absorption in better conditions*".

Positive renal effects: Prevention of development of kidney disease and swelling of hands and legs were among the positive renal effects reported by our participants.

A participant (a 49-year-old male clerk) said: *"When we eat less salt, its benefits are that the legs do not swell and the kidneys do not stop functioning*".

Table 2. Themes, categories, and subcategories of behavioral beliefs among people at risk of hypertension (HTN)

Themes	Categories	Subcategories
The benefits of reducing daily salt intake	Preventing diseases	Positive effects on the heart
		Positive effects on the brain
		Positive GI effects
		Positive renal effects
		Preventing osteoporosis
		Vision enhancement
		Reducing the severity of asthma
		Prevention of obesity
	False beliefs about benefits	Reducing blood lipids
		Reducing blood cholesterol
The disadvantages of reducing daily salt intake	Physical health disorders	Adverse effects on the heart
		Weight loss and thinness
	Difficulty adhering to low-salt diet	Unpleasant taste of low-salt food
		Imposing restrictions on the consumption of some foods
		Family members' disagreement
		Changing the previous dietary habits
	False beliefs about disadvantages	Adverse GI effects
		Adverse biochemical effects
		Muscle contraction impairment

GI: Gastrointestinal

Preventing osteoporosis: Participants reported lower rates of developing osteoporosis and bone health promotion as some other benefits of daily salt intake reduction.

A 42-year-old female faculty member said: *"Reducing salt intake will reduce the risk of osteoporosis"*.

Vision enhancement: Participants mentioned prevention of visual problems and vision enhancement as two benefits of salt intake reduction.

A 50-year-old serviceman said: "*Salt reduction causes our vision not to decline*".

Reducing the severity of asthma: Salt can cause inflammation of the respiratory tract by confining water in the body. Participants in our study also reported the reduction in asthma severity as one of the benefits of salt intake reduction.

A 38-year-old male clerk said: *"When we eat less salt, we don't get asthma and we won't have dyspnea*".

Prevention of obesity: Salt intake reduction prevents overweight by preventing water accumulation in the body.

The participants also reported decreased appetite, reaching an appropriate weight, and prevention of overweight and obesity as the benefits of salt intake reduction.

A 35-year-old female clerk said: "*When salt is consumed in low amounts, because excess water does not accumulate in the body, it causes weight loss*".

False beliefs about advantages: Reducing blood lipids and lowering blood cholesterol were two of the false beliefs about the benefits of salt intake reduction reported by our participants.

Reducing blood lipids: A 49-year-old serviceman said: *"I have diabetes, I don't eat sugar, if I eat low amounts of salt, it is good for lowering blood lipids*".

Reducing blood cholesterol: A 38-year-old female clerk said: *"When we eat less salt, my blood cholesterol lowers*".

Regarding the disadvantages of salt intake reduction, three categories, namely, physical health disorder, difficulty following a low-salt diet, and false beliefs about the disadvantages of salt intake reduction were drawn.

Physical health disorders: This category includes the adverse effects on the heart, thinness, and weight loss subcategories.

Adverse effects on the heart: Participants expressed a drop in blood pressure in people who had hypotension, as one of the disadvantages of salt intake reduction.

A 38-year-old female clerk said: *"When less amounts of salt are consumed, the blood pressure in a person with hypotension decreases further*".

Weight loss and thinness: A participant (a 50-year-old physician) said: "*Using low salt in food causes skinny people to lose their appetite due to its inappropriate taste, and they cannot eat an adequate amount of food so that their weight is lost*".

Difficulty adhering to low-salt diet: Participants considered the unpleasant taste of low-salt foods, restrictions on the consumption of certain foods, the opposition of family members, and the change in previous dietary habits as part of the difficulty of adhering to the low-salt diet.

Unpleasant taste of low-salt food: Food insipidness and the lack of deliciousness as well as unpleasant taste of low-salt food were also reported as the disadvantages of salt intake reduction by our participants.

A 27-year-old female clerk said: *"The reduction in salt intake does not seem to me to be a disadvantage, but it may slightly affect the taste of the food which will be resolved by* [adding] *lemon juice and orange juice*".

Imposing restrictions on the consumption of some foods: A participant (a 27-year-old female employee) said: "*If we consume less salt, we will not be able to eat some of the foods we like*".

Family members' disagreement: The unwillingness of children and other family members was reported as one of the other disadvantages of low salt intake by the participants.

A 49-year-old male clerk said: *"When the food is low-salt, the children don't eat or drink, they don't eat at the table, or the food will be excess and will be thrown away*".

Changing the previous dietary habits: Some participants reported the separate cooking of food and the change in the method of food preparation as some of the disadvantages of salt intake reduction.

A 50-year-old housewife said: *"If I decide to eat low-salt foods, I'll have to eat separately on myself because my kids and husband won't eat*".

False beliefs about disadvantages: Participants said that salt intake reduction would lead to adverse effects on the digestive system and might cause adverse biochemical effects and muscle contraction impairment.

Adverse gastrointestinal effects: Participants said that salt intake reduction could cause gastric acid secretion as well as digestive problems.

A participant (a 31-year-old male accountant) said: "*When we eat low* [*amounts of*] *salt, gastric acid secretion will decrease and our food won't be well digested*".

Adverse biochemical effects: Participants reported disturbed levels of body fluids, iodine deficiency, as well as low blood pH levels as the adverse effects of salt intake reduction.

A participant (a 34-year-old male clerk) said: "*When we eat low* [*amounts of*] *salt, we'll develop iodin deficiency*".

Muscle contraction impairment: Some participants said that reducing salt intake could lead to problems regarding muscle contraction and movement as well as muscle cramps.

One of our participants (a 38-year-old male clerk) said: "*Everything is useful in a specific amount, if we consume too low amounts of salt, our muscles cannot contract and we will develop muscle cramps*".

Discussion

The findings of this study represent a classification of the advantages and disadvantages (behavioral beliefs) of reducing salt intake based on TPB in five main categories, namely, disease prevention, false beliefs about advantages, physical health disorder, difficulty in adhering to a low-salt diet, and wrong beliefs about disadvantages.

Prevention of disease included positive effects for the heart, positive effects for the brain, positive GI effects, positive renal effects, osteoporosis prevention, vision enhancement, asthma severity reduction, and obesity prevention.

The positive effects for the heart included prevention of CVDs, myocardial infarction (MI), and HTN, which is consistent with previous researches. In a study on patients with diabetes in Australia, 88% of patients believed that there was a relationship between high salt intake and HTN.[14]

The findings of a review study also found that 80% of healthy participants were aware of the relationship between high salt intake and HTN and 60% of them were aware of relationship between high salt intake and CVD and/or MI.[17]

But only 32% of people with HTN believed that the main nutritional factor for the risk of CVD was salt intake, which mainly affects the health by increased blood pressure,[16] and participants in the study of Sanchez et al. believed that heart disease and HTN were associated with the incidence of these diseases in one of the family members and were not associated with high salt intake.[24]

The positive effects for the brain were another subcategory drawn in our study, which is in line with the results of the study of Gray et al. in which 78% of people with diabetes believed that high salt intake was associated with stroke.[14]

Salt intake is one of the determinants of urinary calcium excretion and calcium is a major component of kidney stones.[28] One of the other benefits of salt intake reduction that the participants believed in this study was the prevention of kidney disease, which is not consistent with the results of the study of Sanchez et al., where the participants believed that kidney disease was inherited and was not associated with salt intake.[24]

Increased salt in the body also increases urinary calcium excretion, as well as calcium loss from the bone, leading to osteoporosis.[28] Prevention of osteoporosis was another advantage of reducing salt intake as expressed by the participants in the study, which is also consistent with the results of the study in which it was believed by about 30% of the participants.[17]

High salt intake is a risk factor for human cataract.[29] Vision enhancement was reported as one of the other benefits of salt intake reduction. Intake of high amounts of salt is an indirect cause of obesity. Salt absorbs water and motivates non-alcoholic beverages consumption, which will increase the body mass index (BMI).[28] Prevention of obesity was one of the other benefits of salt intake reduction that our participants talked of.

The severity of asthma attacks is associated with salt intake.[28] Reduction in the severity of asthma was reported as one of the benefits of salt intake reduction from the perspectives of the participants in our study.

Studies have shown that salt does not affect the level of blood cholesterol and other lipids,[2,30] and the reduction in lipid levels was among the false beliefs of a few number of our participants who considered it to be a benefit of salt intake reduction.

In the study of Zhang et al., one-third of the participants believed that false self-confidence would reduce physical activity if salt was reduced.[31]

In an international study by Newson et al., intensification of hunger by salt intake was reported as one of the false beliefs.[32]

The difficulty of adhering to a low-salt diet due to its adverse effects on the taste of food, the restrictions on the consumption of certain foods, family members' opposition, and the change in previous dietary habits were reported as the disadvantages of salt intake reduction.

The unpleasant taste of low-salt food is consistent with the findings of a study where the participants believed that salt was essential for the food flavor and that salt-free food was not edible.[24]

Training to use salt substitutes such as lemon juice and vegetables to taste food will resolve this problem.

Disagreement among family members and as a result, individual catering was also highlighted in Keshani and Farvid investigations on the use of high-fiber foods in patients with diabetes[33] and in older women's beliefs about restrictions on dietary salt intake.[34] It can be resolved by educating other family members to support and accompany in adhering to a diet with an appropriate amount of salt and how to prepare low-salt foods.

Disorders of physical health including decreased blood pressure in people with hypotension as well as thinness and weight loss were among the other disadvantages of salt intake reduction reported by our participants.

The participants believed that if the individuals who had low appetite and were thin, reduced their salt intake, their desire to eat food would further decrease and therefore, they would become thinner.

The last drawn category of behavioral beliefs included false beliefs about the disadvantages of salt intake reduction, including adverse effects on digestive system, adverse biochemical effects, and muscle contraction impairment, which few participants talked of.

This can be due to the lack of knowledge about the amount of salt recommended among the participants and the false belief that says reducing salt intake means complete elimination of salt from the diet.

Some participants assumed that reducing salt intake was equivalent to a severe salt deficiency, because they knew that one of the main symptoms of significant reduction in sodium intake was muscular cramping.[35]

Although sodium is an essential nutrient necessary to maintain plasma volume, the balance between acid and alkaline, the transmission of nerve signals, and normal cell function, and although the use of iodized salt plays a role in providing the body's salt, iodized salt is not the only source of iodine supply.

The belief of having difficulty digesting the food and GI problems due to salt intake reduction can also be due to the religious recommendations to eat salt before and after meals.

Considering the recommended intake of salt in a day by the WHO (5 g per day),[36] the participants are less likely to have misconceptions about the disadvantages of salt intake.

There are a number of limitations that should be considered before interpretation of our results. Although this study was based on the perception of people at high risk of developing HTN and it provided valuable information, we did not interview with health care providers. Therefore, their experience was not taken into account to obtain more comprehensive information, which is suggested to be addressed in subsequent researches.

Conclusion

According to the findings of this study, prevention of high blood pressure and CVD is one of the main advantages of reducing salt intake, and undesirable taste of low-salt foods and family members' disagreement were among the most important disadvantages of reducing salt intake.

The misconceptions of our participants included blood lipids reduction and creation of difficulty contracting the muscles. It is recommended to correct misconceptions and strengthen behavioral beliefs to promote salt intake reduction behavior in educational interventions.

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Conflict of Interests

Authors have no conflict of interests.

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The effect of intracoronary versus intralesional injection of eptifibatide on myocardial perfusion outcomes during primary percutaneous coronary intervention in acute ST-segment elevation myocardial infarction; A randomized clinical trial study

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Original Article

Abstract

BACKGROUND: Previous studies have proved that intracoronary injection of eptifibatide is safe and more effective in infarct size reduction and clinical outcomes than intravenously injection in the patients with acute myocardial infarction (AMI). This study aimed to compare the effect of localized and intracoronary injection of eptifibatide on myocardial perfusion improvement and its outcomes.

METHODS: We conducted a randomized clinical trial study of 60 patients presented with thrombotic AMI. The patients underwent percutaneous coronary intervention (PCI), and were randomly divided into two equal number groups. The first group received two bolus doses of 180 µg/kg eptifibatide through guiding catheter. The second group received the same bolus doses through export aspiration catheter into the coronary lesion directly. Thrombolysis in myocardial infarction (TIMI) flow, myocardial blush grade (MBG), and no-reflow phenomenon were primary end points. Secondary end points were pre- and postprocedure cardiac arrhythmia, in-hospital mortality, adverse effects, reinfection, pre-discharge ventricular systolic function, and re-hospitalization and mortality after 6 month of follow up.

RESULTS: The mean ages of group I and group II were 58.3 ± 1.8 and 57.0 ±2.0 years, respectively, and most of patient were men (90% in group I and 80% in group II). Postprocedural TIMI flow grade 3 was achieved in 60.0% and 76.7% of the intracoronary and intralesional groups, respectively (P = 0.307). Postprocedural MBG grade 3 was achieved in 53.3% and 70.0% in intracoronary and intralesional groups, respectively (P = 0.479). There was no significant difference between the groups in no-reflow assessment. Moreover, no significant difference was seen between the two groups in secondary end-point analysis.

CONCLUSION: Both methods of intracoronary and intralesional eptifibatide administration during primary PCI in patients with acute ST-elevation myocardial infarction (STEMI) were safe and similar in myocardial perfusion outcomes.

