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ARYA Atherosclerosis

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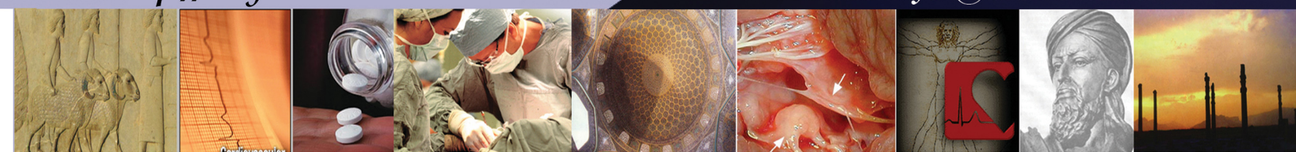

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2. Bonow RO, Mann DL, Zipes DP, Libby P. Braunwald's Heart Disease E-Book: A Textbook of Cardiovascular Medicine. 7th ed. Philadelphia, PA: Elsevier Health Sciences; 2007. p. 1976, 1981, 1982.

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Qualitative Research	3500	7,000,000	2,000,000
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* All the words of the article containing the references; each table is considered as 300 words.

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Risk factors of congenital heart diseases: A hospital-based case-control study in Isfahan, Iran

Alireza Ahmadi[(1)], Mojgan Gharipour[(2)], Zohreh Sadat Navabi[(3)], Hossein Heydari[(4)]

Original Article

Abstract

BACKGROUND: Improving knowledge towards risk factors for congenital heart disease (CHD) is important because of its high mortality and morbidity and trying for prevention of occurrence of CHD.

METHODS: This case-control study was conducted on a total of 898 children with their mothers, who referred to the Clinic of Pediatric Cardiology of School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran, during the years of 2014 to 2016. Cases comprised of 464 children with CHD diagnosed by echocardiography and controls were 434 sex- and age-matched children without any evidence of CHD, who were admitted for a heart check-up at the same study period and in similar conditions. The children's parents completed check lists for collecting demographic characteristics, family history of CHD, history of obesity in mother, history of abortion and diseases in mother, use of medicine during pregnancy, exposure to teratogens during pregnancy, and children characteristics such as birth height and birth weight, etc.

RESULTS: Based on the results of data analyses with multiple logistic regression model [odds ratio (OR) with 95% confidence interval (CI)], history of obesity in mother before pregnancy, history of abortion, parental consanguinity, exposure to cigarette smoke during pregnancy, exposures to teratogens in the first trimester of the pregnancy, and use of medicine during pregnancy were associated with an increased odds of CHDs.

CONCLUSION: Results of this study emphasizes the use of policies that enhance pre-marital counseling, regular counseling during pregnancy, treatment of mothers' disease, and enhancing knowledge of women of childbearing age about exposure to certain teratogens for controlling risk factors of CHD.

Keywords: Congenital Heart Defects; Risk Factors; Pediatrics

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Introduction

Congenital malformations in the heart and great vessels mainly appear during intrauterine development. The global incidence of congenital cardiovascular defects varies in the range of 0.47% to 1.17% of live births.[1] Various etiological factors have been identified; however, the exact reasons for these abnormalities have remained unclear. A multifactorial etiology is now accepted as a combination of both genetic and environmental factors for these defects.[2,3] It seems that the genetically predisposed fetus when exposes to environmental triggers may suffer cardiac morphogenetic abnormalities within intrauterine growth period.[4] In fact, an interaction between genetic susceptibility and exposing to environmental stimulators may lead to congenital heart disease (CHD). A variety of both neonatal and maternal risk factors have been introduced to be related to certain heart defects. Results of studies showed that the incidence rate of CHD increased after exposure of pregnant mother to rubella virus.[5,6]

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Consuming some drugs during pregnancy such as thalidomide, some anticonvulsant drugs, alcohol, lithium, sex hormones, folic acid antagonists, diazepam, corticosteroids, and methamphetamines, phenothiazine, and cocaine is associated with different severities of CHDs.[5,7] Diabetic mothers are also more predisposed to CHD.[8] Moreover, higher incidence of these abnormalities is also identified in some chromosomal anomalies such as Down syndrome (DS), Turner's syndrome (TS), and deletion of chromosome 22.[9-11] Based on the genetic science, the association between some single nucleotide polymorphisms and occurrence of CHDs has been also indicated.[12,13] Thus, the cause of CHDs is largely on the basis of multifactorial inheritance hypothesis. Some types of CHDs are minor without significant effects on physical function of the affected patients. However, emergency surgery may be required in about one-fourth of patients within first year of birth.[14] Also, some complex surgical procedures may be needed to repair these anomalies which may lead to potential complications and prolonged hospitalization.[15] In this regard, discovering risk factors is very important for managing and treatment of CHD. Consequently, in order to make suitable planning for control of causative factors in these anomalies, it is necessary to conduct careful studies for identifying main risk factors in CHD. Therefore, the aim of this study was to investigate risk factors of CHDs in children in Isfahan, Iran.

Materials and Methods

This case-control study was conducted on a total of 898 children with their mothers, who referred to Clinic of Pediatric Cardiology, School of Medicine, Isfahan University of Medical Sciences, during the years of 2014 to 2016. All children were referred to this clinic for heart check-up, and they were visited by pediatric cardiologist with complete physical examination and complementary diagnostic tests such as echocardiography. Then, 464 children with documented CHD were selected as the case group and 434 children without CHD who were sex-and age-matched were selected as the control group.

The inclusion criteria were children with CHD confirmed on clinical manifestations as well as complementary diagnostic tests such as echocardiography, cardiac catheterization and angiography, computed tomography (CT) scan, or magnetic resonance imaging (MRI). The exclusion criteria were children with acquired heart disease such as ischemic or rheumatologic defects, and refusing to participate in the study. This study was approved by the Ethics Committee of Isfahan Cardiovascular Research Institute. Participation in this study was voluntary. All information collected from participants was kept confidential.

After receiving written informed consent from parents in both groups, the study data were collected through checklists. The checklist variables consisted of the following details:

Characteristics of checklist variables included age, sex, parents' level of education, parents' occupation, number of children per family, and birth weight.

Maternal variables characteristics that were collected with checklists included history of obesity in mother before pregnancy, history of abortion, parental consanguinity, radiation and X-rays exposure during pregnancy, history of smoking and exposure to cigarette smoke during pregnancy, the maternal exposure to teratogens in the first trimester of the pregnancy (including hair color, canned food, detergents, insecticides, alcohol, and opioids), use of mobile phone, family history of CHD, history of diseases in mother [including diabetes, heart diseases, hypertension (HTN), hypothyroidism, etc.], and use of medicine during pregnancy. The checklist variables were completed by an expert person through the interview with mothers of children with CHD (self-report) as the case group, and mothers of healthy children as the control group and also the information of hospital records for CHD such as echocardiographic report was used for the case group.

Data were reported as mean and standard deviation (SD) for quantitative variables and frequencies and percentages for qualitative variables. Continuous variables were compared using independent samples t-test. For checking normality assumption of the data, Kolmogorov-Smirnov test (K-S test) was used. Categorical variables were compared using chi-square test or Fisher's exact test if needed.

The multiple logistic regression model [odds ratio (OR) with %95 confidence interval (CI)] was used for estimating the association between risk factors of CHD and CHD. For the statistical analysis, the SPSS statistical software (version 25, IBM Corporation, Armonk, NY, USA) was used. $P < 0.050$ was considered significant.

Results

A total of 474 children with CHD and 436 sex- and age-matched children without any evidence of CHD

and their parents were recruited. The characteristics for case and control groups were presented in table 1. 253 (53.4%) of cases and 231 (53.0%) of controls were male (P = 0.900). The mean age for the case group was 3.22 ± 3.35 years and for the control group was 3.57 ± 3.49 years (P = 0.120). The mean weight for cases and controls were 2.96 ± 0.56 kg and 2.98 ± 0.53 kg, respectively (P = 0.640). The mean height for cases was 48.54 ± 30.30 cm, and for controls was 48.93 ± 2.92 cm (P = 0.060). Results in table 1 showed that parents' occupation, parents' level of education, and the number of children per family were different in case and control groups.

As shown in table 2, compared with mothers in the control group, a number of mothers in CHD group had obesity before pregnancy (27.0% vs. 17.7%, P < 0.001), history of abortion (14.6% vs. 47.0%, P < 0.001), and consanguineous marriage (32.5% vs. 18.6%, P < 0.001). More mothers in case group had exposure to cigarette smoke during pregnancy (23.2% vs. 11.9%, P < 0.001) and teratogens including hair color (9.7% vs. 4.1%, P = 0.001), canned food (17.3% vs. 5.3%, P = 0.001), detergents (21.7% vs. 10.8%, P < 0.001), and using tobacco, alcohol, and opium (3.6% vs. 0.7%, P = 0.003) in the first trimester of pregnancy in both group.

Moreover, results in this study showed that family history of CHD (P = 0.006), mother's diseases such as diabetes and hypothyroidism (P < 0.001), as well as the use of medications such as metformin and levothyroxine (P < 0.001) during pregnancy may have an effect on the occurrence of CHDs.

Variables for determining and identifying the most important risk factors of CHDs were included in a multiple logistic regression model. The risk factors were coded as Yes/No indicator variables. They were obesity in mother before pregnancy, history of abortion, parental consanguinity, radiation and X-rays exposure, history of smoking, and exposure to cigarette smoke during pregnancy.

Table 1. Characteristics variables of cases with congenital heart disease (CHD) and controls

Variables	Case group (n = 474)	Control group (n = 436)	P
Age (year) (mean ± SD)	3.22 ± 3.35	3.57 ± 3.49	0.120
Birth weight (kg) (mean ± SD)	2.96 ± 0.56	2.98 ± 0.53	0.640
Birth height (cm) (mean ± SD)	48.54 ± 3.30	48.93 ± 2.92	0.060
Sex [n (%)]			0.900
Male	253 (53.4)	231 (53.0)	
Female	221 (46.6)	205 (47.0)	
Fathers' occupation [n (%)]			< 0.001
Worker	224 (47.3)	148 (33.9)	
Employed	78 (16.5)	82 (18.8)	
Self-employed	151 (31.9)	191 (43.8)	
Other jobs	21 (4.4)	15 (3.4)	
Father's education level [n (%)]			0.001
Primary school	201 (42.4)	133 (30.5)	
High school	157 (33.1)	178 (40.8)	
College	116 (24.5)	125 (28.7)	
Mothers' occupation [n (%)]			< 0.001
Employed	27 (5.7)	43 (9.9)	
Housewife	386 (81.4)	369 (84.6)	
Other jobs	61 (12.9)	24 (5.5)	
Mother's education level [n (%)]			< 0.001
Primary school	174 (36.7)	100 (22.9)	
High school	175 (36.9)	189 (43.3)	
College	125 (26.4)	147 (33.7)	
Number of children per family [n (%)]			0.010
1	222 (46.8)	223 (51.1)	
2	189 (39.9)	176 (40.4)	
3	43 (9.1)	34 (7.8)	
4	15 (3.2)	2 (0.5)	
More	5 (1.1)	1 (0.2)	