Keywords: Myocardial Perfusion Imaging, Eptifibatide, Myocardial Infarction

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Introduction

Primary percutaneous coronary intervention (PCI) is the standard treatment for patients with acute myocardial infarction (AMI).[1] Embolism, thrombus and vascular debris toward the distal vascular bed may occur during PCI which impairs myocardial perfusion, and thus aggravates clinical outcomes.[2]

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Furthermore, microvascular occlusion can occur in the large proportion of patients that undergoing successful PCI which will be associated with increased infarct size, reduced ventricular systolic function, and increased mortality.[3]

In order to prevent and treat distal embolization and improve myocardial perfusion, the specialists can use mechanical and/or pharmacological intervention methods that will improve clinical outcomes in patients with ST-elevation myocardial infarction (STEMI).[4,5] As a conventional method, glycoprotein (GP) inhibitors injection into infarcted vessels will increase drug concentration dramatically, and thus reduces available GP IIb/IIIa receptors to bind to fibrinogens in the microvessels.[6]

Previous studies have proved that intracoronary injection of eptifibatide (as a GP IIb/IIIa receptors inhibitor) is more effective in reduction of infarct size and clinical outcomes without significant increase in major bleeding than intravenous injection in the patients with AMI.[5-7] As a novelty, we hypothesized that intralesional eptifibatide injection could be more effective than intracoronary injection, because drug infusion through guiding catheter (situated in the left main or right coronary artery) causes drug back flow to the aorta and simultaneous drug entry into the normal vessels. So, the aim of our study was to compare eptifibatide localized and intracoronary injection on myocardial perfusion improvement and its outcomes.

Materials and Methods

Study participants and design: This was a randomized clinical trial study reviewed and approved by the research ethics committees in Isfahan University of Medical Sciences, Isfahan, Iran, and registered by the Iranian Registry of Clinical Trials (IRCT number: IRCT2016122722134N4). All patients gave written informed consent to participate in the study. A total of 160 patients with AMI diagnosis who presented to Shahid Chamran Heart Center (Isfahan, Iran) were selected.

Inclusion criterion was diagnosis of STEMI as defined by chest pain suggestive for myocardial ischemia for at least 30 minutes before hospital admission, and symptoms onset time less than 12 hours with 1 mm ST-segment elevation in 2 or more contiguous leads (for V1-V3, ST elevation was 2 mm) simultaneously. These patients should also have thrombus burden grade three or more on the angiography. Thrombus burden (TB) was graded (G) as G0 = no thrombus, G1 = possible thrombus, G2 = small (greatest dimension ≤ 1/2 vessel diameter), G3 = moderate (> 1/2 but < 2 vessel diameter), G4 = large (≥ 2 vessel diameter), G5 = unable to assess TB due to vessel occlusion.[8] Diagnosis and patient management was done by three specified interventional cardiologists.

Presenting with STEMI more than 12 hours of symptom onset, rescue PCI after thrombolytic therapy, with contraindications for antiplatelets such as bleeding disorder including hematuria, gastrointestinal bleeding, or known any bleeding tendency, recent stroke (less than 6 months), thrombocytopenia (platelet count < 100.000/cm^3), and cardiogenic shock were considered as exclusion criteria.

Finally, 97 patients were excluded and 63 patients were selected for coronary intervention. The patients were randomized in two groups by specified on-call interventional cardiologists via using random number table method. In group I (intracoronary administration group, n = 32), patients received two bolus dosess of eptifibatide through the guiding catheter in the infarct-related artery. In group II or intralesional administration group (n = 31), boluses of eptifibatide were administered through the export aspiration catheter into the lesion of infarct-related artery. These treatment methods were safe, and would not put the patient at higher risk (Figure 1).

Treatment: Standard therapy for all patients with pain reduction (analgesics and/or intravenous nitroglycerin), decreasing oxygen demand (beta-blocker), statin therapy, antithrombotic medications including 325 mg of acetylsalicylic acid, a 600 mg loading dose of clopidogrel, and heparin therapy after electrocardiographic confirmation of STEMI, were done usually in the emergency department. All the patients were transferred to the catheterization laboratory quickly. During PCI, when the wire had crossed the occlusion, the initial treatment step consisted of manual thrombus aspiration (Export aspiration catheter, Medtronic Inc., Santa Rosa, USA) in both groups. Over a period of 1 minute after the thrombus aspiration, in the intracoronary group, two separated bolus doses of eptifibatide with a 5-minute interval (each 180 μg/kg) were administered through the guiding catheter. The same doses of medication were administered through the export aspiration catheter into the lesion of infarct-related artery. Additional pre- or post-intervention dilatation with a balloon might be required in certain patients.

After the PCI, treatment included aspirin (80 mg), clopidogrel (75 mg), beta-blockers, lipid-lowering agents, and angiotensin converting enzyme (ACE)-inhibitors or angiotensin II receptor blocker.

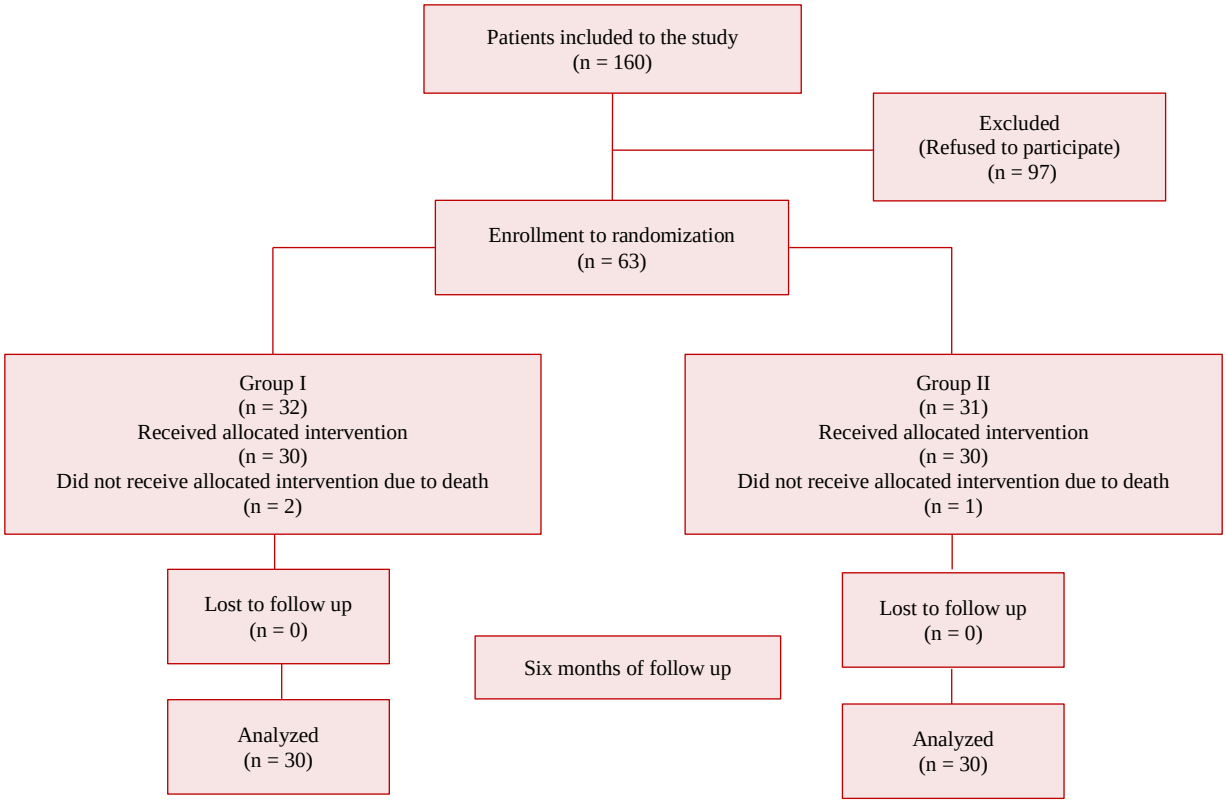

Figure 1. Consort diagram

The primary end points were postprocedural assessment of thrombolysis in myocardial infarction (TIMI) flow, myocardial blush grade (MBG), and no-reflow phenomenon. TIMI flow grade of less than 2, and MBG of less than 2 were described as angiographic no-reflow. These parameters were evaluated by another cardiology interventionist who was blinded to the groups. Secondary end points were pre- and postprocedure cardiac arrhythmia, in-hospital mortality, adverse effects including hemorrhage and stroke, reinfection, global ventricular systolic function (measured by conventional transthoracic echocardiography) before discharge, and re-hospitalization and mortality after 6 months of follow up. Follow-up information would be obtained from hospital records as well as by telephone interviews with the patients.

Statistical analyses: All statistical analysis was conducted on intention to treat basis by using the statistical program for social science (SPSS) software (version 15.0, SPSS Inc., Chicago, IL, USA). Statistician was blind to treatment condition.

Continues and categorical variables were reported as mean ± standard deviation (SD) and absolute number (percent). Pearson's chi-square or fisher's exact test (if needed) and Student's t test were used for comparison categorical and continues variables between groups, respectively. All differences were considered as statistically significant at a P value of less than 0.050.

Results

Finally, sixty patients including two equal group were analyzed. Baseline demographic and clinical characteristics are presented in table 1. There was no significant difference between groups in demographic, clinical, and drugs variables ($P > 0.050$ for all).

No significant difference was between the two groups on AMI level, culprit vessel, and severity of coronary artery diseases (CAD) ($P > 0.050$ for all). In both groups, the most common MI level (63.3%) was inferior MI, and the most common artery involvement (approximately 60.0%) was right coronary artery (Table 2).

Table 3 shows the frequency distribution of arrhythmia before the procedure, and the incidence of AMI and mortality after the PCI. There was not any significant difference in arrhythmia incidence between the two groups ($P = 0.228$). However, the frequency of cardiac arrhythmia in the group I (5 patients) was more than group II (2 patients).

Table 1. Baseline demographic and clinical characteristics for each group

Variables	Group I (n = 30) [n (%)]	Group II (n = 30) [n (%)]	P
Gender (man)	27 (90.0)	24 (80.0)	0.620
History of IHD	5 (16.6)	4 (13.3)	0.802
Diabetes mellitus	7 (23.3)	9 (30.0)	0.506
Hypertension	5 (16.7)	10 (33.3)	0.136
Current smoker	13 (43.3)	14 (46.6)	0.703
Cardiac drug consumption			
Aspirin	6 (20.0)	13 (43.3)	0.052
Clopidogrel	1 (3.3)	1 (3.3)	0.981
Statin	3 (10.0)	12 (40.0)	0.052
Beta-blocker	4 (13.3)	5 (16.6)	0.676
ACEI or ARB	2 (6.6)	7 (23.3)	0.062
	Mean ± SD	Mean ± SD	
Age	58.3 ± 1.80	57.0 ± 2.05	0.091

IHD: Ischemic heart disease; ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; SD: Standard deviation

It should be noted that the frequency of cardiac arrhythmia during the hospitalization was only one person (3.3%) in the intracoronary group, and no patient in the intralesional group (P = 0.310). Remarkably, the incidence of mortality during the hospitalization was very low and not significant (P = 0.554). The incidence of bleeding and stroke after PCI were very low in both groups including 3.3% in group II (only one case with cerebral stroke and no case of bleeding), and 6.7% in group I (one case of gastrointestinal bleeding and one case of cerebral stroke) (P = 0.554).

After six month of follow up, mortality rate was one patient (from group II) (P = 0.312). Two members of group II and one member of group I had to be re-hospitalized (P = 0.554). Figure 2 shows the bar graph of the percentage of cardiac events six months after PCI. No MI was seen among the patients of both groups.

There was no significant difference between the two groups in global ventricular systolic function assessment (38.80 ± 2.68 vs 41.00 ± 3.65 percent in group I and II, respectively; P = 0.440).

Table 4 shows the postprocedural TIMI flow, coronary MBG of infarct-related artery, and no-reflow phenomenon incidence. Postprocedural TIMI flow grade 3 was achieved in 60.0% and 76.7% of the intracoronary and intralesional groups, respectively (P = 0.307). Postprocedural MBG grade 3 was achieved in 53.3% and 70.0% of groups I and II, respectively (P = 0.479). About no-reflow phenomenon, there was no significant difference between the groups according to both methods of TIMI flow and MBG (P = 0.071) (Table 4).

Table 2. The comparison of frequency distribution of myocardial infarction (MI) level, culprit vessels, and severity of coronary artery diseases (CAD) between the groups.

Variables	Group I (n = 30) [n (%)]	Group II (n = 30) [n (%)]	P
AMI level			> 0.999
Inferior ± lateral/posterior	19 (63.3)	11 (36.6)	
Anterior ± septal/lateral	19 (63.3)	11 (36.6)	
Culprit vessels			0.570
LAD	11 (36.6)	11 (36.6)	
LCX	1 (3.3)	0 (0.0)	
RCA	18 (60.0)	19 (63.3)	
Severity of CAD			0.525
1-vessel disease	16 (53.3)	13 (43.3)	
2-vessel disease	9 (30.0)	12 (40.0)	
3-vessel disease	5 (16.6)	5 (16.6)	

AMI: Acute myocardial infarction; LAD: Left anterior descending artery; LCX: Left circumflex artery; RCA: Right coronary artery; CAD: Coronary artery diseases

Table 3. The comparison of frequency distribution of preprocedural cardiac arrhythmia, postprocedural acute myocardial infarction (MI), and in-hospital mortality.

Variables	Group I (n = 30) [n (%)]	Group II (n = 30) [n (%)]	P
Cardiac arrhythmia (preprocedural)	5 (16.6)	2 (6.6)	0.228
Acute MI (postprocedural)	1 (3.3)	1 (3.3)	0.957
In-hospital mortality	2 (6.6)	1 (3.3)	0.554

MI: Myocardial infarction

However, the results were better in group II in terms of TIMI flow, MBG, and no-reflow phenomenon.

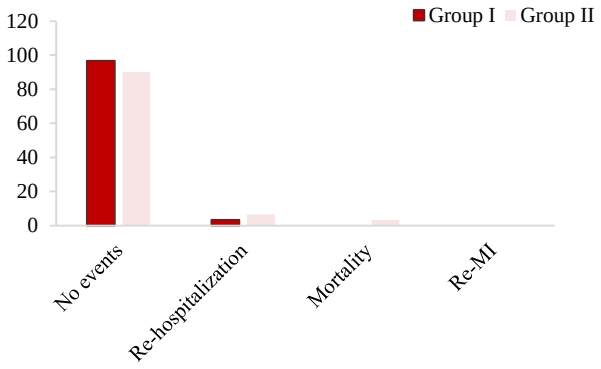

Figure 2. The bar graph showing percentage of cardiac events, after six month follow up
MI: Myocardial infarction

Discussion

The finding of this study showed that both methods of intracoronary and intralesional eptifibatide administration during the primary PCI in patients with acute STEMI were safe and similar in myocardial perfusion outcomes. In this study, PCI outcomes and myocardial perfusion were evaluated by TIMI flow and coronary MBG grading. Cardiac arrhythmia, in-hospital mortality, adverse effects, and pre-discharge left ventricular (LV) function were also similar in both groups.

Several studies have shown that intracoronary injection of glycoprotein GP IIb/IIIa inhibitors (in comparison with systematic injection) increases drug local concentration at the site of thrombosis and infarcted vessels.[9-12] Increased intra-coronary concentrations of GP IIb/IIIa inhibitors, such as abciximab, was safe and effective in infarct size reduction and myocardial perfusion (TIMI flow) improvement.[6] Deibele et al. reported that intracoronary eptifibatide administration during PCI in patients with acute coronary syndromes was accompany with higher occupancy of local platelet glycoprotein IIb/IIIa receptor, which was associated with improved microvascular perfusion.[10] Gu et al. studied about the comparison of intracoronary versus intravenous abciximab administration during emergency reperfusion of STEMI. They concluded that intracoronary abciximab injection through guiding catheter was associated with myocardial perfusion improvement which was evaluated by myocardial blush grade.[11] In addition, Hamza et al.[12] studied 75 patients with acute MI and coronary thrombosis who had angioplasty with stenting.

Table 4. The comparison of postprocedural thrombolysis in myocardial infarction (TIMI)-flow, coronary myocardial blush grade (MBG), and no-reflow phenomenon between the groups

Variables	Group I (n = 30) [n (%)]	Group II (n = 30) [n (%)]	P
TIMI flow			0.307
Grade 0	1 (3.3)	0 (0.0)	
Grade 1	6 (20.0)	2 (6.7)	
Grade 2	5 (16.7)	5 (16.7)	
Grade 3	18 (60.0)	23 (76.7)	
Coronary MBG			0.479
Grade 0	1 (3.3)	0 (0.0)	
Grade 1	5 (16.7)	4 (13.3)	
Grade 2	8 (26.7)	5 (16.7)	
Grade 3	16 (53.3)	21 (70.0)	
No-reflow (Coronary MBG)	6 (20.0)	4 (13.3)	0.071
No-reflow (TIMI flow)	7 (23.3)	2 (6.7)	

TIMI: Thrombolysis in myocardial infarction; MBG: Myocardial blush grade

In comparison to intracoronary eptifibatide administration and mechanical aspiration, pharmaceutical therapy had significantly better results in terms of MBG and corrected TIMI frame count.[12] The same results also were seen about the effectiveness and safety of intracoronary administration of GP IIb/IIIa inhibitors (lower bleeding risk) by Stone et al.[13] and Hassan et al.[14]

In contrast to those studies, researches on comparison of intracoronary and intralesional injection of GP IIb/IIIa inhibitors are fewer.[15-17] In a case report by Dziewierz et al., intralesional infusion of abciximab using a dedicated therapeutic perfusion catheter accompanied with increased concentrations of abciximab at the culprit lesion and in the distal vascular bed and finally, optimal clinical results.[15] In another trial by Stone et al., it was shown that intralesional abciximab and thrombus aspiration may have long-term benefits in patients with anterior STEMI in regard to mortality and ischemic events.[16] Prati et al. indicated that local intracoronary administration of abciximab by means of a dedicated perfusion catheter reduced thrombus burden, improved coronary microcirculation (shorter TIMI frame count), and tented to lower procedure-related MI and major adverse cardiac event (MACE) after 1 year of follow up in comparison to intracoronary drug delivery.[17] In our study, there was no significant difference between the intracoronary and intralesional group in terms of TIMI flow grade, MBG, no-reflow phenomenon, and clinical outcomes; however, the intralesional eptifibatide injection had better results.

The small number sample size and shorter follow-up period in comparison to previous studies were some limitations of this study. It is recommended to make further studies with more groups with comparison of systemic, intracoronary, and intralesional administration of GP IIb/IIIa inhibitors.

Conclusion

The results of this study indicates that intracoronary and intralesional administration of eptifibatide during primary PCI in patients with acute STEMI are safe, and have similar outcomes regarding myocardial perfusion evaluated by TIMI flow and coronary MBG grading. Cardiac arrhythmia, in-hospital mortality, adverse effects, and pre-discharge LV function were also similar in both groups.

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Conflict of Interests

Authors have no conflict of interests.

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Factors in relation with fatigue and illness perception in patients with myocardial infarction and the changes in fatigue due to intervention on illness perception: Research design, methodology, and preliminary results

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Original Article

Abstract

BACKGROUND: In physical diseases including cardiovascular diseases (CVDs), illness perception (IP) plays an important role in illness outcomes. Fatigue is a major bothersome symptom after myocardial infarction (MI). This manuscript presents the research design, methodology, and primary findings of a study on factors in relation with fatigue and IP in patients with MI, and changes in fatigue after intervention on IP.

METHODS: 241 patients with MI who experienced a first-time acute MI (AMI) participated in this study in 2016-2017. During hospitalization, the demographic and clinical information of participants were collected. After four months, the information regarding fatigue, IP, coping with stress, type D personality, perceived social support (PSS), and locus of control of the participants was collected at their houses. About one year later, based on the results of phase one of the study, a psychoeducation course was conducted for 35 of the patients as intervention group while 36 patients were supervised as control group. Two months later, the role of IP in fatigue changes of the participants was assessed.

RESULTS: 155 (65%) of the patients had positive family history of coronary heart disease (CHD). 103 (43%) were cigarette smokers, 100 (43.5%) had high blood cholesterol, and 72 (30%) had sedentary life style before MI.

CONCLUSION: The overview of the factors related to fatigue and IP of the patients with MI could help the care teams to provide better care in the recovery period of the illness.

Keywords: Myocardial Infarction, Perception, Fatigue, Education, Structural Equation Modeling

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Introduction

The number one cause of death all around the world is cardiovascular diseases (CVDs). Every year, 17.7 million people die because of CVDs. This forms 31% of all global deaths, and 13% of that is because of coronary heart disease (CHD). 80% of all CVD deaths are due to heart attack and stroke.[1] A major part of underlying causes of death and disability in Iran is due to CVDs. The first cause of death in Iran (39.3%) is because of CVDs, and 19.5% of that is due to myocardial infarction (MI).[2] The cognitive representation of illness which is called illness perception (IP) is formed by patients' beliefs and understood information about their condition, and the individual's mental health and dealing with the illness can be affected by these factors.[3]

In physical illnesses including CVDs, illness outcomes are considerably varied by IP.[4] It has been shown that IP is capable of affecting patients' taking part in care, obeying physician order and health behaviors, responses to illness, and the strategies chosen while suffering from illness.[5-7]

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In some studies on patients with MI, it has been shown that their IP (attitude and feelings regarding their disease) extensively impacts on recovery process.[8] IP is a set of psychological ideas. It has been developed as a basic construct of Leventhal's Common Sense Model (CSM).[9] Each patient makes her/his own illness representation in this model. The dimensions of this representation are: identity, timeline, cure/control, consequences, and causation of the illness.[5] A symptom is a subjective experience[10] and after MI, fatigue is a tormenting symptom.[11] Andersson et al.,[12] one year post-MI found an extreme and constant physically and mentally fatigue that was difficult to manage and caused obvious restrictions. Fatigue remains in nearly half of patients for four months[13,14] and two years after MI.[15] In a study regarding symptom experiences in post-MI period, four months after treatment, fatigue was reported by 50% of the participants[13] and this proportion remained after two years.[15] Tiredness is a response to stressors which is adaptive, and fatigue shows a reduced adaptability. Inability to respond to stressors may lead to exhaustion.[16] Normal tiredness is different from post-MI fatigue, and also is unintelligible because it is not related to any specific activity, and hence it is unpredictable and coping with it is difficult.[11] Persons think in different ways about their illness (symptoms). In the experience of symptoms many factors may take part, though, physical, cognitive, behavioral, and motivational factors are important.[17]

In post-MI period, negative IPs are related with fatigue. Those who experience fatigue expect longer duration for their illness and more serious consequences. They have more negative emotional beliefs. More fatigue is related with limited personal control of perceptions and not being sure about the cure.[13,14] Some of the negative beliefs were associated with fatigue such as: IP changes over time from feeling the MI as an acute event to a more chronic illness, and feeling decreased personal and treatment control.[14]

The interventions on IP usually consist of brief classes regarding pathophysiology of MI and associated symptoms, exploration of the patients' ideas about the disease, the role of life style modification in management of MI, discussing and explanation of identity, timeline, cure/control, consequences, and causation of MI. It is very important to alter the highly-negative perceptions, address the misconceptions of the patients, broaden the patients' causal model to alter the patients' views of the timeline and consequences of their illness, and provide them with a recovery plan.[18-20] The external and internal factors affect formation of IP such as: social environment and support, attachment styles, demographics, health conditions of individuals for example past history of MI which makes more negative cognition, locus of control, personality traits such as type D, depression, information obtained through other people, mass media, or health workers, mood, and personal beliefs.[3,5,20-24]

In this paper, the focus is on the methodology of the study, on factors related to fatigue and IP in patients with MI, and the changes in fatigue due to intervention on IP.

The objective of this study was exploring the relations between some psychological, clinical, and demographic factors and fatigue and IP, then exploring the effect of intervention of IP on fatigue changes.

The specific aim was identifying the relationship between the followings in patients with MI:

I- Relationship of the demographic factors of age, sex, and education with perceived social support (PSS), type D personality, coping with disease, locus of control, fatigue, and IP.

II- Relationship of some of the clinical factors with PSS, type D personality, coping with disease, locus of control, fatigue, and IP.

III- Relationship of PSS, type D personality, coping with disease, locus of control with fatigue and IP.

Materials and Methods

Study design and participants' recruitment

The design of this cross-sectional study (which is the corresponding author's PhD thesis) has been approved by Vice Chancellor for Research (registration No. 395045) and the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.REC.1395.3.045).

Settings: The two main cardiac care units in Isfahan were the places of conducting this study: Shahid Chamran Hospital (the main academic heart center) and Shariati Hospital (affiliated to the Social Security Insurance Organization).

Sample size: By means of formula $n = (z1 + z2)^2 * S^2/d^2$ and considering 95% confidence interval (CI), coefficient (Z1) of 1.96, study power of 80% equal to 0.84, standard deviation (SD) of IP questionnaire which is one sixth of the changing range of its score (8 to 80) equal to 13.3, and sampling error (d) equal to 2.5,

the calculated sample size was 181. To have a safety factor, 241 patients were included in the study.

Conducting procedure: The observational cross-sectional phase of the study included two steps of data collection. During a 9-month period (from April 2016 to January 2017) nearly 750 patients with MI were admitted in Chamran (600) and Shariati (150) Hospitals. The necessary permissions obtained from hospital authorities. The related staff was informed about the study; hence, they had a very good cooperation. In the first week of post-MI period, two questionnaires of clinical and demographic information were completed by the researcher for 350 consecutive MI patients who captured the inclusion criteria in either coronary care unit (CCU) or cardiac ward of the mentioned hospitals. After delivering an introduction including the aim of the study to the patients and collecting the written informed consent (only if they were ready), the questionnaires were completed by conducting an interview. The time needed to complete the said questionnaires for each patient was about 20 minutes. Also some information was collected from the patients' hospital files. The obtained information was kept secret carefully. To complete this step of the study, the researcher has gone nearly 90 times to Chamran and 60 times to Shariati Hospitals.