SD: Standard deviation

Table 2. Mother's risk factors in cases with congenital heart disease (CHD) and controls

Variables	Group		P
	Case group (n = 474)	Control group (n = 436)	
History of obesity in mother before pregnancy*	128 (27.0)	77 (17.7)	< 0.001
History of abortion	69 (14.6)	25 (47.0)	< 0.001
Consanguineous marriage	154 (32.5)	81 (18.6)	< 0.001
Exposure to cigarette smoke during pregnancy	110 (23.2)	52 (11.9)	< 0.001
Exposure to radiation during pregnancy	9 (1.9)	11 (2.5)	0.520
Family history of CHD	36 (7.6)	15 (3.4)	0.006
Mother's diseases**	70 (14.8)	31 (7.1)	< 0.001
Use of medicine during pregnancy***	94 (19.8)	47 (10.8)	< 0.001
Exposure to teratogens in the first trimester of pregnancy			
Hair color	46 (9.7)	18 (4.1)	0.001
Canned foods	82 (17.3)	23 (5.3)	< 0.001
Detergents (bleaches)	103 (21.7)	47 (10.8)	< 0.001
Insecticides	18 (3.8)	11 (2.5)	0.270
Tobacco, opium, alcohol	17 (3.6)	3 (0.7)	0.003
Use of mobile phone during pregnancy	421 (88.8)	396 (90.8)	0.310

Data are reported as number (%)

* History of obesity was assessed by mother's self-report (weight and height of mother before pregnancy); ** Mother's diseases included diabetes and hypothyroidism; *** Many drugs were used during pregnancy including metformin and levothyroxine

CHD: Congenital heart disease

For comparison of effective factors between case and control groups, chi-square test or Fisher's exact test was used.

Moreover, variables such as exposure to teratogens in the first trimester of the pregnancy (exposure to at least one of teratogens including hair color, canned foods, detergents, insecticide, alcohol, tobacco, and opium), use of mobile phone in pregnancy, family history of CHD, history of diseases in mother, and use of medicine during pregnancy were studied.

According to the results of table 3, variables that entered into the multiple logistic regression model, variables of history of obesity in mother before pregnancy (OR: 1.54, %95 CI: 1.10-2.17), history of abortion (OR: 2.16, %95 CI: 1.29-3.60), parental consanguinity (OR: 2.02, %95 CI: 1.46-2.81), exposure to cigarette smoke during pregnancy (OR: 2.00, %95 CI: 1.36-2.92), exposure to teratogens in the first trimester of the pregnancy (OR: 2.32, %95 CI: 1.68-3.20), and use of medicine during pregnancy (OR: 1.78, %95 CI: 1.16-2.71) were associated with an increased odds of CHDs.

Discussion

CHD is one of the most common causes of mortality in children. The studies about etiology of CHD has showed that there are multifactorial causes as a combination of both genetic and environmental factors for these defects.

Table 3. Odds ratio (OR) and 95% confidence interval (CI) for congenital heart disease (CHD) according to risk factor in the multiple logistic regression model

Variables	OR	%95 CI	P
History of obesity in mother before pregnancy	1.54	1.10-2.17	0.012
History of abortion	2.16	1.29-3.60	0.003
Smoking mother during pregnancy	5.20	0.56-48.37	0.147
Consanguineous marriage	2.02	1.46-2.81	< 0.001
History of diseases in mother	1.41	0.83-2.33	0.168
Use of medicine during pregnancy	1.78	1.16-2.71	0.007
Radiation and X-rays exposure during pregnancy	0.53	0.20-1.41	0.207
Exposure to cigarette smoke during pregnancy	2.00	1.36-2.92	< 0.001
Exposure to teratogens during pregnancy*	2.32	1.68-3.20	< 0.001
Use of mobile phone in pregnancy	0.89	0.55-1.44	0.650
Family history of CHD	1.68	0.86-3.27	0.124

Risk factors were considered as a binary variable (Yes/No) in the multiple logistic regression model

* Exposure to teratogens during pregnancy: Exposure to at least one of teratogens including hair color, canned food, detergents, insecticides, tobacco, opium, and alcohol

OR: Odds ratio; CI: Confidence interval; CHD: Congenital heart disease

In our survey, we attempted to determine risk factors of CHD to help early prediction of these abnormalities. Results of this study showed that among studied main factors for CHD, maternal weight in pregnancy, history of abortion, consanguineous marriage, drug use during pregnancy, and exposure to cigarette smoke and teratogens had significant relationship with incidence of CHD. According to the results, prevention of risk factors of CHD before pregnancy may lower the incidence of CHD.

As previously pointed, both genetic and environmental factors can be major causes of congenital heart anomalies. Similar findings to our observations can be found in previous studies.

Results of this study revealed the maternal weight in CHD group more than that of the control group. The results of studies of Brite et al.,[16] Persson et al.,[17] and Kmietowicz[18] showed that increased maternal weight had a significant statistical relationship with increased risk for CHD.

Also, in the present study among investigated diseases, hypothyroidism and diabetes in case group were more than that of the control group. The results of this study are consistent with the results of Grattan et al.[19] and Naghavi-Behzad et al.,[20] based on the results, more attention to the treatment of a mother's illnesses before pregnancy is necessary.

In this study, there was a significant relationship between the history of abortion and increased risk for CHD. Regarding association between history of abortion and increased risk for CHD, epidemiological studies have reported conflicting results on the association of CHD risk in offspring with a maternal history of prior pregnancies and abortions. A recent meta-analysis showed a positive effect of maternal gravidity on increased CHD risk. Also, a history of abortion was associated with a 24% higher risk of these defects. When stratified by abortion category, risk for heart defects increased by 18% and 58% with a history of spontaneous abortion and induced abortion, respectively.[21] In another study by Taksande et al., 10.61% of those with heart defects had a history of previous abortions, while only 2.79% had a history of CHD in previous child or malformed babies.[22]

The result of a data analysis showed that consanguineous marriage had a significant relationship with CHD. In Ul Hag et al.[23] study, consanguineous marriage and family history of CHD were known as independent risk factors for CHD. Because of the major role of consanguineous marriage in developing CHD and also due to the high prevalence of consanguineous marriage in Iran population especially in rural areas, higher prevalence of these defects can be predicted in such population.

Results of multiple regression in this study showed that history of treatment with drug by mother and exposure to cigarettes smoke and teratogens during pregnancy had a significant relationship with CHD. Results of study by Nicoll showed that in addition to smoking mother during pregnancy and some of the many components of cigarette smoke, exposure to teratogens such as pesticides, metals, and detergents had a significant relationship with CHD.[24] This data was consistent with the results of the present study. Therefore, mothers must be aware of risk factors of CHD and their effects on their infant's health during pregnancy.

The strong point of this study is that at first, the diagnosis of each CHD in case group was confirmed by a pediatric cardiologist and documented by echocardiography. Second, the children's age and sex between cases and controls were matched.

There are also a number of limitations in this study. Most data in this study were based on the parents' self-report, which could be a source of recall bias. As in any case-control study, we cannot rule out differential recall in cases and controls.

Conclusion

We could show that among all neonatal and maternal factors as well as demographic and socioeconomic factors, maternal obesity, history of abortion, consanguineous marriage, also exposure to teratogens could affect the incidence of CHD. Based on the results of this study, it seems necessary to make programs for preventing maternal obesity before pregnancy, improving pregnancy health care, lowing consanguineous marriage, prompt treatment of mothers' disease, and decreasing exposure to cigarette smoke and teratogens during pregnancy.

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Conflict of Interests

Authors have no conflict of interests.

References

1. Ren YY, Li XT, Gui YH, Yan YL, Chang C, Zhang JH, et al. Evaluation of the prenatal screening mode for fetal congenital heart diseases by ultrasound. Zhonghua Fu Chan Ke Za Zhi 2008; 43(8): 589-92.
2. Lage K, Greenway SC, Rosenfeld JA, Wakimoto H, Gorham JM, Segre AV, et al. Genetic and environmental risk factors in congenital heart disease functionally converge in protein networks driving heart development. Proc Natl Acad Sci U S A 2012; 109(35): 14035-40.
3. Wong P, Denburg A, Dave M, Levin L, Morinis JO, Suleman S, et al. Early life environment and social determinants of cardiac health in children with congenital heart disease. Paediatr Child Health 2018; 23(2): 92-5.
4. Sun R, Liu M, Lu L, Zheng Y, Zhang P. Congenital heart disease: Causes, diagnosis, symptoms, and treatments. Cell Biochem Biophys 2015; 72(3): 857-60.
5. Liang Q, Gong W, Zheng D, Zhong R, Wen Y, Wang X. The influence of maternal exposure history to virus and medicine during pregnancy on congenital heart defects of fetus. Environ Sci Pollut Res Int 2017; 24(6): 5628-32.
6. Tan MJ. A case-control study on the environmental factors and children congenital heart disease during early pregnancy. J Environ Health 2006; 23: 427-30.
7. Kallen B, Otterblad Olausson P. Antidepressant drugs during pregnancy and infant congenital heart defect. Reprod Toxicol 2006; 21(3): 221-2.
8. Simeone RM, Devine OJ, Marcinkevage JA, Gilboa SM, Razzaghi H, Bardenheier BH, et al. Diabetes and congenital heart defects: A systematic review, meta-analysis, and modeling project. Am J Prev Med 2015; 48(2): 195-204.
9. Kim MA, Lee YS, Yee NH, Choi JS, Choi JY, Seo K. Prevalence of congenital heart defects associated with Down syndrome in Korea. J Korean Med Sci 2014; 29(11): 1544-9.
10. Bondy C. Congenital cardiovascular defects in Monosomy X or Turner Syndrome. In: Muenke M, Kruszka PS, Sable CA, Belmont JW, Editors. Congenital heart disease: Molecular genetics, principles of diagnosis and treatment. Basel, Switzerland: Karger Medical and Scientific Publishers; 2015. p. 91-9.
11. Qin YF, Xie CH, Yang JB, Wu DW, Shao J, Zhao ZY. Relationship between 22q11 microdeletion syndrome and congenital heart disease. Zhonghua Xin Xue Guan Bing Za Zhi 2011; 39(7): 631-5.
12. Wolf M, Basson CT. The molecular genetics of congenital heart disease: A review of recent developments. Curr Opin Cardiol 2010; 25(3): 192-7.
13. Weismann CG, Gelb BD. The genetics of congenital heart disease: A review of recent developments. Curr Opin Cardiol 2007; 22(3): 200-6.
14. Vener DF, Tirotta CF, Andropoulos D, Barach P. Anaesthetic complications associated with the treatment of patients with congenital cardiac disease: Consensus definitions from the multi-societal database committee for pediatric and congenital heart disease. Cardiol Young 2008; 18(Suppl 2): 271-81.
15. Pasquali SK, He X, Jacobs ML, Shah SS, Peterson ED, Gaies MG, et al. Excess costs associated with complications and prolonged length of stay after congenital heart surgery. Ann Thorac Surg 2014; 98(5): 1660-6.
16. Brite J, Laughon SK, Troendle J, Mills J. Maternal overweight and obesity and risk of congenital heart defects in offspring. Int J Obes (Lond) 2014; 38(6): 878-82.
17. Persson M, Cnattingius S, Villamor E, Soderling J, Pasternak B, Stephansson O, et al. Risk of major congenital malformations in relation to maternal overweight and obesity severity: Cohort study of 1.2 million singletons. BMJ 2017; 357: j2563.
18. Kmietowicz Z. Risk of major birth defects rises with severity of mother's overweight. BMJ 2017; 357: j2911.
19. Grattan MJ, Thomas DS, Hornberger LK, Hamilton RM, Midodzi WK, Vohra S. Maternal hypothyroidism may be associated with CHD in offspring. Cardiol Young 2015; 25(7): 1247-53.
20. Naghavi-Behzad M, Alizadeh M, Azami S, Foroughifar S, Ghasempour-Dabbaghi K, Karzad N, et al. Risk Factors of Congenital Heart Diseases: A Case-Control Study inNorthwest Iran. J Cardiovasc Thorac Res 2013; 5(1): 5-9.
21. Feng Y, Wang S, Zhao L, Yu D, Hu L, Mo X. Maternal reproductive history and the risk of congenital heart defects in offspring: A systematic review and meta-analysis. Pediatr Cardiol 2015; 36(2): 253-63.
22. Taksande A, Vilhekar K, Chaturvedi P, Jain M. Congenital malformations at birth in Central India: A rural medical college hospital based data. Indian J Hum Genet 2010; 16(3): 159-63.
23. Ul Hag F, Jalil F, Hashmi S, Jumani MI, Imdad A, Jabeen M, et al. Risk factors predisposing to congenital heart defects. Ann Pediatr Cardiol 2011; 4(2): 117-21.
24. Nicoll R. Environmental contaminants and congenital heart defects: A re-evaluation of the evidence. Int J Environ Res Public Health 2018; 15(10).

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The effect of a lifestyle management educational program on blood pressure, heart rate, and body mass index in patients with hypertension

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Original Article

Abstract

BACKGROUND: Hypertension (HTN) is one of the most prevalent risk factors for arteriosclerosis and coronary artery disease (CAD). Its side effects can be decreased through the use of some methods and interventions. The present study was conducted with the aim to evaluate the effects of a lifestyle management on blood pressure, heart rate, and body mass index (BMI) of patients with HTN who have undergone angioplasty.

METHODS: This clinical trial was conducted on 2 groups in 3 stages in an educational hospital in Isfahan, Iran, in 2014. The study participants consisted of 60 patients with HTN who had undergone angioplasty. The participants were randomly allocated to the study and control groups. The intervention was implemented in 6 educational sessions during 3 weeks, and then, follow-up was conducted through phone calls in the study group. The collected data were analyzed using independent t-test, chi-square, Mann-Whitney U test, and ANOVA in SPSS software.

RESULTS: Repeated measures ANOVA results indicated that the effect of time ($P < 0.001$) and group ($P = 0.027$) on systolic blood pressure (SBP) was significant. The effect of time ($P = 0.015$) and group ($P = 0.040$) on diastolic blood pressure (DBP) was also significant. In terms of BMI, both effects of time ($P = 0.010$) and group ($P = 0.034$) were significant. However, the effect of time ($P = 0.899$) and group ($P = 0.900$) on heart rate was not significant.

CONCLUSION: The lifestyle management program implemented in the present study was effective on decreased DBP, SBP, and BMI in patients with HTN who had undergone angioplasty. Thus, nurses could implement this program as a part of their care provision program for patients.

Keywords: Lifestyle; Hypertension; Body Mass Index; Heart Rate; Angioplasty

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Introduction

Hypertension (HTN) is a serious medical condition that significantly increases the risk of heart attack, stroke, kidney failure, and blindness. It is one of the leading causes of premature death worldwide.[1] According to the World Health Organization (WHO), 33% of adults in the world are suffering from HTN and it is predicted that its prevalence will increase to 60% by 2025.[2] HTN is a manageable and identifiable risk factor for stroke, myocardial infraction (MI), heart failure, aorta dissection, and atrial fibrillation.[3]

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Moreover, HTN is one of the most common risk factors for coronary artery disease (CAD)[4], and uncontrolled HTN could lead to extent CAD, which needs different surgical and therapeutic-diagnostic procedures like angioplasty.[5]

Angioplasty is the most common beneficial therapeutic-diagnostic methods for CAD[6] and a low-cost and low-risk method compared to coronary artery bypass. Due to its low risk and high success, today, in the USA, 400000 angioplasties are performed every year.[7] In Shahid Chamran Hospital of Isfahan, Iran, alone, 1516 cases of angioplasty and 2550 angioplasties with stent were conducted in the first 6 months of 2003.[8]

After coronary artery angioplasty, permanence of risk factors, especially HTN, could result in the recurrence of stenosis of the coronary artery or decrease the success rate of treatment.[9] Therefore, appropriate interventions to decrease risk factors, especially HTN, are necessary.[10]

Of the estimated 1.13 billion people who have HTN, fewer than 1 in 5 have it under control.[1] According to Eighth Joint National Committee (JNC8) criteria, the algorithm of HTN treatment initiates with correction of lifestyle and continues with different drug regimens.[11] Different studies on lifestyle management have showed that changes such as weight loss, Dietary Approaches to Stop Hypertension (DASH), reduced salt consumption, and exercising are effective on lowering blood pressure (BP) and decreasing its complications.[12,13]

Most people assume themselves healthy and do not sense the necessity to alter their way of life, modify their diet, lower their weight, exercise, and give up smoking until they begin displaying complications.[10,14] Only when their disease has reached a progressive phase or they have been diagnosed with diseases such as CAD, do individuals come to the decision to change their lifestyle.[15] However, an improvement in the health status of patients with HTN after undergoing angioplasty may cause them to return to their former unhealthy lifestyle. This can potentially result in disease recurrence. However, multiple lifestyle management interventions will hearten and stimulate patients with HTN to adopt and continue lifestyle changes in their everyday life.[16]

Different methods have been carried out as lifestyle management programs on subjects with HTN and many existing studies have focused on the consequence of a single lifestyle modification plan on BP, pulse rate (PR), and body mass index (BMI). Some previous studies have shown didactic interventions to be effective on the lifestyle of patients with HTN.[17-21] Nevertheless, Cook et al. found that their 18-month educational intervention did not have a significant effect on BP monitoring in patients with prehypertension.[22]

Mokhtari et al. studied a didactic intervention program and found that it was effective on controlling HTN in women suffering from CAD, but it did not have an effect on heart rate (HR).[23] Moreover, the study by Paula et al. showed that lifestyle interventions were effective on BP in patients with HTN and diabetes mellitus (DM) type 2, but had no effect on BMI.[24] Dekkers et al. conducted a lifestyle intervention among people at risk of ischemic heart disease (IHD) and found that it did not have a significant effect on weight, physical activity, and BP.[25]

Samiei et al. showed that 4 sessions of lifestyle education during 2 weeks had no effect on reducing BP in patients with HTN.[26] Furthermore, the result of another study indicated that purposeful intervention for managing BP did not have a significant effect.[27]

Due to the difference in the results of studies on the effects of lifestyle modification on hemodynamic parameters and the lack of a comprehensive study with emphasis on all the features of lifestyle change in subjects with HTN who had undergone angioplasty, this research was performed to assess the effect of a management educational program on BP, PR, and BMI in subjects with HTN after angioplasty in Iran.

Materials and Methods

Study design and Participants: This clinical trial was conducted with a 2-group and 3-stage design from November 2014 to April 2015 in an educational hospital in Isfahan, Iran. The trial registration number in the Iranian Registry of Clinical Trials (IRCT) was 2015062420912N3. This study was part of a bigger study titled "Effects of a lifestyle modification program on knowledge, attitude and practice on hypertensive patients with angioplasty." Another aspect of the results was previously published as another article.[28]

Based on the studies by Babu,[18] and Jafari et al.,[28] with the confidence interval (CI) of 95% and test power of 80%, sample size was calculated as 25 subjects in the study and control group. Based on the researchers' assumption of a 20% drop in the number of subjects, 30 subjects were assigned to each of the two groups.

The study participants were selected using convenient sampling method from among those

patients who met the inclusion criteria. A random number table was used to assign the participants to either the study group (n = 30) or the control group (n = 30) which was continued until the predetermined number of subjects was reached.

Using the table of random numbers and moving along the table with odd and even numbers, we selected the number of participants and then put in a block. After the participants were singled out, a numbered cart was opened, whether it was odd or even, the subjects were assigned to each control and study group.

The study inclusion criteria were age of over 40 years, ability to read and write, no experience of dieting, no knowledge of any relaxation technics such as yoga, meditation, and etcetera, lack of any cardiovascular diseases (CVDs) like secondary HTN, DM type 1 and 2, hormone disorders, kidney disorders, and psychiatric diseases, no previous experience of educational programs on BP management, and the presence of the clinical conditions for the intervention. More than 2 sessions of absence from the educational program, experiencing severe acute stress throughout the study, and unexpected changes in BP, which required a change in the dose of drugs, were considered as the exclusion criteria.

To organize the group educational sessions, the study group participants were divided into 2 groups of 8 participants and 2 groups of 7 participants. The follow-up was conducted through contacting each participant by phone call the day before each session.

The educational program was performed in 6 sessions (each lasting 45-60 minutes) during 3 weeks.[28,29] Each session consisted of different educational methods such as lecture, question and answer, group discussions and reviewing scenarios, videos, and educational booklets.[30] All aspects of lifestyle were included in the lifestyle management program based on the preventive and therapeutic guidelines for HTN (Table 1).[31] Moreover, educational booklets were distributed among the participants at the beginning of every session. From the second session onward, after reviewing the previous topics and answering the questions, the performance of patients during the last week was evaluated. Furthermore, one session was held for the patients' families and the summary of a healthy lifestyle was presented to them. After the last educational session, BP, PR, and weight of each participant in the study and control group were measured. Then, every week for 1 month, the performance of each patient was followed up through phone call conversations about the educational program,[30] elimination of performance obstacles, patients' questions, and presentation of encouraging feedback about a healthy lifestyle. The BP, PR, and weight of the participants in both groups were measured again 1 month after the intervention.

Moreover, 2 question and answer sessions were held in the control group on the experience of patients regarding HTN, diet, weight loss, and exercise. Educational booklets were distributed among the participants 1 month after the end of the study.