About four months after the first step, at the second one, 6 questionnaires namely PSS, type D personality, locus of control, coping with stress, fatigue, and IP were completed for 241 patients. Before commencement of the second step, 109 participants were excluded from the study due to some reasons such as undergoing a surgical operation, suffering from another MI, changing address, or death. After briefing, 10 questioners (with psychology or health education bachelor degree) completed the questionnaires by the means of interview at the patients' houses which were located in different districts and locations of Isfahan Province such as Shahreza, Shahinshar, Mobarekeh, etc. Prior to interview, the patients were informed by phone. If they were ready, the interview would be set. The average time for each interview was less than one hour, though because of long distances in some instances, 1 to 3 hours was needed to reach the participants. The questioning fee was paid to the questioners after completion of the work.

One year after completion of the phase one, the second phase of the study was conducted and an educational intervention was performed on some of the patients participated in the phase one, by means of determining the contribution and the role of each variable in IP variance and the role of IP in the patients' fatigue. 35 patients as the case group and 36 patients as the control group were randomly selected. The case group was divided into two batches. Five psychoeducation classes including following topics were held for each batch of the case group: mechanism of atherosclerosis and MI, the role of life style in developing heart diseases, life style modification, mindfulness and its role in stress management, self-control, self-evaluation, self-reinforcement, self-value, self-care, and IP and its role in management of MI and fatigue. During the classes, participants were actively involved in the discussions. Two brochures containing necessary information regarding post-MI period and angiography were given to the control as well as case group participants. The aim of the intervention was assessing the role of IP improvement in fatigue status of the patients with MI. Before holding the classes and 2 months after that, IP and fatigue of the participants in the case and control groups were assessed. Figure 1 shows the steps of the phase one of the study.

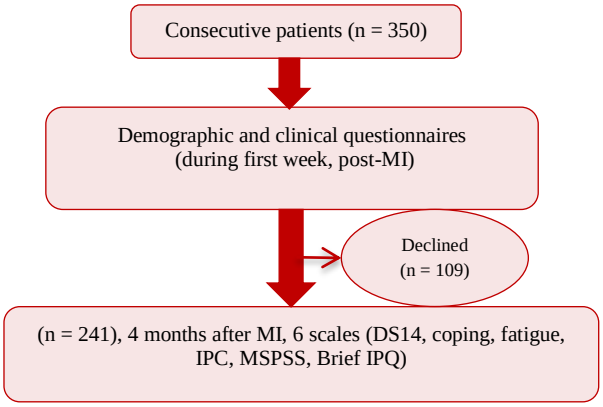

Figure 1. Data collection, handling, and quality assurance (12 months)
MI: Myocardial infarction; DS14: 14-item Type D Personality Scale; IPC: Internal, powerful others, chance; MSPSS: Multidimensional Scale of Perceived Social Support; IPQ: Illness perception questionnaire

Study instruments

Clinical characteristics: Data regarding the clinical characteristics of the participants were collected mainly by means of history taking, though some data were collected from the patients' hospital files. The participants answered to some of the questions regarding important items such as: the critical time needed to be hospitalized after commencement of symptoms, family history of CHD, if any of the consanguineous relatives had the disease, past history of CHD, if in the past the participant suffered from CHD, past history of intervention for CHD, if the

participant in the past had undergone any intervention for CHD such as medical, surgical, or percutaneous coronary intervention (PCI), physician visit prior to hospitalization, type of vehicle which transported the patient to hospital, cigarette smoking before MI, suffering from high blood cholesterol (> 240 mg/dl) and/or high blood triglyceride (TG) (> 200 mg/dl) before MI, suffering from high blood pressure (systolic > 140 mmHg and/or diastolic > 90 mmHg), history of diabetes, fasting blood sugar (FBS) > 120 mg/dl and/or hemoglobin A1c (Hb A1c) > 6.5%, history of obesity [body mass index (BMI) > 30 kg/m^2] before MI, and having a sedentary life style (less than 20 minutes regular physical activity per day, five days per week).

Illness perceptions: For basic evaluation and follow-up of IP score, a short form of IP Questionnaire (IPQ) called Brief IPQ was used. In various conditions, this questionnaire has been reported as a reliable and valid tool. It has a good test–retest reliability.[25] Except the causal, the other questions of the nine subscales have a 10-point (1 to 10) response scale. Each subscale assesses one component of IP: 1) consequences, 2) timeline, 3) personal control, 4) treatment control, 5) identity, 6) concern, 7) illness comprehensibility, and 8) emotional response. The cause of the illness is assessed by an open-ended question.[21] Item 9 was excluded in this study since the cause of the illness was not considered.

For each of the subscales, the reliability coefficient by test-retest method was from r = 0.48 (understanding) to r = 0.70 (consequences).[25] Cronbach's alpha was 0.84 for the Farsi version of the Brief IPQ. Its correlation with Farsi version of the revised version of IPQ (IPQ-R) was 0.71. The Farsi version of the Brief IPQ has a good validity.[22]

Type D personality: It refers to individuals with a joint propensity toward negative affectivity (NA) as well as social inhibition (SI) and is related to poor prognosis of heart failure.[26] Its related scale, 14-item Type D Personality Scale (DS14), has two subscales. Each of them consists of 7 questions and are answered on a five-point Likert scale from 0 (false) to 4 (true). The maximum score is 28 for NA and for SI as well.[26,27] Denollet conducted a study on psychometric properties of DS14. According to that, NA and SI scales were internally consistent (α = 0.88 and α = 0.86, respectively; N = 3678) and also were stable over a period of 3 months (test–retest r = 0.72 and 0.82, respectively).[26] For the Farsi version of the 14-item scale over a 2-month period, the subscales of NA and SI have a good reliability (test–retest r = 0.86 and 0.77, respectively) and internal consistency of Cronbach's alpha coefficient as 0.84 and 0.86, respectively, in patients' group and 0.87 for NA and 0.75 for SI subscales in healthy group. Also for this version (Farsi DS14), a structural validity was confirmed by factor analysis of the NA and SI items.[28]

Multidimensional Scale of Perceived Social Support (MSPSS): Zimet et al. developed the first version of this 12-item scale. It has three subscales: family, friends, and significant others.[29] From the psychometric properties point of view, the MSPSS showed high internal consistency, reliability, validity, and utility of the scale in a sample of urban, largely African-American adolescents.[30] A study was carried out in Iran on 176 patients with MI admitted to the CCU as well as 71 subjects from the general population for assessing the psychometric properties of the Farsi version of the MSPSS. A three-factor structure of family, friends, and significant others was provided by factor analysis of the scores of the patients and healthy samples. The percentages of variance of the three factors were 77.87% in the patient sample and 78.55% in the healthy sample and the scale's Cronbach's α coefficient was 0.84 among MI patients and healthy samples. The Farsi version of the MSPSS is a reliable and valid scale.[31]

Iowa Fatigue Scale (IFS): Hartz et al. developed an 11-item scale. On a data set of 409 primary care patients, factor analysis was used and validated on 816 additional subjects. In that study, correlations of the overall measure with other overall measures ranged from 0.82 to 0.96. This scale synthesizes information from several fatigue instruments.[32] We used its Farsi manuscript which was translated (forward and backward method) under supervision of an English language professor from Shiraz University of Medical Sciences, Shiraz, Iran. Two specialists (an endocrinologist and a social medicine specialist) approved validity of the questionnaire. Cronbach's alpha test was used for reliability (r = 0.84). These aspects of fatigue are assessed by the scale: cognitive aspects (4 questions), physical fatigue (2 questions), energy rate (3 questions), and work output (2 questions).[33]

Levenson Multidimensional Locus of Control Scale (IPC): Internal, powerful others, chance **(**IPC) scale of the Levenson includes 24 items for three components of internal, powerful others, and chance, eight questions for each. It is rated on a six-point Likert scale. The validity of this scale has been verified with Rotter's Internal-External (I-E) scale (1996). Kuder-Richardson's reliability coefficient of 0.50, 0.61, and 0.77 was reported by Levenson for the IPC subscales, respectively. The validity and

reliability of the Farsi version of this scale were reported by Farahani et al. The reliability coefficients for I, P, and C components were 0.76, 0.56, and 0.67, respectively, in a sample of students.[34] On the first and second administration, the mean differences between scores were non-significant and internal consistency estimates were moderately high. The construct validity of the scale was supported by the differences among diagnostic categories and between normal and hospitalized subjects.[35] In a study, the concurrent validity of the Farsi version of the Multidimensional Health Locus of Control (MHLC) scale was measured by Levenson's IPC Scale and showed satisfactory results for all of the three subscales.[36]

Coping Inventory for Stressful Situations (CISS): Endler and Parker developed this reliable and valid multidimensional coping scale. The CISS has three dimensions: task, emotion, and avoidance. Respondents were asked to rate each of the 48 items of the scale on a five-point Likert-type rating scale.[37-39] It can be concluded from the results of four studies that the CISS is a valid and reliable scale as far as the basic coping styles are concerned.[40] To validate Farsi version of Endler and Parker's CISS, a study was carried out with participation of 410 high school students. It revealed that this scale had suitable validity and there was relation and correlation between scale factors. The scale and its subscales have an acceptable validity and reliability.[41]

Data collection, entry, handling, and quality assurance

The researcher supervised the process of interviews continuously during the 12 months of data collection, and in different stages, the credibility of the data was investigated. The questionnaires were checked regularly. By using the computerized process, the data were entered into the electronic sheets and to identify missing values and outlier items, the computerized data were rechecked.

Statistical method: To describe the quantitative data, mean and SD and to describe the qualitative data, frequency and percentage indicators were used. In analyzing the data, to explore the relationship between demographic, clinical, and psychological variables, Structural Equation Modeling (SEM) was used. The indicators which were used to examine the goodness of fit of the model are: Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), probability of Root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI), Tucker-Lewis index (TLI), and probability of Standardized Root Mean Square Residual (SRMR). Figure 2 shows the diagram representing the possible relationships of demographic, clinical, psychological, IP, and fatigue variables in patients with MI.

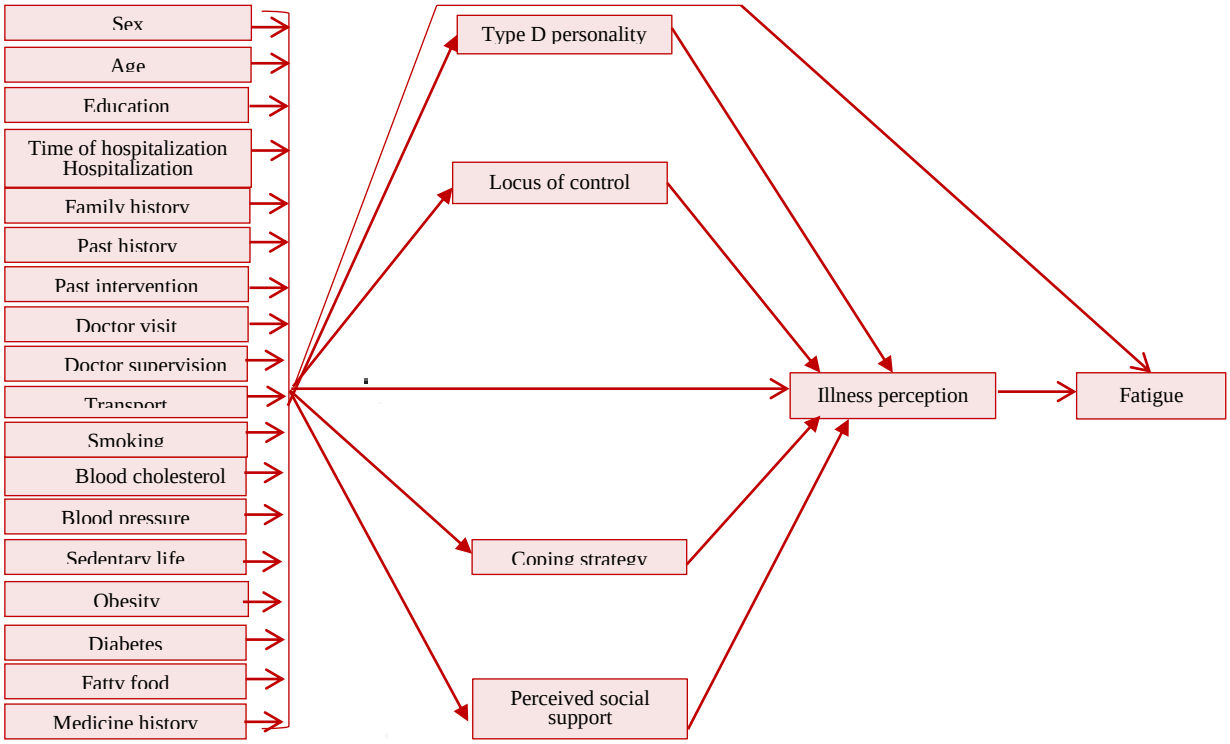

Figure 2. The possible relationships of demographic, clinical, psychological, illness perception (IP), and fatigue variables in patients with myocardial infarction (MI)

Results

Demographic: 241 patients with MI participated in the study, 173 (72%) from Chamran and 68 (28%) from Shariati hospital; finally, we had 1 missing case. The mean age of participants was 54.53 years (SD = 9.76). Demographic characteristics of the participants can be seen in table 1.