Table 1. Lifestyle management educational program

Sessions	Content of the educational program
First	Definition of HTN, sorting and diagnosing HTN, number of follow-ups and referring to the physician, complications and risk factors of HTN, and methods of treating and controlling HTN
Second	"DASH" diet, the importance of diet and its effect on BP control, foods that could lower BP, foods that could increase BP, the right method of cooking food and its importance
Third	Appropriate exercise, the importance of increasing physical activity, how to lose weight and its effect on BP control, the risks of weight gain, the advantages of increase in physical activity
Fourth	The importance of regular medicine treatment, different types of medicines for lowering BP, medicine interactions and the right consumption method of medicines based on their dose and timing and considering medicine interactions, medicines' side effects At the end of this session, a scenario about some patients who have experienced acute complications due to lack of BP control was given to the participants and they were asked to study it before the next session.
Fifth	Reviewing scenarios in groups, presenting a video about a patient with HTN, methods to manage stress, the advantages of stress management and the effect of stress and tension on BP, relaxation and muscle releasing methods
Sixth	The participation of the subjects' families was demanded to support patients. Participants' families were informed about the disease, healthy lifestyle, the ways to control the disease, the complications of not controlling the disease, and the role of family's participation in supporting the patient. At the end of the session, a question and answer session was held for participants and their families.

HTN: Hypertension; DASH: Dietary Approaches to Stop Hypertension; BP: Blood pressure

Data were collected by the researcher's assistant by studying medical records, and measuring BP, PR, height, and weight of the participants.

The researcher-made checklist consisted of information about the disease and background variables (including age, height, sex, education, marital status, and occupation). BP was measured by means of a mercury sphygmomanometer and a standard stethoscope that was calibrated at the beginning and middle of the present research for validity by 2 expert nurses (man and woman) who were authorized by the professors of the School of Nursing and Midwifery in Isfahan University of Medical Sciences, Isfahan, Iran. The study was a single-blind trial, meaning that the assistant researcher who performed the measurements had no knowledge of the study procedure, and BP measurements were controlled. To evaluate BMI, the same digital meter and calibrated scale were used for all participants.

The sphygmomanometer was calibrated by the equipment unit of the hospital, and BP of 10 people was measured twice in 5 minutes to verify its reliability. The interclass correlation coefficient was 0.89, which indicated an acceptable consistency in measurements. To calibrate the scale, a 1 kg sample weight was used. To confirm the reliability of the scale, the weight of 10 people was measured twice in 1 minute. The interclass correlation coefficient was 0.97, which indicated an acceptable consistency in measurements. To calibrate the meter, a metallic meter was used. For calculate BMI, the formulae of weight (kg)/high (m^2) was used.

After sampling, written informed consent forms were obtained from all participants. Then, the demographic characteristics form and disease information checklist were completed by the researcher. Considering all the scientific principles, the systolic blood pressure (SBP) and diastolic blood pressure (DBP) of the participants in both groups were measured on their right hand and in sitting position.[5,31] A plastic meter was placed on the wall to measure the height of the participants. To measure their weight, the participants were asked to stand on the calibrated scale without shoes and with light clothing.

Verbal and written explanations regarding the study goals and procedures were provided for all the participants and they could leave the study at any stage.

The collected data were analyzed in SPSS software (version 20, IBM Corporation, Armonk, NY, USA). Continuous and categorical variables were reported as mean and standard deviation and absolute number with percentage, respectively. The demographic variables (sex and marital status) were compared between the two groups using chi-square test. In addition, Mann-Whitney test was used for the comparison of education level and economic status, and independent t-test was utilized for the comparison of age, height, and duration of HTN between the groups.

We used dependent t-test to compare mean weight, BMI, SBP, DBP, and PR in each group at three times. In addition, the repeated measures ANOVA with Mauchly's sphericity test were applied for comparisons between the two groups in the 3 stages in order to show the effect of time and group. P values of lower than 0.05 were considered as significant.

Results

Of the 70 patients with HTN who were entered into the study, 10 were excluded due to their reluctance to continue (8 participants), severe stress (1 participant), and hospitalization during the study (1 participant). Thus, the remaining 60 participants were divided into two groups and their data were analyzed (Figure 1).

The results showed no statistically significant differences between the two groups in terms of demographic variables. Frequency distribution of marital status was quite similar in the two groups. Chi-square test results showed no significant difference between the groups in terms of the distribution of occupation ($P = 0.286$). Mann-Whitney test showed no significant differences between the groups in educational level ($P = 0.880$) and economic level ($P = 0.421$). Furthermore, independent t-test results showed that the differences in the mean of age ($P = 0.114$), weight ($P = 0.159$), height ($P = 0.866$), and duration of HTN ($P = 0.820$) between the two groups were not significant before the intervention (Table 2).

Independent t-test showed no significant differences between the groups concerning the mean of SBP ($P = 0.673$), DBP ($P = 0.815$), BMI ($P = 0.231$), and PR ($P = 0.572$) before the intervention.

Mauchly's sphericity test supported homogeneity of variances ($P > 0.050$). Repeated measures ANOVA showed that the effect of time ($P < 0.001$) and group ($P = 0.027$) on SBP was significant.

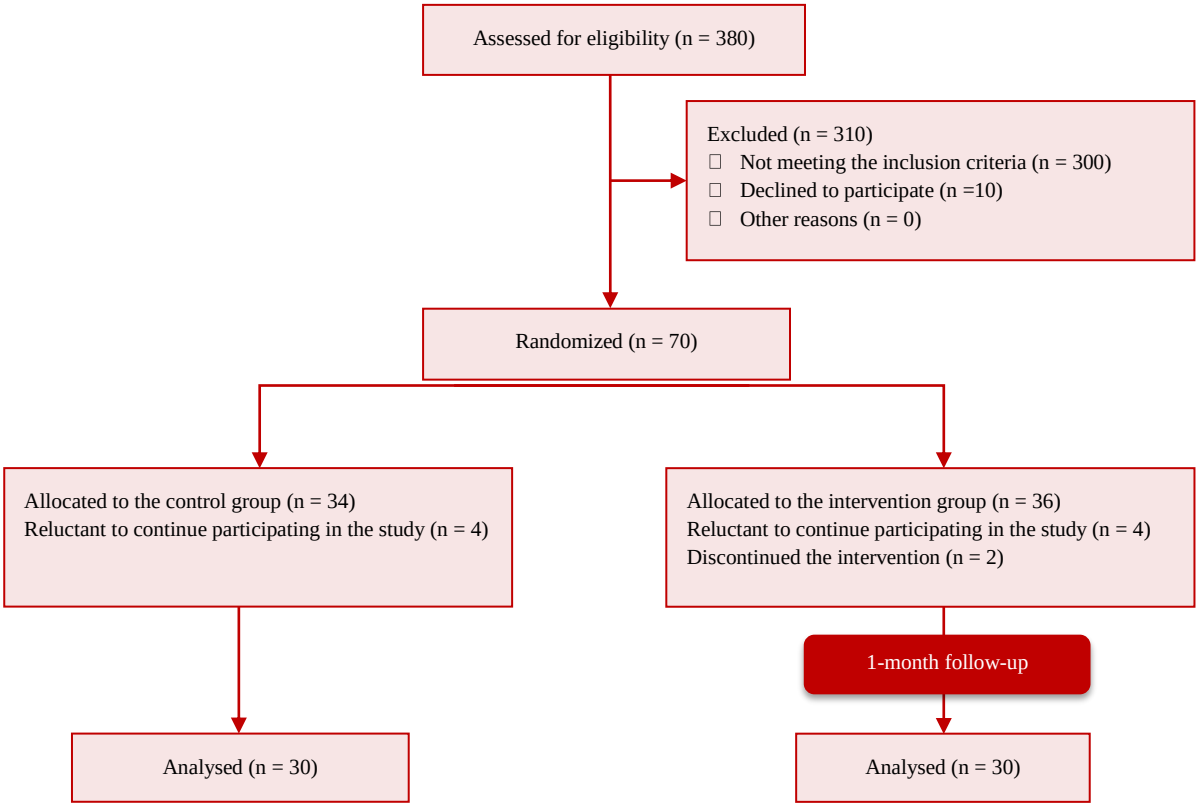

Figure 1. CONSORT flow diagram of the participants

The effect of time (P = 0.015) and group (P = 0.040) on DBP was also significant. Regarding BMI, both effects of time (P = 0.010) and group (P = 0.034) were significant. However, the effect of time (P = 0.899) and group (P = 0.900) on heart rate was not significant (Table 3).

Table 2. Comparison of the mean of demographic variables in the study and control groups before the intervention

Variable		Study group	Control group	P
		Mean ± SD	Mean ± SD	
Age (year)		58.4 ± 6.5	55.6 ± 6.5	0.114*
Height		169.3 ± 7.9	166.2 ± 8.8	0.159*
Weight		79.2 ± 9.5	78.8 ± 7.1	0.866*
BMI		27.6 ± 3.1	28.7 ± 3.5	0.231*
Duration of hypertension (year)		3.5 ± 3.4	3.3 ± 3.1	0.820*
		n (%)	n (%)	
Occupational status	Employee	1 (3.3)	0	0.286**
	Housekeeper	4 (13.3)	4 (13.3)	
	Retired	7 (23.3)	11 (36.7)	
	Businessman	16 (53.3)	10 (33.3)	
	Worker	2 (6.7)	5 (16.7)	
Economic level	Low	12 (40.0)	9 (30.0)	0.421***
	Moderate	16 (53.0)	18 (60.0)	
	Good	2 (7.0)	3 (10.0)	
Educational level	Primary school	21 (70.0)	24 (80.0)	0.880***
	Pre-diploma	3 (10.0)	3 (10.0)	
	Diploma	6 (20.0)	3 (10.0)	

* Independent t-test; ** Chi-Square test; *** Mann-Whitney U test
BMI: Body mass index; SD: Standard deviation
P-value of less than 0.050 was considered as significant.

Table 3. Comparison of the mean changes in scores of systolic and diastolic blood pressure, pulse rate, and body mass index in the two groups before and immediately and one month after the intervention

Variable	Time	Study group	Control group	Repeated measures ANOVA	
		Mean ± SD	Mean ± SD	P*	P**
Systolic blood pressure	Before the intervention	144.4 ± 18.1	142.5 ± 15.2	0.027	< 0.001
	Immediately after the intervention	135.6 ± 13.7	140.9 ± 15.3		
	One month after the intervention	131.7 ± 13.0	138.0 ± 15.0		
Diastolic blood pressure	Before the intervention	84.3 ± 9.0	84.9 ± 10.7	0.040	0.015
	Immediately after the intervention	80.5 ± 6.5	83.3 ± 8.8		
	One month after the intervention	78.9 ± 6.4	83.0 ± 7.3		
Pulse rate	Before the intervention	81.9 ± 10.0	80.6 ± 7.3	0.900	0.899
	Immediately after the intervention	79.6 ± 4.6	81.8 ± 4.3		
	One month after the intervention	80.9 ± 5.8	80.8 ± 3.8		
BMI	Before the intervention	27.7 ± 3.2	28.7 ± 3.5	0.0340	0.010
	Immediately after the intervention	26.7 ± 3.2	28.9 ± 3.6		
	One month after the intervention	26.6 ± 2.7	28.9 ± 3.6		

BMI: Body mass index; SD: Standard deviation
* Effect of group; ** Effect of time

Discussion

In the present study, the lifestyle management educational program was found to be effective on DBP, SBP, and BMI in patients with HTN who had undergone angioplasty. However, it was not effective on their PR.

Moreover, no significant differences were observed between the two groups in terms of the mean DBP and SBP before and immediately after the intervention. Nevertheless, mean SBP and DBP were significantly lower in the study group compared to the control group 1 month after the intervention. Thus, it seems that the studied lifestyle management program has been effective on these variables during the study period. In different studies, different effects have been reported for non-medical interventions on BP management. Navidian et al. reported a significant reduction in mean SBP and DBP in patients with HTN in the study group compared to the control group 2 months after motivational interviews and lifestyle education.[32] No significant difference was observed in SBP between the two groups, but a significant reduction was observed in DBP in the study group compared to the control group in the follow-up period.[32] Paula et al. reported a significant reduction in mean SBP 1 month after the intervention (messaging and phone call about dieting and exercising) in patients with HTN and DM type 2 compared to the control group.[24]

However, they did not observed a significant difference between the two groups in terms of DBP.[24] Moreover, the results of a systematic review study showed that multilateral lifestyle interventions implemented during at least 4 weeks could help to reduce SBP in patients with HTN.[33] A study conducted in America on a lifestyle management intervention based on the operation the patients had undergone found a reduction in SBP and DBP 3 and 6 months after the interventions.[17]

Nevertheless, Siavoshi et al. reported that lifestyle management interventions did not have a significant effect on BP.[21] Pandit et al. showed that health education did not have a significant effect on BP reduction among patients with HTN.[34] Dekkers et al. showed that lifestyle modification interventions did not have a significant effect on BP among individuals at risk of IHD.[25] The results of

another systematic review study by Aucott et al. showed that magnesium and calcium supplements did not have a significant effect on BP control.[16] Furthermore, Reuther et al. found that purposeful interventions regarding BP management did not have a significant effect on SBP and DBP.[27]

These differences in the results of the present study and that of previous studies could be due to the different educational methods used in these studies (lecture, question and answer, group discussion, reviewing scenarios, videos, and booklets), and the use of an educational program for all aspects of the participants' lifestyle, supporting the family, and following up on patients who had undergone angioplasty. A decrease in the BP of the study group could be the result of the effectiveness of this lifestyle management program on BP in patients with HTN who had undergone angioplasty.

The results of the present study showed no significant differences between the groups in terms of BMI before the intervention. However, it showed a significant reduction in mean BMI in the study group compared to the control group immediately after the intervention and 1 month after the intervention. This could be indicative of the effectiveness of this lifestyle management program. Moreover, in the study group, synchronous to the reduction in BP, a reduction was also observed in BMI due to utilization of appropriate interventions, trainings, and diets. Mahajan et al. implemented health education interventions regarding BP in the form of group sessions among patients with HTN in India; they reported a reduction in SBP, BMI, and weight in these patients.[35]

The results of this study showed that after reducing BMI, SBP and DBP had also reduced. Reduction in BMI is one aspect of a healthy lifestyle that could be achieved through an appropriate diet and increase in physical activity. This indicates a relation between a reduction in BP and lifestyle management in the form of losing weight and BMI. It also indicates the effectiveness of the multilateral lifestyle management program in this study.

The findings of Paula et al. were not in accordance with that of the present study; their results indicated that although lifestyle interventions were effective on BP of patients with HTN and DM type 2, they did not have a significant effect on the BMI of these patients.[24] Dekkers et al., in their study, displayed that lifestyle management interventions did not have a significant effect on the weight and physical activity of individuals at risk of IHD.[25]

In the present study, during the study period, a reduction was observed in mean PR in the study group, but this difference was not statistically significant, which could be due to the small sample size or the 1-month follow-up that was not enough for a reduction in PR. Moreover, in the study by Siavoshi et al., the presentation of a cardiac rehabilitation program along with lifestyle educational interventions among coronary artery patients, in addition to the reduction of SBP, reduced PR in these patients.[21] Furthermore, Aizawa et al. found that lifestyle intervention, in addition to reducing BMI, decreased PR in patients with prehypertension.[36] In the study by Farsi et al., educational interventions had a significant effect on BP and PR of patients with HTN who had undergone coronary artery angiography.[37] Mokhtari et al. found that the effect of educational interventions on BP control among women with CAD was significant, but their effect on the patients' heart rate was not significant.[23]

The short follow-up period (1 month after the intervention) was an important limitation of this study. Due to the time limitation of the student thesis, we had to limit the follow-up time of these patients after the intervention. Sample volume was another limitation of this study and the selection of a greater number of subjects with the two variables of HTN and angioplasty required more time. Thus, it is recommended that future studies be performed on a larger study population and the follow-up periods be extended.

Conclusion

The present study results showed that the lifestyle management program presented with different educational methods such as group discussion and lectures influenced all aspects of lifestyle along with companionship and support of families. Furthermore, follow-up was effective on reducing SBP, DBP, and BMI in patients with HTN who had undergone angioplasty. Moreover, introducing effective support to families and educating them on how to perform it could be an important factor in improving the lifestyle of patients with HTN. Thus, it seems that in this educational HTN management program, the patients' families should be regarded as an important factor. In addition, comprehensive lifestyle management programs could be more effective on the well-being of these patients; therefore, it is suggested that nurses use this

program as part of their care providing routines for these patients.

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Conflict of Interests

Authors have no conflict of interests.

References

1. World Health Organization. Cardiovascular disease: World Hypertension Day 2019 [Online]. [cited 2019]; Available from: URL: https://www.who.int/cardiovascular_diseases/world-hypertension-day-2019/en
2. Dananagowda H. A study to assess the knowledge and attitude regarding life style modifications to prevent hypertension among bank employees in selected banks at tumkur [Thesis]. Karnataka, India: Rajiv Gandhi University of Health Sciences; 2013.
3. Kwan MW, Wong MC, Wang HH, Liu KQ, Lee CL, Yan BP, et al. Compliance with the Dietary Approaches to Stop Hypertension (DASH) diet: A systematic review. PLoS One 2013; 8(10): e78412.
4. Eskandarian R, Ghorbani R, Shiyasi M, Momeni B, Hajifathalian K, Madani M. Prognostic role of Helicobacter pylori infection in acute coronary syndrome: A prospective cohort study. Cardiovasc J Afr 2012; 23(3): 131-5.
5. Woods SL, Sivarijan Froelicher ES, Motzer SU, Bridges EJ. Cardiac nursing. Philadelphia, PA: Lippincott Williams & Wilkins; 2009.
6. Rodrigo R, Hasson D, Prieto JC, Dussaillant G, Ramos C, Leon L, et al. The effectiveness of antioxidant vitamins C and E in reducing myocardial infarct size in patients subjected to percutaneous coronary angioplasty (PREVEC Trial): Study protocol for a pilot randomized double-blind controlled trial. Trials 2014; 15: 192.
7. Yousef Nejad K. Analysis of survival data in patients with coronary artery after angioplasty to help Kalks regression model [Thesis]. Sari, Iran: Mazandaran University of Medical Sciences; 2012. p. 101-7. [In Persian].
8. Shahid Chamran Hospital. Medical Record Archive. Isfahan, Iran: Shahid Chamran Hospital; 2013. [Unpublished].
9. Van Belle E, Ketelers R, Bauters C, Perie M, Abolmaali K, Richard F, et al. Patency of percutaneous transluminal coronary angioplasty sites at 6-month angiographic follow-up: A key determinant of survival in diabetics after coronary balloon angioplasty. Circulation 2001; 103(9): 1218-24.
10. Sadeghzadeh V, Raoufi Kelachayeh SS, Naserian J. The effect of self-care documented program on performance of patients undergoing coronary angioplasty. Intl Res J Appl Basic Sci 2013; 4(1): 86-90.
11. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: Report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014; 311(5): 507-20.
12. Ariff F, Suthahar A, Ramli M. Coping styles and lifestyle factors among hypertensive and non-hypertensive subjects. Singapore Med J 2011; 52(1): 29-34.
13. Svetkey LP, Pollak KI, Yancy WS Jr, Dolor RJ, Batch BC, Samsa G, et al. Hypertension improvement project: randomized trial of quality improvement for physicians and lifestyle modification for patients. Hypertension 2009; 54(6): 1226-33.
14. Demaio AR, Otgontuya D, de Court Bygbjerg IC, Enkhtuya P, Meyrowitsch DW, et al. Hypertension and hypertension-related disease in mongolia; findings of a national knowledge, attitudes and practices study. BMC Public Health 2013; 13: 194.
15. Song IH, Kim SA, Park WS. Effects of a hypertension management program by Seongcheon primary health care post in South Korea: An analysis of changes in the level of knowledge of hypertension in the period from 2004 to 2009. Health Educ Res 2012; 27(3): 411-23.
16. Aucott L, Rothnie H, McIntyre L, Thapa M, Waweru C, Gray D. Long-term weight loss from lifestyle intervention benefits blood pressure?: A systematic review. Hypertension 2009; 54(4): 756-62.
17. Schoenthaler A, Luerassi L, Teresi JA, Silver S, Kong J, Odedosu T, et al. A practice-based trial of blood pressure control in African Americans (TLC-Clinic): Study protocol for a randomized controlled trial. Trials 2011; 12: 265.
18. Babu A. Effectiveness of structured teaching programme on knowledge of hypertensive patients regarding dash diet at selected kumbalagudu phc area bangalore [Thesis]. Karnataka, India: Rajiv Gandhi University of Health Sciences; 2013.
19. Dawes MG, Kaczorowski J, Swanson G, Hickey J, Karwalajtys T. The effect of a patient education booklet and BP 'tracker' on knowledge about hypertension. A randomized controlled trial. Fam Pract 2010; 27(5): 472-8.

20. Sharma S, Kc B, Alrasheedy AA, Kaundinnyayana A, Khanal A. Impact of community pharmacy-based educational intervention on patients with hypertension in Western Nepal. Australas Med J 2014; 7(7): 304-13.

21. Siavoshi S, Roshandel M, Zareiyan A, Etefagh L. The effect of cardiac rehabilitation on hemodynamic status in patients after coronary artery bypass surgery. J Cardiovasc Nurs 2013; 2(4): 19-27.

22. Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK, et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: Observational follow-up of the trials of hypertension prevention (TOHP). BMJ 2007; 334(7599): 885-8.

23. Mokhtari Z, Alipor A, Hasanzadeh Pashang S, Exirifard M. Effect of emotional intelligence on physical health among heart patient's bed ridden. J Jahrom Univ Med Sci 2014; 12(2): 1-12. [In Persian].

24. Paula TP, Viana LV, Neto AT, Leitao CB, Gross JL, Azevedo MJ. Effects of the DASH diet and walking on blood pressure in patients with type 2 diabetes and uncontrolled hypertension: A randomized controlled trial. J Clin Hypertens (Greenwich) 2015; 17(11): 895-901.

25. Dekkers JC, van Wier MF, Ariens GA, Hendriksen IJ, Pronk NP, Smid T, et al. Comparative effectiveness of lifestyle interventions on cardiovascular risk factors among a Dutch overweight working population: A randomized controlled trial. BMC Public Health 2011; 11(1): 49.

26. Samiei Siboni F, Alimoradi Z, Sadegi T. Impact of corrective life style educational program on controlling stress, anxiety and depression in hypertensives. J Birjand Univ Med Sci 2013; 19(6): 1-9. [In Persian].