Table 1. Demographic characteristics of participants

Characteristics	n (%)
Sex	
Male	200 (83.0)
Female	41 (17.0)
Marital status	
Married	231 (96.0)
Single	10 (4.0)
Education	
Completed high school	63 (26.0)
Below high school	147 (61.0)
University degree	30 (12.5)
Occupation	
Non-governmental	101 (42.0)
Government employee	33 (13.7)
Non-employed	5 (2.1)
Retired	63 (26.1)
Housewife	39 (16.2)

Clinical findings: The clinical findings of the participants can be seen in table 2.

Conclusion

Surviving an MI is often the beginning of a long period of rehabilitation. Cardiac rehabilitation and lifestyle modifications are essential components of successful recovery after MI.[13] We hope to help the promotion of MI rehabilitation process by identifying the relations of some of the psychological factors in order to optimize patients' recovery.

Exploring the relationships between demographic and clinical characteristics and psychological variables of locus of control, coping with stress, type D personality, and PSS with fatigue and IP in patients with MI could help the care teams to provide better care in the post-MI period by considering these important factors.

Acknowledgments

None.

Conflict of Interests

Authors have no conflict of interests.

Table 2. Clinical findings

Characteristics	n (%)
Hospitalized within 1st hour after symptoms commencing	84 (35.0)
Hospitalized within 1 to 2 hours after symptoms commencing	29 (12.0)
Hospitalized after 12 hours of symptoms commencing	83 (34.0)
Positive family history of CHD	155 (65.0)
Past history of CHD	61 (25.0)
Having some intervention for CHD (66% medical, 30% PCI, 4% surgery)	51 (22.0)
Having a physician visit prior to hospitalization	125 (52.0)
Being regularly under supervision of a physician before MI	53 (22.5)
Being transported to hospital by ambulance	72 (30.0)
Being transported to hospital by a taxi or a private car	165 (70.0)
Being cigarette smoker before MI	103 (43.0)
Having high blood cholesterol before MI	100 (43.0)
Having high blood pressure before MI	87 (37.0)
Having diabetes	55 (23.0)
Having sedentary life style before MI	72 (30.0)
Presence of obesity	49 (21.0)
Used to have fatty (greasy) food before MI	156 (65.0)
Used to take medicine regularly before MI	124 (52.0)

CHD: Coronary heart disease; PCI: Percutaneous coronary intervention; MI: Myocardial infarction

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Prevalence of medication adherence in patients with hypertension in Iran: A systematic review and meta-analysis of studies published in 2000-2018

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Meta-Analysis

Abstract

BACKGROUND: Medication adherence (MA) has a crucial role in controlling of hypertension (HTN). A difference was observed in the prevalence of anti-hypertensive MA reported in different studies in Iran, so we aimed to determine the overall prevalence of MA.

METHODS: Using the English and Persian keywords extracted from Mesh, the databases of MagIran, Barakat Knowledge Network System, Scientific Information Database (SID), Web of Sciences, PubMed, Science Direct, and Google Scholar were reviewed from 2000 to 2018. The overall prevalence of MA was estimated using Random effect mode. The I^2 and Egger's tests were used to assess heterogeneity and publication bias, respectively. Meta-regression and subgroup analysis were conducted based on variables such as age, marital status, regions, and tools.

RESULTS: The overall prevalence of MA was 33%. Moreover, the prevalence of MA based on the 8-Item Morisky Medication Adherence Scale (MMAS-8), Hill-Bone Medication Adherence (HBMA) scale, researcher-made tools, and self-care tools, were 13%, 34%, 48%, and 47%, respectively. A higher MA prevalence (38%) was observed among older adults compared to other age groups, and married patients (32%) compared to single (23%) individuals. The highest MA prevalence (50%) was related to region 5 of the country. Meta-regression results showed a significant relationship between the used tools and MA prevalence.

CONCLUSION: The overall prevalence of MA is low in Iran. Furthermore, MA was measured using different questionnaires, such as standard international scales and researcher-made tools. It is proposed that a standard international questionnaire should be used in future studies.

Keywords: Medication Adherence, Prevalence, Hypertension, Systematic Review, Meta-Analysis, Iran

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Introduction

Despite recent advances in the prevention, diagnosis, and treatment of hypertension (HTN), the health and economic impacts of the disease are increasing.[1,2] The US Healthy Population Program's goal is for over half of patients with HTN to control their disease by 2020. The control rate of HTN is generally less than 50% in most countries. For example, in the UK and Japan, 32% and 24.8% of patients, respectively, were able to control their HTN in 2009.[3] The results of various studies in Asia show that the control rates of HTN in Taiwan and China were 29% and 9%, respectively.[4,5] Uncontrolled blood pressure levels have been generally undocumented in Iran, and only in Golestan province, Iran, it was reported that 42.7% of patients with HTN succeeded in controlling their blood pressure.[6]

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Lifestyle modification and accurate use of antihypertensive drugs are the two main strategies for controlling HTN.[5] In fact, recent studies have shown that antihypertensive drugs can effectively control HTN and its related complications.[5,7,8] However, for the drugs to be effective in HTN management, it is required that patients follow and adhere to their medicines.[5] Studies have shown that non-adherence is the most common cause of uncontrolled blood pressure.[9-12] Patients with HTN who are poorly treated are more likely to suffer complications, including coronary artery diseases (CAD), heart failure, and cerebrovascular diseases.[13] No meta-analysis study has been conducted on medication adherence (MA) in Iran. In order to increase the effectiveness of interventional programs for HTN control and the reduction of its consequences in Iran, comprehensive information is required on the status of MA in this group of patients. The goal of this study was to obtain the precise and general prevalence of MA and its related factors in patients with HTN in Iran.

Materials and Methods

The present systematic review and meta-analysis was conducted based on preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines[14] to determine the exact prevalence of MA in patients with HTN in Iran. The protocol of this study was registered by the registration system of systematic review studies (PROSPERO) with the ID number of CRD42017069512.

In the present systematic review and meta-analysis, the prevalence of MA in patients with HTN was reviewed in the Iranian society based on articles published in national and international journals between 2000 and 2018. The reason for excluding studies conducted before 2000 was the different definition of blood pressure offered by the World Health Organization before this date.[15] To search for studies conducted on MA in patients with HTN, databases such as MagIran, Barakat Knowledge Network System, SID, Web of Sciences, PubMed, Science Direct, and Google Scholar were utilized. The search was performed using standard keywords extracted from MESH, including compliance, non-compliance, adherence, non-adherence, medication adherence, medication non-adherence, medication persistence, and blood pressure.

All observational (non-interventional) studies addressing the prevalence of MA in patients with HTN in the Iranian society were included. Interventional articles, letters to the editors, and review studies were excluded from the analysis. If several articles were published from a demographic sample, the article with a more complete content was entered into the analysis.

Based on the inclusion and exclusion criteria, titles and abstracts of studies were independently analyzed by two researchers (M.J. and R.GG.). After the removal of irrelevant articles, the full-texts of the studies were evaluated. Observational studies reporting the prevalence of MA in a hypertensive population were reviewed. In case of any disagreement between the two researchers, the article would be judged by the third author. Subsequently, the full texts of the articles were reviewed and data were extracted by two of the authors (M.J. and R.GG.) independently. For the data extraction process, a form was used including items related to the first author, the publication year, setting, the location of the study, the sample size, the sample size in men and women, the prevalence of MA in general and by sex, and the MA measurement method.

To assess the quality of the studies, a scale for rating methodological quality of studies was used to assess the quality of the methodology of articles in various internal and external studies.[16-19] A Systematic Review of Psychosocial Factors Affecting Survival after Bone Marrow Transplantation. The tool consists of 5 items related to research design, sampling method, comparison group, sample size, and psychometric properties of the tool. Each item is scored on a scale of 0-3, with the overall score ranging from 0 to 15. Accordingly, the studies were divided into three groups of weak studies (0 to 5), moderate studies (5 to 10), and strong studies (above 10). The quality of the studies was assessed by two authors (M.J and R.G.), and any disagreements were solved by asking the opinion of the third author (F.M).

Data analysis was performed using STATA 12 software (version 12, StataCorp, College Station, USA). Results are presented in forest plots. In two studies, the prevalence of MA was directly reported, so researchers estimated its ratio by dividing the number of cases by the total sample size. Confidence interval (CI) was estimated at 95% for each prevalence. The prevalence has a binomial distribution, so the variance in prevalence was calculated using the binomial distribution variance formula. To evaluate the heterogeneity of the selected studies, Cochran's Q test and I2 statistic were used. Significant heterogeneity results were found throughout studies ($P < 0.001$) ($I2 = 99.50$), so the random effect model was used to estimate

the prevalence of MA. To combine different prevalence rates of the studies, the weighted mean was used in each study, and the weight of each study would be the inverse of the variance. Egger's test was used to examine the bias of the publication. Using subgroup analysis and meta-regression, the effects of the underlying variables, including sex, age, five regions of provinces in Iran, the tool used, the population studied, the year of studies, and marital status, were assessed on the prevalence of MA and the heterogeneity of studies. it is necessary to mention that the five regions of the country (based on territorial division of the country) were divided as follows: Region 1: Tehran, Alborz, Qazvin, Mazandaran, Semnan, Golestan, and Qom provinces; Region 2: Isfahan, Fars, Bushehr, Chaharmahal Bakhtiari, Hormozgan, and Kohkiloyeh and Boyerahmad provinces; Region 3: East Azarbaijan, West Azarbaijan, Ardebil, Zanjan, Gilan and Kurdistan provinces; Region 4: Kermanshah, Ilam, Lorestan, Hamedan, Central, and Khuzestan provinces; Region 5: Khorasan Razavi, Southern Khorasan, Northern Khorasan, Kerman, Yazd, and Sistan and Baluchestan provinces. Meta-analyses were not carried out for MA predictors; only the correlation between them and MA were estimated in the studies. Therefore, only the most important factors related to MA were explained and categorized based on the existence or non-existence of a significant relationship.

Results

Selection of studies: In this study, all studies on the prevalence of MA in patients with HTN between 2000 and 2018 were systematically selected according to PRISMA guidelines.

In the initial search, 317 papers were identified. Finally, 17 studies were entered into the final analysis (Figure 1).

Characteristics of the studies: The total sample size was 7941with the mean being 467 samples per study. The characteristics of the articles selected are presented in table 1. Like other meta-analysis studies,[20] among our primary studies, there was some with large sample size like a study conducted by Zinat Motlagh et al.[21] The highest MA rate was reported in the study by Barati et al.[22] and the lowest MA rate was related to the studies by Mahmoudian et al.[23] and Najimi et al.[24] In all primary studies, the self-reporting method was used to measure MA. Questionnaires used were the 8-Item Morisky Medication Adherence Scale (MMAS-8),[24-27] Hill-Bone Medication Adherence (HBMA) scale,[28-30] self-care questionnaires,[21,27] researcher-made questionnaires,[31,32] a one-item questionnaire,[33] and the 4-Item Morisky Medication Adherence Scale (MMSA-4).[34] All of these tools measure medication adherence. The self-care questionnaires were multi-sectional including MA, diet adherence, exercise, weight control, and smoking.

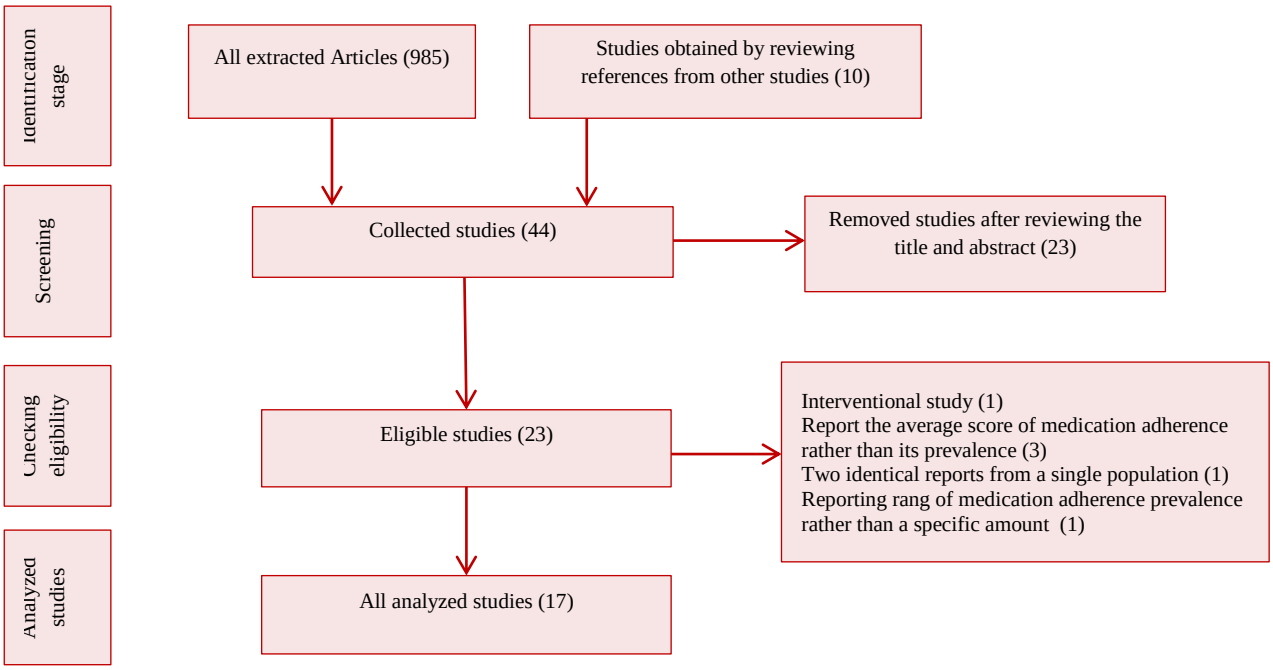

Figure 1. The process of selecting the primary articles according to preferred reporting items for systematic reviews and meta-analyses (PRISMA)