27. Reuther LO, Paulsen MS, Andersen M, Schultz-Larsen P, Christensen HR, Munck A, et al. Is a targeted intensive intervention effective for improvements in hypertension control? A randomized controlled trial. Fam Pract 2012; 29(6): 626-32.

28. Jafari F, Shahriari M, Sabouhi F, Khosravi FA, Eghbali Babadi M. Effects of a lifestyle modification program on knowledge, attitude and practice of hypertensive patients with angioplasty: A randomized controlled clinical trial. Int J Community Based Nurs Midwifery 2016; 4(4): 286-96.

29. Rocha-Goldberg MP, Corsino L, Batch B, Voils CI, Thorpe CT, Bosworth HB, et al. Hypertension Improvement Project (HIP) Latino: Results of a pilot study of lifestyle intervention for lowering blood pressure in Latino adults. Ethn Health 2010; 15(3): 269-82.

30. Webber J. The effect of a lifestyle modification adherence tool on risk factors in patients with chronic hypertension compared to usual management [MSc Thesis]. Johannesburg, South Africa: University of the Witwatersrand; 2011.

31. Wilson DE, Van Vlack T, Schievink BP, Doak EB, Shane JS, Dean E. Lifestyle factors in hypertension drug research: Systematic analysis of articles in a leading cochrane report. Int J Hypertens 2014; 2014: 835716.

32. Navidian A, Abedi MR, Baghban I, Fatehizadeh MA, Poursharifi H. Effect of motivational interviewing on blood pressure of referents suffering from Hypertension. Kowsar Medical Journal 2010; 15(2): 115-21.

33. Li J, Zheng H, Du HB, Tian XP, Jiang YJ, Zhang SL, et al. The multiple lifestyle modification for patients with prehypertension and hypertension patients: A systematic review protocol. BMJ Open 2014; 4(8): e004920.

34. Pandit AU, Tang JW, Bailey SC, Davis TC, Bocchini MV, Persell SD, et al. Education, literacy, and health: Mediating effects on hypertension knowledge and control. Patient Educ Couns 2009; 75(3): 381-5.

35. Mahajan H, Kazi Y, Sharma B, Velhal GD. Health education: An effective intervention in hypertensive patients. International Journal of Recent Trends in Science and Technology 2012; 4(2): 77-82.

36. Aizawa K, Shoemaker JK, Overend TJ, Petrella RJ. Effects of lifestyle modification on central artery stiffness in metabolic syndrome subjects with pre-hypertension and/or pre-diabetes. Diabetes Res Clin Pract 2009; 83(2): 249-56.

37. Farsi Z, Eslami R, Sajadi A, Afaghi E. Comparing the effect of peer education and orientation tour on the hemodynamic indices of patients candidate for coronary angiography. Medical-Surgical Nursing Journal 2016; 4(4): 65-72. [In Persian].

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10-year risk of cardiovascular disease and body mass index in association with the obesity paradox

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Original Article

Abstract

BACKGROUND: Some recent studies reported an inverse association between obesity and risk of cardiovascular diseases (CVD), heart failure related mortality rate, outcomes of myocardial infarction (MI), and the consequences of cardiovascular events interventions; this inverse association was named the obesity paradox. The present study was conducted with the aim to determine whether the obesity paradox will be detectable when the 10-year risk of CVD is estimated using CVD risk assessment tools.

METHODS: The related data of 2910 subjects aged 40-74 years obtained in our cohort study that was carried out among 6140 subjects in Amol, in northern Iran, was included in this study. CVD risk assessment tools were used to estimate the 10-year risk of CVD. Obesity was evaluated using 4 indices, including waist circumference (WC), waist to height ratio (WHtR), waist to hip ratio (WHR), and body mass index (BMI). The receiver operating characteristic (ROC) curve analysis was utilized to evaluate the discriminatory power of obesity indices for 10-year risk of CVD.

RESULTS: Categorizing the participants to with and without obesity according to BMI showed that a significantly higher proportion of men with obesity had a 10-year risk of CVD ≥ 7.5% and ≥ 10% according to American College of Cardiology/American Heart Association (ACC/AHA) and the Framingham approaches, respectively. A higher proportion of women without obesity had a 10-year risk of CVD ≥ 7.5% than women with obesity based on the ACC/AHA equation (28.54% vs. 24.15%; P = 0.0707). BMI had a non-significant AUC (< 0.5) according to the the ACC/AHA equation.

CONCLUSION: BMI showed a weak and non-significant inverse association with 10-year risk of CVD estimated using pooled cohort equations of ACC/AHA in women. However, this result cannot directly provide enough evidence for the obesity paradox.

Keywords: Obesity; Cardiovascular Diseases; Risk Assessment; Body Mass Index

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Introduction

Obesity is a very common condition worldwide. Between 1980 and 2013, the proportion of over-weigh adults and those with obesity increased from 28.8% to 36.9% in men, and from 29.8% to 38.0% in women.[1]

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The rising trend of obesity in many countries led to very serious consequences at both individual and community levels.[2] Obesity is an independent and modifiable risk factor for all-cause mortality including cardiovascular disease (CVD) related mortality rates.[3-5] However, some recent studies have reported an inverse association between obesity and CVD risk, heart failure related mortality rate, myocardial infarction (MI) outcomes, and the consequences of CVD events interventions; this inverse association was named the obesity paradox.[6,7]

CVD risk assessment tools have been utilized to estimate the 10-year risk of CVD for years. In these tools, several modifiable and non-modifiable risk factors of CVD are utilized to predict the 10-year risk of CVD. The pooled cohort equations of the American College of Cardiology/American Heart Association (ACC/AHA) and the Framingham general cardiovascular risk profile (for use in primary care) were developed using some CVD risk factors including age, history of diabetes mellitus (DM), current smoking status, systolic blood pressure (SBP), total cholesterol and high density lipoprotein (HDL) in men and women, separately.[8,9]

Two versions of the Systematic Coronary Risk Evaluation (SCORE) equations were also developed according to the abovementioned risk factors, except for HDL and history of DM.[10] None of the obesity indices are utilized in the abovementioned CVD risk assessment tools, Although, there are several simple indices to evaluate obesity, none of the obesity indices are utilized to predict the 10-year CVD risk in the abovementioned CVD risk assessment tools. Since the obesity paradox was confirmed for some CVD outcomes based on some obesity indices, particularly BMI, we aimed to determine whether the obesity paradox would be detectable when the 10-year risk of CVD and obesity are determined by mentioned risk assessment tools and obesity indices, respectively.

Materials and Methods

The present cohort study was conducted among 6140 subjects aged 10-90 years in northern Iran (Amol) in 2009-2010. We obtained the study sampling frame from health centers, where all residents had a health record file. The population of the city was categorized into 16 categories based on sex and age at the intervals of 10 years. We randomly selected the study participants from each category based on the proportion to size approach. All study arrangements were in accordance with the Helsinki Declaration. Informed consent was obtained from all study subjects, and the study was approved by the Ethics Committee of Iran University of Medical Sciences, Iran. Since the risk assessment tools are generally applied to the population aged 40-74 years (8-10), the data of 2910 subjects (1623 men and 1287 women) aged 40-74 years were utilized in this study. The study population and the study inclusion and exclusion criteria are displayed in figure 1.

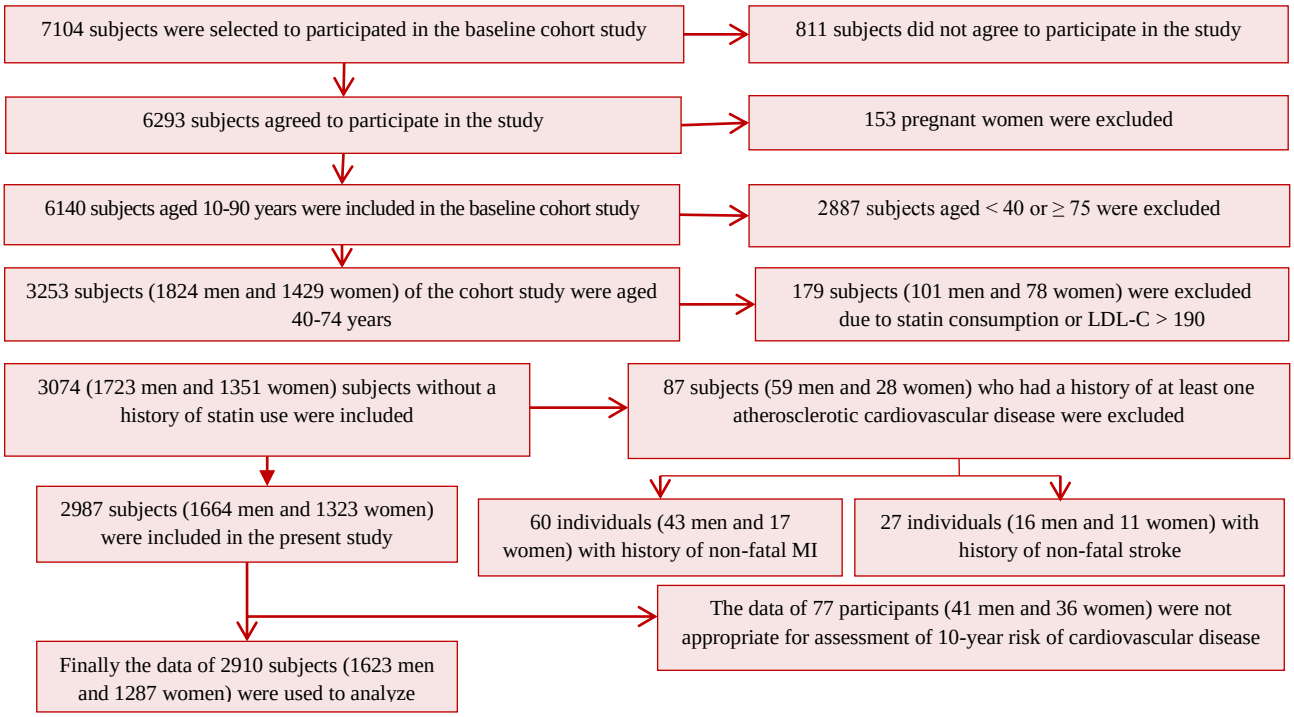

Figure 1. Flowchart of the study participants, inclusion and exclusion criteria

Anthropometric data and BP were measured by trained health care providers for each participant. The participants' weight was measured without excess clothes and shoes. Their height was measured while they stood upright with their heels and buttocks in contact with the wall. The midpoint of the distance between the lowest costal ridge and the upper border of the iliac crest was considered as the waist circumference (WC). The largest circumference between the waist and knee was considered the hip circumference (HC). The health care providers measured BP in sitting position using a fitted cuff, following at least 5 minutes of rest.

Lipid profiles and fasting blood sugar (FBS) were evaluated following 12 hours of fasting. All tests, including FBS and lipid profiles, were assessed enzymatically according to protocol using an autoanalyzer (BS200, Mindray, China).

To determine the 10-year risk of CVD in the present study, 4 risk assessment tools, including pooled cohort equations of the ACC/AHA, SCORE equations for low and high risk European countries, and the Framingham general cardiovascular risk profile (for use in primary care), were used.[8-10] While the ACC/AHA equations and Framingham tool estimate fatal and non-fatal 10-year risk of CVD, SCORE equations only estimate the fatal risk.

We changed the estimated risks into dichotomous scales according to a cut off point of 0.075 (7.5%) for ACC/AHA, 0.05 (5%) for SCORE equations, and 0.1 (10%) for the Framingham tool (8-10). Receiver operating characteristic (ROC) curve was used to assess the capability of BMI, WC, waist to hip ratio (WHR), and waist to height ratio (WHtR) in the discrimination of people with a 10-year risk ≥ 5%, ≥ 7.5%, and ≥ 10% (according to the related thresholds of the abovementioned CVD risk assessment tools) from people with a lower risk. In ROC curves, the sensitivities of infinite thresholds of obesity measures were plotted versus the associated false positive rates. Consequently, the associated areas under the curves (AUCs) were computed. The lowest threshold for AUC was considered as 0.5, meaning a significantly greater area than 0.5 signifies the power of obesity indices to distinguish participants with a higher 10-year risk of CVD than related thresholds in participants without those indices.

Furthermore, the values of obesity indices were categorized into dichotomous variables according to related data in previous literature. Thus, BMI was classified into a dichotomous variable based on a cut off point of 30 kg/m^2 in women and men, WC was categorized based on a cut off point of 88 cm in women and 102 cm in men, WHR was categorized based on a cut off point of 0.85 in women and 0.9 in men, and WHtR was categorized based on a cut off point of 0.5 in women and men.[11-13] Obesity was defined based on the abovementioned thresholds of each related obesity indice, and the 10-year risk of CVD was estimated in participants with and without obesity. The proportion of individuals who had a 10-year risk of CVD ≥ 7.5% based on ACC/AHA, ≥ 5% based on SCORE equations (low and high risk European countries), and ≥ 10% based on Framingham approach were compared between the groups with and without obesity using independent two group proportion test. Since the 10-year risk of CVD was estimated based on 4 risk assessment tools and obesity was determined according to 4 indices, 16 two group proportion tests were performed in men and women, separately.

Finally, several logistic regression analyses were separately performed in which each of the categorized obesity indices was considered a predictor and a 10-year risk of CVD ≥ 7.5%, ≥ 5%, and ≥ 10% was considered an outcome based on pooled cohort equations, SCORE equations, and the Framingham tool, respectively. In multiple logistic regression analyses, in addition to the evaluated obesity indices, LDL-C level, TG level, and diastolic blood pressure (DBP) were entered into the associated models. It is worth noting that these risk factors are not directly utilized in risk assessment tools to compute the 10-year risk of CVD.

A threshold of 0.05 (less than 0.05) was taken into account as the significance level for all analyses. All analyses were performed using Stata software (version 12; StataCorp, Texas, USA).

Results

The demographic characteristics of the participants are presented in table 1. The prevalence of diabetes in women was significantly higher than men (26.01% vs 13.4%; P < 0.0001). While the percentage of current smoking was 30.2% in men, it was only 0.84% in women (P < 0.0001).

Table 2 shows the percentage of study population who had a 10-year risk of CVD ≥ 7.5%, ≥ 5%, ≥ 5%, and ≥10% according to pooled cohort equations of ACC/AHA, SCORE equations for low risk European countries, SCORE equations for high risk European countries, and the Framingham general cardiovascular risk profile in men and women with and without obesity, respectively.

Table 1. Characteristics and clinical biomarkers of the study participants (n = 2910)

Characteristics	Men (n = 1623)	Women (n = 1287)	P*
	Means ± SD		
Age (year)	53.91 ± 9.36	53.50 ± 9.01	0.1890
BMI (kg/m^2)	27.23 ± 4.27	31.23 ± 5.04	< 0.0010
WC (cm)	93.54 ± 11.23	96.20 ± 11.55	< 0.0010
WHR	0.93 ± 0.07	0.89 ± 0.08	< 0.0010
WHtR	0.56 ± 0.07	0.62 ± 0.08	< 0.0010
DBP (mm Hg)	78.10 ± 13.15	79.32 ± 12.90	0.0080
SBP (mm Hg)	119.01 ± 16.87	120.93 ± 18.21	0.0020
FBS (mg/dl)	103.01 ± 34.86	113.16 ± 48.67	< 0.0010
TG (mg/dl)	155.21 ± 100.19	159.04 ± 108.57	0.3080
Total cholesterol (mg/dl)	187.13 ± 41.13	200.57 ± 43.28	< 0.0010
LDL (mg/dl)	110.16 ± 30.61	117.48 ± 31.52	< 0.0010
HDL (mg/dl)	42.83 ± 11.61	44.67 ± 12.01	0.0010

* Significance level was considered at P < 0.0500.

SD: Standard deviation; BMI: Body mass index; WC: Waist circumference; WHR: Waist to hip ratio; WHtR: Waist to height ratio; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; FBS: Fasting blood sugar; TG: Triglyceride; LDL: Low-density lipoprotein; HDL: High-density lipoprotein

The categorization of individuals to with obesity and without obesity according to BMI showed that a higher proportion of women without obesity had a 10-year risk of CVD ≥ 7.5% compared to women with obesity based on the ACC/AHA equations (28.54% vs. 24.15%), although the difference was not statistically significant (P = 0.0707).

Table 3 shows the results of the univariate logistic regression analysis in which obesity indices were separately considered as predictors and 10-year risk of CVD ≥ 7.5%, ≥ 5%, and ≥ 10% were considered outcomes based on pooled cohort equations, SCORE equations, and the Framingham tool, respectively. According to these results, WHR and WHtR had a significant relationship with estimated 10-year risk of CVD in all risk assessment tools. Furthermore, WHR showed the strongest relationships with 10-year risk of CVD compared to other obesity indices, particularly in women. In multiple logistic regression analysis with the elimination of the effects of other risk factors, which were applied to calculate 10-year risk of CVD, none of the obesity indices showed a significant association with the related 10-year risk of CVD.

The present study results showed that BMI had a non-significant AUC (< 0.5) based on pooled cohort equations of ACC/AHA tool [0.4742 (0.4391-0.5093)] and SCORE equations for high-risk European countries [0.4717 (0.4022-0.5412)] in women.

Discussion

The present study was conducted to determine whether the obesity paradox will be detectable when 10-year risk of CVD and obesity are determined by related risk assessment tools and obesity indices, respectively.

The results showed a weak and non-significant obesity paradox in women whose obesity and 10-year risk of CVD were determined based on BMI and ACC/AHA equation, respectively. A lower proportion (but non-significant) of women with obesity, based on a BMI ≥ 30, had a10-year risk of CVD ≥ 7.5% compared to women without obesity when the ACC/AHA equation was applied. BMI had the lowest discriminatory ability among the mentioned obesity indices. The discriminatory ability of BMI was even less than 0.5 in women whose 10-year risk of CVD was estimated based on pooled cohort equations of ACC/AHA and SCORE equations for high risk European countries.

McAuley et al. showed that obesity (BMI ≥ 30) was related to a lower mortality risk in a clinical population of individuals without heart failure, which was in agreement with the obesity paradox.[7] While a high WHR is primarily associated with increased central fat stores (notably with visceral fat), decreased thigh muscle mass, and reduced physical fitness, a high BMI is associated with increased thigh muscle mass and peripheral fat stores without association with visceral fat.[14] A growing body of evidence still supports purposeful weight reduction in the control and treatment of CVDs.[15] Moreover, it has been suggested that the obesity paradox is largely confounded by fitness.

Consequently, individuals who are more fit usually have a better prognosis than others, and no clear obesity paradox is apparent in these individuals.[7]

Table 2. The proportion [confidence interval (95%CI)] of the study population who had a 10-years risk of cardiovascular disease (CVD) ≥ 7.5%, ≥ 5%, ≥ 5%, and ≥ 10% based on related risk assessment tools in individuals with and without obesity defined by different obesity indices

Obesity indices (BMI)	BMI < 30 in men and women	BMI ≥ 30 in men and women	P*	BMI < 30 in men and women	BMI ≥ 30 in men and women	P*
Risk assessment tools	**Men (n = 1623)**			**Women (n = 1287)**		
A risk of ≥ 7.5% based on pooled cohort equations of ACC/AHA £	54.46 (51.76-57.16)	62.04 (57.44-66.64)	0.0060	28.54 (24.77-32.32)	24.12 (21.13-27.11)	0.0710
A risk of ≥ 5% based on SCORE equations for low risk European countries £	10.28 (8.66-11.90)	10.47 (7.63-13.31)	0.9130	2.23 (1.03-3.43)	2.03 (1.08-2.99)	0.8030
A risk of ≥ 5% based on SCORE equations for high risk European countries £	24.44 (22.15-26.73)	25.00 (20.99-29.01)	0.8140	5.49 (3.64-7.34)	4.91 (3.44-6.38)	0.6270
A risk of ≥ 10% based on the Framingham general cardiovascular risk profile for use in primary care £	50.47 (47.76-53.18)	59.02 (54.35-63.68)	0.0020	21.62 (18.18-25.06)	21.86 (18.98-24.74)	0.9180
Obesity indices (WC)	**WC < 102 in men**	**WC ≥ 102 in men**	**P***	**WC < 88 in women**	**WC ≥ 88 in women**	**P***
Risk assessment tools	**Men (n = 1623)**			**Women (n = 1287)**		
A risk of ≥ 7.5% based on pooled cohort equations of ACC/AHA £	52.95 (50.27-55.63)	67.55 (63.00-72.10)	< 0.0010	18.32 (13.86-22.78)	27.90 (25.20-30.60)	0.0010
A risk of ≥ 5% based on SCORE equations for low risk European countries £	9.73 (8.17-11.29)	12.80 (9.61-15.98)	0.0710	1.66 (0.22-3.10)	2.23 (1.37-3.09)	0.5370
A risk of ≥ 5% based on SCORE equations for high risk European countries £	22.75 (20.54-24.96)	30.80 (26.40-35.20)	0.0080	4.30 (2.01-6.59)	5.35 (4.03-6.67)	0.4640
A risk of ≥ 10% based on the Framingham general cardiovascular risk profile for use in primary care £	48.74 (46.06-51.42)	65.34 (60.71-69.97)	< 0.0010	12.46 (8.65-16.26)	24.20 (21.62-26.78)	<0.0010
Obesity indices (WHR)	**WHR < 0.9 in men**	**WHR ≥ 0.9 in men**	**P***	**WHR < 0.85 in women**	**WHR ≥ 0.85 in women**	**P***
Risk assessment tools	**Men (n = 1623)**			**Women (n = 1287)**		
A risk of ≥ 7.5% based on pooled cohort equations of ACC/AHA £	42.27 (38.33-46.21)	63.86 (61.06-66.65)	< 0.0010	10.41 (7.49-13.32)	32.93 (29.90-35.96)	<0.0010
A risk of ≥ 5% based on SCORE equations for low risk European countries £	6.70 (4.74-8.66)	12.43 (10.55-14.31)	0.0010	0.45 (-0.17-1.07)	2.86 (1.82-3.90)	0.0340
A risk of ≥ 5% based on SCORE equations for high risk European countries £	16.11 (13.23-18.99)	29.16 (26.57-31.75)	< 0.0010	1.81 (0.57-3.05)	6.64 (5.08-8.02)	0.0010
A risk of ≥ 10% based on the Framingham general cardiovascular risk profile for use in primary care £	36.80 (32.95-40.65)	61.04 (58.20-63.87)	< 0.0010	6.87 (4.46-9.28)	28.47 (25.56-31.38)	<0.0010
Obesity indices (WHtR)	**WHtR < 0.5 in men and women**	**WHtR ≥ 0.5 in men and women**	**P***	**WHtR < 0.5 in men and women**	**WHtR ≥ 0.5 in men and women**	**P***
Risk assessment tools	**Men (n = 1623)**			**Women (n = 1287)**		
A risk of ≥ 7.5% based on pooled cohort equations of ACC/AHA £	38.87 (33.56-44.18)	60.38 (57.83-62.93)	< 0.0010	10.45 (3.12-17.77)	26.64 (24.22-29.06)	0.0030
A risk of ≥ 5% based on SCORE equations for low risk European countries £	6.57 (3.91-9.22)	11.32 (9.70-12.94)	0.0100	0.00 (0.00-0.00)	2.22 (1.43-3.00)	0.2080
A risk of ≥ 5% based on SCORE equations for high risk European countries £	15.22 (11.38-19.07)	26.78 (24.52-29.04)	< 0.0010	0.00 (0.00-0.00)	5.40 (4.19-6.60)	0.0460
A risk of ≥ 10% based on the Framingham general cardiovascular risk profile for use in primary care £	33.31 (28.18-38.44)	57.05 (54.47-59.63)	< 0.0010	7.46 (1.17-13.75)	22.43 (20.14-24.72)	0.0040