Table 1. Characteristics of the primary studies

First author	Sample size	Target community	City	Questionnaires	Scoring of questionnaires	Overall prevalence	Prevalence•			Article quality score	Article language
							High	Moderate	Low		
Mahmoudian et al.[23]	300	adults	Isfahan	MMAS-8	Score 8 = adherent / score 1-7: Non- adherent to medication	12.0	-	-	-	10	English
Behnood-Rod et al.[26]	280	adults	Tehran, Bafq, and Kermanshah	MMAS-8	Score < 6: Poor adherence / Score 6-7: moderate adherence / Score 8: high adherence	-	16.0	34.00	50.0	8	English
Zinat Motlagh et al.[21]	1836	adults	Kohgiloyeh and Boyerahmad	Self-care questionnaire	Score 21: adherent / Score lower than 21: Non- adherent	36.1	-	-	-	8	English
Arbabshastan et al.[29]	400	adults	Zahedan	HBMA	Poor / moderate / high adherence	-	45.4	41.00	31.6	9	English
Izadirad and Zareban[31]	358	adults	Zabul	Researcher-made	score 0-9: poor adherence / score 10-15: moderate adherence / score > 15: high adherence	-	53.35	3.44	16.2	5	English
Roohafza et al.[30]	1055	People over 19	Isfahan, Najafabad, and Arak	Researcher-made	Answer Yes: adherent / Answer No: Non–adherent	45.0	-	-	-	9	English
Roohafza et al.[30]	619	people over 19	Isfahan, Najafabad, and Arak	Researcher-made	Answer Yes: adherent / Answer No: Non–adherent	45.0	-	-	-	9	English
Najimi et al.[24]	390	adults	Isfahan	MMAS-8	Score 8 = adherent /score 1-7: Non- adherent	12.0	-	-	-	8	English
Saadat et al.[27]	280	adults	Tehran, Bafq, and Kermanshah	MMSA-8	Score < 6: poor adherence / Score 6-7: moderate adherence / Score 8: high adherence	-	16.4	34.00	49.6	8	English
Dehghan et al.[30]	280	adults	Kerman	HBMA	poor / moderate / high adherence	-	51.0	42.60	6.4	7	English
Taher et al.[37]	130	adults	Tehran	HBMA	poor / moderate / high adherence	-	5.4	85.40	9.2	6	English
Moharamzad et al.[35]	200	adults	Tehran, Bafq and Kermanshah	MMAS-8	Score < 6: poor adherence / Score 6-7: moderate adherence / Score 8: high adherence	-	15.0	31.00	54.0	7	English
Kamran et al.[34]	671	adults	Ardebil	MMSA-4	Score 4 = adherent / Score 1-3: Non–adherent	24.0	-	-	-	7	English
Masror Roudsari et al.[32]	264	adults	Tehran	Researcher-made	Score < 500: poor adherence / score 500-750: moderate adherence / score > 750: high adherence	-	10.0	82.00	8.0	9	Persian
Asayeshi et al.[25]	300	elderly	Isfahan	MMAS-8	Score < 6: poor adherence / Score 6-7: moderate adherence / Score 8: high adherence	-	10.3	34.00	55.7	9	Persian
Barati et al.[22]	328	adults	Hamedan	Self-care questionnaire	score 0-5: poor adherence / score 6-10: moderate adherence / 11-16: high adherence	-	84.1	11.60	3.3	8	Persian
Hadi and Rostami-Gouran[33]	250	adults	Isfahan	One item with Yes / No answer	Adherent = Consumption of 90-100% of prescription / Non-adherent: Consumption of less than 90% of prescription	39.6	-	-	-	7	English

The low, moderate, and high MA are based on questionnaire scoring, for example, for the MMAS-8: scores of 0, 1-2, and 3-8 mean high, moderate, and low MA, respectively.
MMAS-8: 8-Item Morisky Medication Adherence Scale; MA: Medication adherence; HBMA: Hill-Bone Medication Adherence

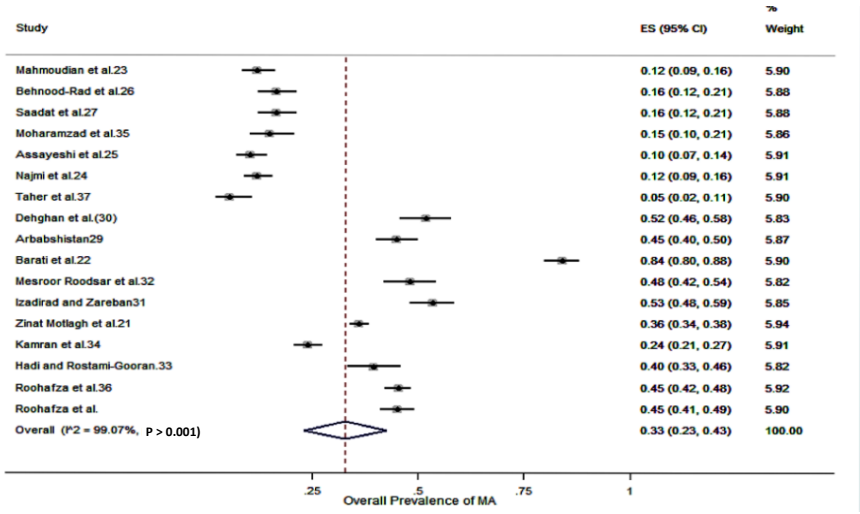

Figure 2. The forest plot of the overall prevalence of medication adherence
CI: Confidence interval; MA: Medication adherence

We used only the MA part of these questionnaires. All of the mentioned questionnaires were valid and reliable. For example, the MMAS and the HBMA scale have been used in many Iranian studies and various studies have reported their validity and reliability.[26,30,35]

Prevalence of medication adherence: In the primary studies, various prevalence rates of MA have been reported. The lowest MA rate (12%) was related to the studies of Mahmoudian et al.[23] and Najimi et al.[24], and the highest prevalence of MA (84%) was reported by Barati et al.[22] The lowest prevalence of MA was related to the MMAS-8 tool, and the highest was related to the researcher-made tools. According to figure 2, the overall prevalence of MA was 33% (95% CI: 23%-43%).

MA was reported as dichotomous (Yes/No) in 7 studies and as high, moderate, and poor on the Likert scale in 10 studies. Thus, we estimated the overall prevalence of MA for dichotomous and Likert scale questionnaires separately. For the studies with dichotomous response, overall prevalence was 31% (95% CI: 20-41). The prevalence of high, moderate, and low MA was 31% (95% CI: 14% -47%), 42% (95% CI: 28% -58%), and 27% (95% CI: 15% -38%), respectively (Figure 3).

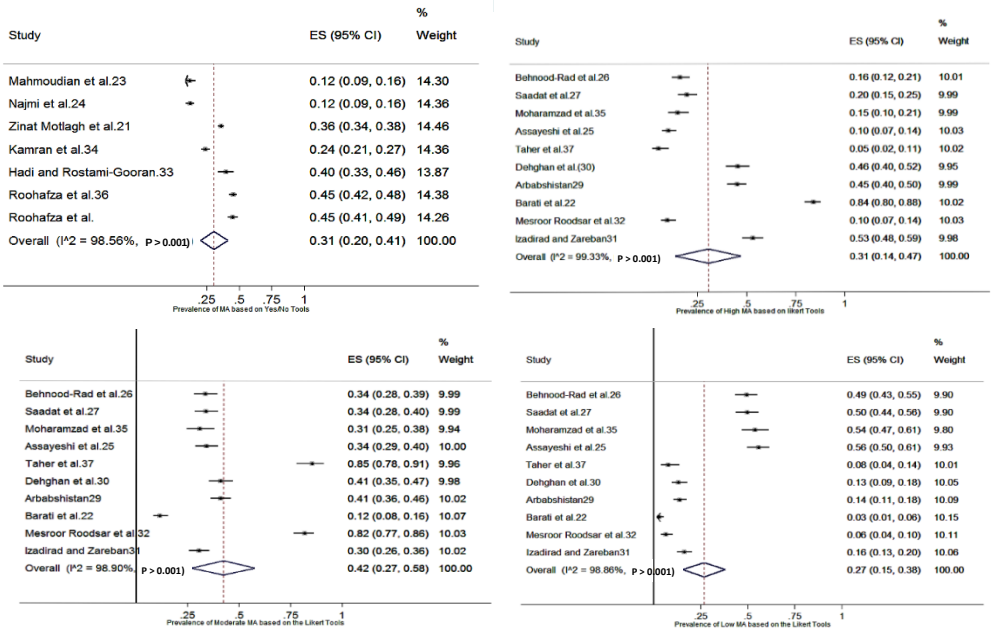

Figure 3. The forest plot of the prevalence of medication adherence in the studies with dichotomous and Likert scales
CI: Confidence interval; MA: Medication adherence

Analysis of subgroups: The tools used to measure MA in the primary studies were the MMAS in 7 studies (6 studies with the MMAS-8 and 1 with the MMAS-4), the HBMA scale in 3 studies, a researcher-made tool in 4 articles, a self-care tool in 2 studies, and an one-item tool in 1 study. From among the studies conducted using the MMAS tool, the 6 studies using the MMAS-8 tool were analyzed and the 1 study with the MMAS-4 was excluded from the analysis. The prevalence of MA on the basis of the MMAS-8 tool was 13% (95% CI: 0.11-0.15). In the studies done using the HBMA, the prevalence of MA was measured as poorly, moderately, and highly adherent; but in this study, we reported only the highest prevalence of MA as 34% (95% CI: 0.4-0.44). The prevalence of MA in 4 studies conducted using the researcher-made tools was 48% (95% CI: 0.4-4.0). There was much heterogeneity among other tools. The 2 self-care questionnaires showed a prevalence of 47% (95% CI: 0.46-0.49). Because the studies conducted using the MMAS-4 and the one-item tool were not similar to those with other tools, the meta-analysis was not performed on them. Based on the tools, the findings showed that the highest prevalence of MA is related to the researcher-made tools (Figure 4).

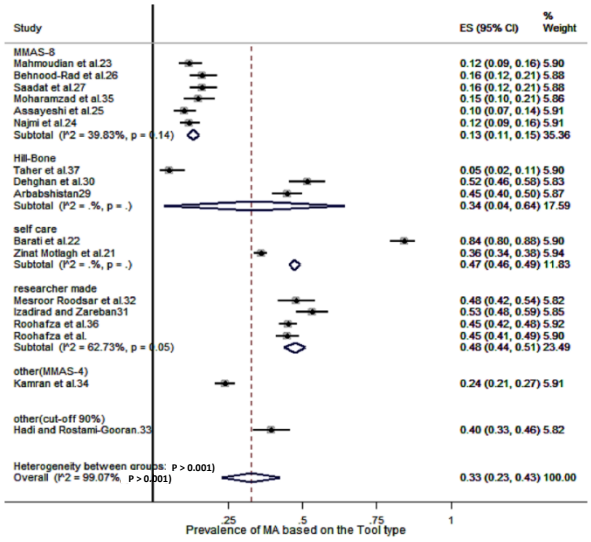

Figure 4. Forest plot, the prevalence of medication adherence based on questionnaires
CI: Confidence interval; MA: Medication adherence

Regarding Iran's regions, the findings also showed that the highest prevalence of MA was related to region 5 (50% with a 95% CI of 45-55). The prevalence of MA in regions 1 and 2 was 30% (95% CI: -51% -0.09%) and 29% (95% CI: 17% - 40%), respectively. In the 6 studies using MMAS-8, the prevalence of MA in region 2 and region 1 was 11% and 16%, respectively (Figure 5).

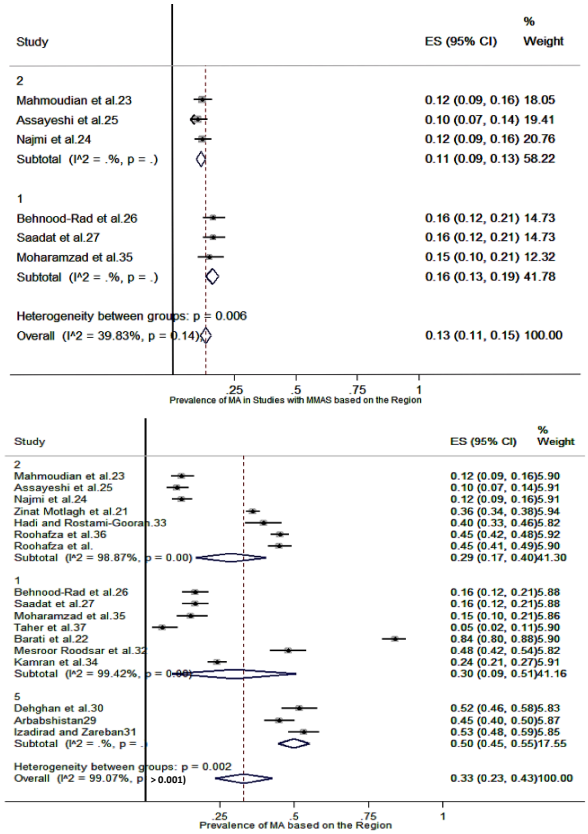

Figure 5. Forest plots of the prevalence of MA based on the five regions* of the country for all studies (Left) and the 6 studies using the MMAS-8 tool (Right)
CI: Confidence interval; MA: Medication adherence; MMAS-8: 8-Item Morisky Medication Adherence Scale
*(Region 1: Tehran, Alborz, Qazvin, Mazandaran, Semnan, Golestan, and Qom provinces ; Region 2: Isfahan, Fars, Bushehr, Chaharmahal Bakhtiari, Hormozgan, and Kohkiloyeh and Boyerahmad provinces; Region 3: East Azarbaijan, West Azarbaijan, Ardebil, Zanjan, Gilan, and Kurdistan provinces; Region 4: Kermanshah, Ilam, Lorestan, Hamedan, Central, and Khuzestan provinces; Region 5: Khorasan Razavi, Southern Khorasan, Northern Khorasan, Kerman, Yazd, and Sistan and Baluchestan provinces)

In relation to demographic variables, only in three studies the prevalence of MA was reported by age, gender, and marital status that allowed us to estimate MA prevalence by demographic variables (Table 2).

Meta-regression analysis: To investigate the relationship between the variables of tools, regions, and language of the studies with the prevalence of MA, a meta-regression was conducted once for all studies and once for studies performed using the MMDS-8 tool.

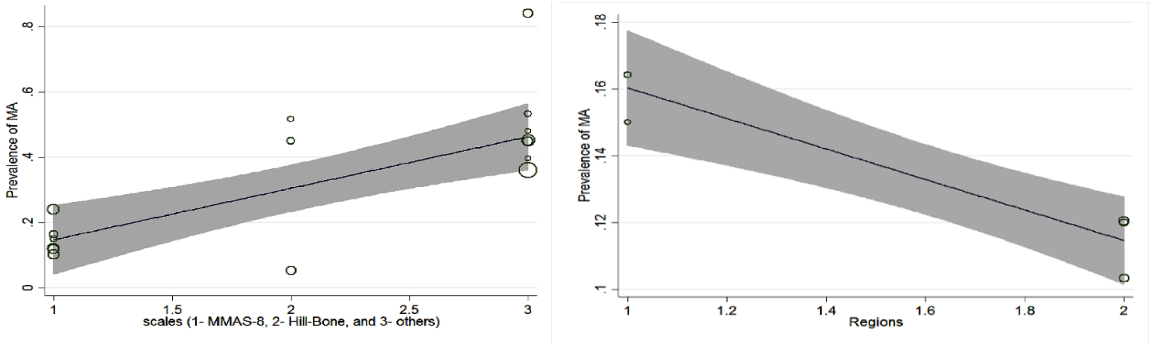

Figure 6. The meta-regression graph of the relationship of the used scales (Right) and the regions (Left) with the prevalence of medication adherence
MMAS-8: 8-Item Morisky Medication Adherence Scale; MA: Medication adherence

Table 2. Prevalence of medication adherence based on demographic variables

Demographic variables	Categories	Prevalence (%)	CI
Age (year)	30-39	30	24-35
	40-49	26	22-30
	50-59	32	28-35
	≥ 60	38	35-41
Gender	Male	33	30-36
	Female	32	30-34
Marital status	Single	23	16-29
	Married	32	30-34

CI: Confidence interval

The findings showed that, in all studies, only the tool type was associated with the prevalence of MA (Z = 4.02, P = 0.001), and among studies which used the MMDS-8 tool, only the regions of the study had a significant relationship with the prevalence of MA (Z = 2.73, P = 0.006). For the rest of the cases, there was no significant relationship among the variables and the prevalence of MA (P > 0.050) (Figure 6). According to figure 7, the results of Egger's test showed no bias in the publication of studies (t = 0.6; P = 0.550).

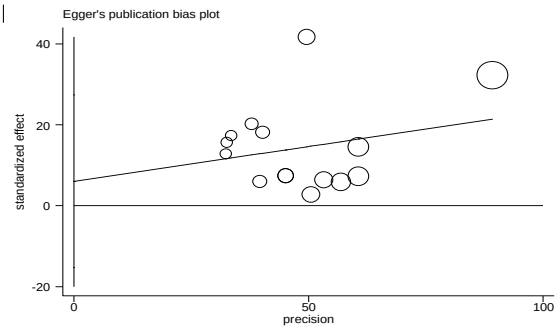

Figure 7. Egger's test diagram

Finally, we extracted and categorized predictors of MA in studies based on the existence of a significant or non-significant correlation between them and MA. We did not report odd ratio, because it was not possible to calculate using the data of the primary studies (Table 3).

Discussion

The findings of this meta-analysis showed a low prevalence of MA among patients with HTN in Iran. Based on the MMAS-8, HBMA scale, researcher-made tools, and self-care tools, the prevalence of MA was reported at different ranges. Nielsen et al. assessed the prevalence of MA in countries of medium and lower income in 2015 and estimated the overall prevalence of medication nonadherence in studies using MMAS-8 and tools with cut-off points of 80%-90% as 63.35%.[38] In other words, the prevalence of MA in the study conducted by Nielsen et al.[38] for studies using the MMAS-8 tool was 36.65%, and for articles with a cut-off point of 80%-90%, it was 55.54%. Abegaz et al. investigated the prevalence of MA in 15 countries in 2016.[39] They found that 54.8% of the patients had MA based on the MMAS-8 tool.[39] The results of the systematic review and meta-analysis by Durand et al. showed that the prevalence of MA in patients with HTN was 69% in European countries.[40] The results of the studies conducted in Palestine also showed that 54% of patients with HTN were non-adherent to medicine.[41] The findings of the study conducted by Lemstra and Alsabbagh in 2014 that assessed the prevalence of MA in patients with HTN in European countries showed that 48.5% (95% CI: 47.0-49/2-2.0) of patients adhere to their medication for up to one year. Comparing these findings with the findings of our study, it is evident that the MA rate among Iranian patients with HTN is lower compared with other countries.[42]

Table 3. Predictors of medication adherence based on the significant or non-significant relationship

First author	Variables non-significantly correlated with medication adherence	Variables significantly correlated with medication adherence
Behnood-Rod et al.[26]	Gender, age, insurance, location of residence, smoking	Systolic and diastolic blood pressure, body mass index (BMI), experience of referring to the emergency room because of hypertension
Arbabshastan et al.[29]	-	Internal locus of control, social support
Taher et al.[37]	-	Understanding the necessity of taking medicines, concerns about drug use, age, sex, education, occupation, place of residence, duration of disease, duration of drug intake, polypharmacy, and history of comorbidity
Hadi and Rostami Gouran[33]	Duration of disease	Systolic and diastolic blood pressure, age, duration of drug intake, polypharmacy, stage of hypertension, knowledge of hypertension, forgetfulness, side effects of drugs, number of visits
Mahmoudian et al.[23]	Age, sex (patient), gender (physician), duration of disease	Education, satisfaction with communication with the doctor
Roohafza et al.[36]	-	Stress, knowledge
Saadat et al.[27]	Comorbidity	-
Zinat Motlagh et al.[21]	Duration of disease, body mass index (BMI), income, education level, place of residence, marital status, gender	Age
Asayeshi et al.[25]	Drug-related beliefs	Education and occupation
Kamran et al.[34]	-	Physical activity, being a non-smoker, perceived sensitivity, perceived severity, perceived damage
Najimi et al.[24]	-	Stressful life events, depression, interpersonal conflict

This difference may be attributed to the cultural context of people of different countries in relation to follow-up of their treatments. From the researcher's point of view, people in developed countries have a culture of self-care, pay attention to their health, and are more aware of the role of antihypertensive drugs in disease control, so they try to take their medications correctly.

In this study, the MA rate was measured only using self-report method. In studies that utilized the MMAS-8 tool, a low rate of MA was observed, and in studies that used tools with the cut-off point of 80%-90%, a high MA rate was reported; this was consistent with the results of previous similar study.[38] In a study by Durand et al., the highest rate of non-adherence to medication was related to biological tests (measuring the amount of the drug in the blood and the urine of patients) and the directly observed therapy (DOT), and the lowest rate of non-adherence was related to the medication possession ratio (MPR) measurement method.[40] In the present study, the MA rate was measured only through self-report method using questionnaires. The advantages of self-report questionnaires over other methods of measuring MA rate are that self-reporting can address the underlying causes of medication non-adherence such as disease perception, treatment beliefs, or cognitive impairment where other methods are unable to address them.[40]

The primary studies in our study used different tools to measure MA. The HBMA scale and tools with a cut-off point of 80%-90%, compared with MMAS-8, are associated with a high prevalence of MA. In a recent study, it was found that by using the MMAS-8 tool, the prevalence of MA was estimated as low compared with other tools, and tools with a cut-off point of 80%-90% provided a high MA prevalence.[38] By comparing the prevalence of MA based on different tools, researchers have concluded that using an international standard tool instead of a researcher-developed tool would provide an accurate measurement of MA rate and simplify the comparison and analysis of MA between different studies.

Regarding the geographical location, the findings showed that region 5 of Iran had high MA rates compared with the other regions. The reason for this difference is that, in the studies conducted in region 5, the HBMA scale and researcher-made tools were mostly used, and these tools show a high MA rate compared with the MMAS-8; therefore, a high MA rate was observed in the studies performed in this region.

The correlation of age with the prevalence of MA indicated that elderly people have a higher MA rate compared with other age groups, which was consistent with the findings of similar studies.[29,41,43,44] In a study by Tong et al., it was demonstrated that 75% of the group under 25 years of age had 59% of MA rates, the age group of 18-44 years showed 55% of MA rate, and the age group of 45-40 years indicated 71% of MA rates, and the age group of 65 years showed 78% of MA, indicating a high MA rate in the elderly compared with other age groups.[43] Although the comparison shows that both the elderly in the study by Tong et al.[43] and the elderly in the current study had a high MA rate, the MA rate for the elderly in their study was higher than the MA rate for the elderly in our study. The possible cause can be traced back to the difference in the method of measuring the MA rate. In the study by Tong et al., the HealthStyles survey was used to measure the MA rate, yet in our study, the MMAS-8 tool was mostly used. A study in Hong Kong indicated that more than half of the elderly did not follow their treatment regimen.[43] Al-Ramahi reported that 52% of the elderly have poor MA and the rest of them have moderate and high MA.[41] Based on the experiences of researchers and their relationship with older adults, the elderly think that medicines are the best factors that can control their diseases, and due to their multiple chronic diseases compared with other age groups, they try to control their diseases by timely medicine intake. However, the physical and mental problems of the elderly hinder the correction of the way they take medicines.[1,45-47]

The findings of the current study showed that married women demonstrate a higher MA rate in comparison with single men. In the current study, married couples were compared with single individuals, and it was indicated that married individuals show a higher MA rate, which was similar to the results of previous studies.[43]

The results of our study showed different predictors of MA based on significant and non-significant correlations. These factors could be different based on the context of the study and the culture of the community and are mostly different in various individuals.

Study Limitations and Strengths: The following limitations of our study should be noted when generalizing our results to larger populations. The first limitation was the fact that the primary studies were limit to 17 articles. Moreover, although MMAS-8 as a standard questionnaire was used more in the primary studies, researcher-made questionnaires were also used. This could reduce the generalizability of our findings. However, the study also has strengths. Covering more databases and comprehensive reviews made it possible to access the majority of related primary studies. This is the first study to ascertain the overall prevalence of MA in Iran in patients with HTN.

Conclusion

The results of the current study show that the prevalence of MA among patients with HTN in the community is low. Given that HTN is easily controlled by adherence to treatment, it is essential to provide necessary trainings and interventional programs to increase MA rates in affected patients.

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Conflict of Interests

Authors have no conflict of interests.

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Our first experience in stenting of coarctation of aorta in infants and small children; A case series study

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Case Series

Abstract

BACKGROUND: One of the congenital heart defects which can cause severe cardiac symptoms and cardiac failure in early childhood and neonatal duration is coarctation of aorta. Balloon angioplasty or surgical approach could be done for management of these defects. This study aimed to evaluate the efficacy and safety of coarctation stenting to improve the condition of these patients.

METHODS: Five patients with severe coarctation of aorta participated in this study. Balloon angioplasty performed for these patients initially. Each of five patients had a gradient decline after the initial balloon angioplasty, and againing gradients increased during the follow-up; then, they were treated by implanting a stent. We used Cook Formula stents for these patients.

RESULTS: The pressure gradient decreased in all 5 patients with maximum and minimum reduction of 55 and 35 mmHg; and we had not severe complication during or after the procedure and during the follow-up period.

CONCLUSION: Performing a stent in selected small children and infants that have sever and symptomatic coarctation of aorta can be effective and safe in improving patients' clinical state, and preventing surgery.

Keywords: Coarctation of Aorta, Stents, Infants

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Introduction

One of the congenital heart defects defined as a narrowing or partially closure of the aortic arch or descending aorta, mostly located near the insertion of patent ductus arteriosus (PDA) at the beginning of descending aorta, is coarctation of aorta (CoA).[1] The prevalence is 4 per 10000 live births, represents about 8% of all congenital cardiac anomalies, and is the fourth most common lesion requiring treatment during infancy.[1] CoA may be seen as in combination with other diseases, most commonly left-sided heart diseases such as bicuspid aortic valve and ventricular septal defect, or in isolation form. CoA can be presented at any age, but mostly presents in infancy or early childhood because of opportunities of its symptoms such as heart failure. In severe and critical patients, during the early life period, the severity of the narrowing may be seen such as in the physiology of the interrupted aortic arch; in such case, the baby's life is mostly related to the functioning and opening of the PDA. In these patients, continuous prostaglandin infusion could be helpful in opening the ductus arteriosus prior to doing appropriate treatment as soon as possible. After childhood or during the life, the patient may face with hypertension, and CoA diagnosis may be missed until that time. Untreated patients have shorter long-life than normal population, and may die during third-fourth decades of their life. The most prevalent reasons of death are bacterial endocarditis, intracranial hemorrhage, and heart failure.[1]

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Different treatments were suggested for the CoA during the past years. Crafoord described surgical approach of the CoA repair.[2] Surgical approach of CoA in young children has good results and low risk of reoperation, even in pediatrics with low body weights.[3] There are many surgical procedures suggested for repair of CoA, such as end-to-end anastomosis and subclavian artery patch technique, and each of these methods has advantages and disadvantages. To manage discrete CoA, an alternative approach named balloon angioplasty (BA) was suggested; it is less invasive, has much less complication, and has been used since 1982 to treat CoA. For recoarctation after surgical method compared to native CoA, because of lower mortality and morbidity and higher success rate, BA is more accepted among interventionists.[4-7] BA approach includes inflation and expansion of the inserted balloon in constricted segment zone, and results in tearing and mild rupture of the media and intima layers of the aorta. In long segment form of CoA or hypoplasia of aortic arch, compared to simple form of CoA, less arbitrary results have been reported. Complications such as arterial injury or other vessel sites, restenosis of the aortic wall, and aneurysm formation after CoA zone were reported after BA.[8,9]

Use of balloon-expandable or self-expandable stents is an acceptable alternative management for CoA in older patients. Stents can decrease aneurysm formation in descending aorta and restenosis related to arterial structure, and diminish the gradient pressure of CoA zone to less than 5-10 mmHg.[8,9] The indications of using stents for CoA are generally as long-segment CoA, an aneurysm formation after previous therapies, tortuosity of aortic arch or descending aorta, recurrent of CoA, and associated sever narrowing or hypoplasia of aortic arch.[10] The use of stent is recommended for patients that have at an older age and weighing more than 20 kg. Using stents in small children or infant have been reported in few studies.[11]

This study aimed to evaluate the efficacy and safety of coarctation stenting for long segment or recurrent CoA in infants and small children referred to Shahid Chamran hospital affiliated to Isfahan University of Medical Sciences, Isfahan, Iran.

Materials and Methods

Five patients with long segment form of CoA or discrete CoA (recoarctation after previous balloon angioplasty) underwent stenting of CoA between May 2017 and May 2018 at Shahid Chamran cardiovascular heart center. Detailed explanations were provided for the patients' parents, and the procedures were done with their complete consent. This study was approved by the Ethics Committee of Isfahan University of Medical Sciences with the code of IR.MUI.MED.REC.1397.159.

4 patients were boys and 1 was girl. At the first procedure, the age and body weight ranged from 1 to 2 months and 3 to 5 kg, respectively. One of them had 2 times balloon angioplasty before stent implantation, and others had one time. Initially, all patients were completely examined by the pediatric cardiologist. For complete evaluation, echocardiography, chest radiography, and 12-lead electrocardiogram (ECG) were done before procedure.

The procedures were performed under general anesthesia or deep sedation with 3-5 mg/kg ketamine and 0.1-0.2 mg/kg midazolam, which repeated every 5-10 minutes depending on the patient's condition. Anticoagulation with heparin (50-100 U/kg) was maintained throughout the procedure. Appropriate antibiotic (mostly cefazoline) was prescribed to the patient during the procedure, and was continued for 24 hours after it. Vascular balloon-expandable stents (Cook Formula Blomington, IN, USA) were used in all patients. We used a radial sheath No. 5 French to prevent arterial injury. We marked the CoA zone on the cath lab's monitor using the pen, and after that, the stent moved to relevant place over the wire without using long sheath. When the stent was positioned in appropriate place, the balloon was inflated and dilated the stent up to 6-8 mm (Figure 1). The gradient before and after procedures were measured.

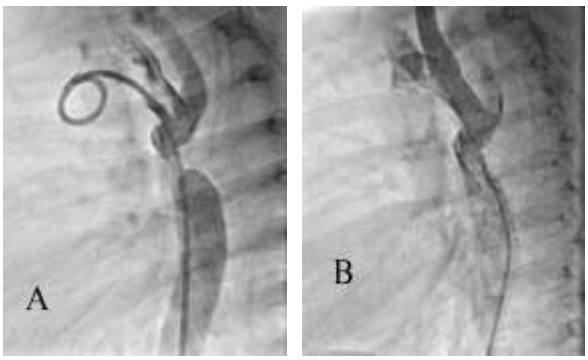

Figure.1 Lateral injection in descending aorta before (A) and after (B) coarctation stenting

After procedure, radio-contrast agent was injected for evaluation and imaging of the anatomy. No damage and side effect was seen at site of procedure. Echocardiography and Doppler echocardiography were performed one day before

Table 1. Clinical data of studied patients

Patients	Sex	Age 1	Long segment CoA	Age 2	BW1 (kg)	BW2 (kg)	Balloon size (mm)	Stent size (mm)
1	Boy	25 days	-	4 months	3	6	7 × 20	17 × 8
2	Boy	2 months	*	9 months	5	7	7 × 20	24 × 7
3	Boy	30 days	*	7 months	4.5	8	7 × 30	24 × 7
4	Girl	35 days	-	24 months	3.5	10	7 × 20	24 × 7
5	Boy	20 days	-	6 months	3	7	6 × 20	17 × 7

CoA: Coarctation of aorta; Age 1: Age at balloon angioplasty; Age 2: Age at CoA stenting; BW 1: Body weight at balloon angioplasty; BW 2: Body weight at CoA stenting

procedure, and one day, one week, one month, three months, and six months after stenting. Pressure gradient less than 5-10 mmHg across the CoA zone, and increasing of 50% in the diameter of the stenosis segment after stent implantation was a successful outcome.

SPSS software (version 22.0, IBM Corporation, Armonk, NY, USA) used for data analysis. Mean ± standard deviation (SD) was expressed for the interval data. For paired data, the paired t-test was used to evaluate utilizing statistical significance. P value of less than 0.05 was considered statistically significant.

Results

5 patients with recoarctation or long segment form of CoA underwent stent implantation (Table 1).

Stenting decreased pressure gradient significantly across the coarctation zone in all 5 patients with a maximum of 55 and a minimum of 35 mmHg (mean of 45 mmHg). A small residual gradient of 5-10 mmHg was remained after stent implantation. Moreover, ejection fraction increased in all patients with a maximum of 28 and a minimum of 5% percent (Table 2). One patient had complete heart block during the first ten minutes after the procedure that changed to 2:1 block for two hours, and finally returned to normal rhythm after procedure.

During stent implantation, immediate dangerous complications such as massive bleeding and blood transfusion, vascular injuries, contrast sensitivity or need for emergency surgical intervention did not occur. Moreover, delayed complications such as retroperitoneal hematoma due to vascular injury, arterial dissection, aneurysm formation, stents fracture, stents migration, arteriovenous fistulas, and infection were not seen. Deaths related to the procedure was not seen during or after the procedure.

Discussion

During the early life period, severe CoA could be presented by heart failure, shock, and subsequent other organs failure. Different approaches are recommended for management of CoA and in some patients, the first step is surgical approach. The results are influenced by arch anatomy, additional defects, and comorbidities.[3] An alternative to surgery is balloon angioplasty, and many interventionists and articles confirmed this method for management of this defect.[4,12] Recoarctation is reported in infants treated with balloon dilatation before 6 months of age.[13,14] CoA stenting is a good alternative method in older patients with CoA. Surgical repair is recommended if percutaneous interventional approach is unsuccessful, or in existence of contraindications. In pediatric, because of smaller size of arterial diameter, using stents is limited in older patients. Kang et al. described using the stent in children with body weight of less than 30 kg with a mean weight of 20.8 kg.[15]

Table 2. Outcomes after procedure.

Patients	PPG1 (mmHg)	PPG2 (mmHg)	PPG3 (mmHg)	PPG4 (mmHg)	Mean difference of pressure	P	EF1 (%)	EF2 (%)	Mean difference of ejection fraction	P
1	40	10	50	10	-0.45 ± 0.093	< 0.001	45	60	0.014 ± 0.09	0.025
2	100	15	50	10	(-0.57,-0.33)		62	70	(-0.028,-0.25)	
3	40	10	60	5			40	68		
4	50	20	40	5			60	65		
5	30	5	60	5			50	63		

PPG1: Peak to peak pressure gradient before balloon angioplasty; PPG2: Peak to peak pressure gradient after balloon angioplasty; PPG3: Peak to peak pressure gradient before coarctation stenting; PPG4: Peak to peak pressure gradient after coarctation stenting; EF1: Ejection fraction before coarctation stenting; EF2: Ejection fraction after coarctation stenting

Neonates with severe CoA in critical hemodynamic state have a high risk of surgical treatment. In these babies, the lifesaving emergency interventional treatment using coronary stents is advocated. According to several case reports and published small series, stabilization of clinical condition can be achieved for a few weeks allowing later elective surgical treatment.[16-18]

Use of low-profile stents were described by Grohmann et al. in 4 patients with low weight that had the average weight of 3.8 kg, and long-term follow-up did not reported side effects.[11] The results and follow-up of using stents in sick and low-weight infants with contraindication for surgical approach also was reported by Al-Ata et al.[16] and Arfi et al.[19]

Stegeman et al. based on a study of 4 very low birth weight (VLBW) infants reported that coronary stent implantation in VLBW neonates with severe CoA was a safe management, and could be a bridging approach to surgical management when prostaglandin therapy failed, and the patients had not good condition. Recoarctation and mortality had lower rates in this two-steps management compared to surgical method or BA.[20]

Gendera et al. published retrospective analysis of implantation of balloon-expandable stents for recoarctation in small children, based on experience of two centers. Immediate, early, and midterm results were reported in 34 patients, treated for recoarctation. All the stenting procedures were successful, and resulted in significantly diminished systolic gradient from a median of 31 to 0 mmHg before and after stenting, respectively, with a concomitant increase of the stenotic segment diameter of the aorta from a median of 3 to 7 mm.[21]

Mohan et al. described effectiveness and facility of stent using for CoA in young children. When stents were used in small children because of short diameter of aorta and not reaching to adult size, we must concerns other options, such as not using stents in discrete CoA. This study on 60 patients confirmed safety and effectiveness of using stents for treatment of CoA in small children, as in larger patients, in the short term.[22]

Re-dilation of the stents can be used as a good option to treat residual CoA from past procedure or to increase narrowing during the life. It seems largely effective and feasible, although such conclusions and recommendations are mostly based on limited experience. On the other hand, based on Cheng et al. study, stenting is usually recommended for a patient older than 10 years or weighing more than 35 kg.[23]

In this study, our patients were selected from patients who had already had a balloon angioplasty procedure, and did not respond to the treatment, or had long segment CoA. In patients with long segment form of CoA, balloon angioplasty is not effective, and these patients are candidates for surgery or stent therapy. Except for one patient that had two time, each of the patients had angioplasty one time in the infancy, and re-admitted with recoarctation. The first procedure was performed for less risky procedures, and in the second stage, CoA stenting was performed because the patients were candidates for surgical approach. The major problem in these patients is the small size of the vessels, which can cause severe complications during or after the procedure. Moreover, with the growth of the children, the vessels grow and need frequent procedures. We used stent to prevent vascular damage without using a long sheath. We used a vascular balloon-expandable stent which had the ability to dilate up to double primary size during the time. The used stents were up to 16 mm in diameter to be opened and this property, along with other collaterals, could be benefit for the patients and could help us to prevent surgery during the life. Mean duration of follow-up period in our patients was 12 months. The pressure gradient in our patients decreased after the stent, and did not increase in follow-up until the time of this report. The weight gain of our patients was normal, symptoms of heart failure decreased, and ejection fraction increased. Unlike previous studies, in this study we did not use stent at the first stage, and after balloon angioplasty, CoA stenting was performed at the next levels. We did not see particular complications in the follow-up period. In the future, due to the growth of patients, there is need to increase the diameter of the stents, and manage other complications if occurred.

Limitations: Each center has a few number of these patients, and does not allow for detailed conclusions, so it is recommended to design a multicenter study or a study with larger sample for better results. Longer follow-up is required to better determine the outcome. With regard to infant's vascular size, this procedure can be complicated in VLBW children. Due to the elegance of stents, we may see stent fractures in the future, and may need for more procedures such as using other stents. The design of better stents for these complications is necessary in the future.

Conclusion

During neonatal and infancy period, surgical

approach and BA in patients with CoA may have some complications. Due to this complications, the use of stents that have the ability of re-dilation in carefully selected patients such as recoarctation of aorta or long segment CoA could be in mind after primary treatment, and may be an alternative way in these patients with safety and efficacy.

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Conflict of Interests

Authors have no conflict of interests.

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