£ The proportion (percentage) of individuals with a 10-year risk of CVD of ≥ 0.075 for pooled cohort equations, ≥ 0.05 for SCORE equations (both low and high risk countries versions), and ≥ 0.1 for the Framingham general cardiovascular risk profile for use in primary care

* Significance level was considered at P < 0.0500.

BMI: Body mass index; ACC/AHA: American College of Cardiology/American Heart Association; SCORE: Systematic Coronary Risk Evaluation; WC: Waist circumference; WHR: Waist to hip ratio; WHtR: Waist to height ratio; CVD: Cardiovascular disease

Table 3. Univariate logistic regression results

Obesity indices	Men (n = 1623)			Women (n = 1287)		
	Wald	OR (95%CI)	P*	Wald	OR (95%CI)	P*
	Outcomes of risk assessment tools					
	A 10-year CVD risk ≥ 0.075 of pooled cohort equations for ACC/AHA tool£					
BMI ≥ 30 kg/m^2 both in men and women	6.50	1.34 (1.07-1.69)	0.0110	2.250	0.83 (0.64-1.06)	0.1340
WC ≥ 102 cm in men and ≥ 88 cm in women	26.92	1.89 (1.48-2.40)	< 0.0010	10.420	1.73 (1.24-2.24)	0.0010
WHR ≥ 0.9 in men and ≥ 0.85 in women	81.65	2.56 (2.08-3.13)	< 0.0010	63.600	4.12 (2.91-5-83)	< 0.0010
WHtR ≥ 0.50 both in men and women	51.47	2.47 (1.95-3.16)	< 0.0010	10.570	5.42 (1.96-15.00)	0.0110
	A 10-year CVD risk ≥ 0.050 of SCORE equations for low risk European countries£					
BMI ≥ 30 kg/m^2 both in men and women	0.01	1.02 (0.72-1.45)	0.9130	0.060	0.91 (0.44-1.89)	0.8030
WC ≥ 102cm in men and ≥ 88cm in women	3.24	1.36 (0.97-1.91)	0.0720	0.380	1.36 (0.51-3.57)	0.5390
WHR ≥ 0.9 in men and ≥ 0.85 in women	13.94	1.98 (1.38-2.83)	0.0020	6.490	6.49 (1.54-27.37)	0.0110
WHtR ≥ 0.50 both in men and women	6.43	1.82 (1.14-2.80)	0.0110	- $	- $	- $
	A 10-year CVD risk ≥ 0.050 of SCORE equations for high risk European countries£					
BMI ≥ 30 kg/m^2 both in men and women	0.06	1.03 (0.81-1.32)	0.8140	0.235	0.89 (0.55-1.43)	0.6280
WC ≥ 102 cm in men and ≥ 88 cm in women	11.17	1.51 (1.19-1.92)	0.0080	0.534	1.26 (0.68-2.32)	0.4650
WHR ≥ 0.9 in men and ≥ 0.85 in women	36.60	2.14 (1.68-2.75)	< 0.0010	12.722	3.87 (1.84-8.13)	0.0040
WHtR ≥ 0.50 both in men and women	19.03	2.04 (1.48-2.80)	< 0.0010	- $	- $	- $
	A 10-year CVD risk ≥ 0.100 of Framingham general cardiovascular risk profile for use in primary care£					
BMI ≥ 30 kg/m^2 both in men and women	9.33	1.41 (1.13-1.76)	0.0020	0.010	1.01 (0.78-1.32)	0.9180
WC ≥ 102 cm in men and ≥ 88 cm in women	33.79	1.98 (1.57-2.50)	< 0.0010	17.750	2.25 (1.54-3.27)	< 0.0010
WHR ≥ 0.9 in men and ≥ 0.85 in women	90.41	2.69 (2.19-3.30)	< 0.0010	67.160	5.40 (3.61-8.08)	< 0.0010
WHtR ≥ 0.50 both in men and women	57.01	2.66 (2.06-3.43)	< 0.0010	7.400	3.59 (1.43-9.01)	< 0.0010

* Significance level was considered at P < 0.0500.

£ outcomes are a 10-year risk of CVD ≥ 0.075 for pooled cohort equations, ≥ 0.05 for SCORE equations (both low and high risk countries versions), and ≥ 0.1 for the Framingham general cardiovascular risk profile for use in primary care.

$ No women with WHtR < 0.5 had a 10-year risk of CVD ≥ 0.05 based on SCORE equations (based on both high and low risk European countries).

OR: Odd ratio; CI: Confidence interval; CVD: Cardiovascular disease; ACC/AHA: American College of Cardiology/American Heart Association; BMI: Body mass index; WC: Waist circumference; WHR: Waist to hip ratio; WHtR: Waist to height ratio; SCORE: Systematic Coronary Risk Evaluation

Some theories attempted to explain the protective effect of obesity by altered cytokines, plasma rennin, epinephrine, and larger coronary arteries.[16] Some other studies proposed smoking as a confounding variable in the obesity paradox; smokers usually lose weight and they also have a higher risk of CVD.[16-18] However, in the present study, the obesity paradox was weakly confirmed only in women and only 0.84% of them were currently smoking, suggesting that smoking might not play a critical role in this context.

Although no obesity indices showed a

relationship with 10-year risk of CVD in a multivariate model, WHR had the strongest association with 10-year risk of CVD in a univariate binary regression model. Previous studies showed that WC and HC have an independent relationship with MI. Consequently, it is reasonable that a combined measure of these two indices (such as WHR) has a strong association with CVD events, as the present study results suggested. An inverse association was observed between HC and risk of DM, hypertension (HTN), dyslipidemia, and CVD.[19-22] Furthermore, DM, HTN, and lipid profiles are the variables commonly utilized to estimate the 10-year risk of CVD. From a different perspective, estrogens have an important role in the accumulation of subcutaneous gluteal and femoral fat, and a higher WHR indicates decreased muscle mass in the legs and gluteal region.[21] Furthermore, the protective effect of estrogen on the cardiovascular system was emphasized in a previous study.[23] Thus, it is reasonable to assume that a higher WHR, which is usually associated with a lower estrogen level, can lead to a higher CVD risk.

This study had some limitations. Although we utilized 4 popular risk assessment tools, none of these risk assessment tools were developed for our country. However, similar results particularly in the context of the association between obesity indices and CVD risk may approve the validity of our findings. In addition, a weak inverse relationship between BMI and estimated CVD risk is not equal to the inverse association between BMI and CVD events. However, this can signify that there is at least a non-strong, negative relationship between BMI as a general index of obesity and a cluster of CVD risk factors that may lead to CVD events in the next decade.

Conclusion

BMI showed a weak and non-significant inverse association with 10-year risk of CVD estimated by pooled cohort equations of ACC/AHA in women. However, this result cannot directly provide enough evidence for the obesity paradox.

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Conflict of Interests

Authors have no conflict of interests.

References

1. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014; 384(9945): 766-81.
2. Flegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. JAMA 2012; 307(5): 491-7.
3. Eckel RH, Krauss RM. American Heart Association call to action: Obesity as a major risk factor for coronary heart disease. AHA Nutrition Committee. Circulation 1998; 97(21): 2099-100.
4. Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, et al. National, regional, and global trends in body-mass index since 1980: Systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet 2011; 377(9765): 557-67.
5. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: A systematic review and meta-analysis. JAMA 2013; 309(1): 71-82.
6. Lavie CJ, McAuley PA, Church TS, Milani RV, Blair SN. Obesity and cardiovascular diseases: implications regarding fitness, fatness, and severity in the obesity paradox. J Am Coll Cardiol 2014; 63(14): 1345-54.
7. McAuley P, Myers J, Abella J, Froelicher V. Body mass, fitness and survival in veteran patients: another obesity paradox? Am J Med 2007; 120(6): 518-24.
8. D'Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: The Framingham Heart Study. Circulation 2008; 117(6): 743-53.
9. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB Sr, Gibbons R, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 63(25 Pt B): 2935-59.
10. Conroy RM, Pyorala K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: The SCORE project. Eur Heart J 2003; 24(11): 987-1003.
11. World Health Organization. Waist circumference and waist-hip ratio: Report of a WHO expert consultation. Geneva, Switzerland: WHO; 2011.
12. Hsieh SD, Yoshinaga H. Waist/height ratio as a

simple and useful predictor of coronary heart disease risk factors in women. Intern Med 1995; 34(12): 1147-52.
13. Ware LJ, Rennie KL, Kruger HS, Kruger IM, Greeff M, Fourie CM, et al. Evaluation of waist-to-height ratio to predict 5 year cardiometabolic risk in sub-Saharan African adults. Nutr Metab Cardiovasc Dis 2014; 24(8): 900-7.
14. Seidell JC, Bjorntorp P, Sjostrom L, Sannerstedt R, Krotkiewski M, Kvist H. Regional distribution of muscle and fat mass in men-new insight into the risk of abdominal obesity using computed tomography. Int J Obes 1989; 13(3): 289-303.
15. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: Risk factor, paradox, and impact of weight loss. J Am Coll Cardiol 2009; 53(21): 1925-32.
16. Gruberg L, Mercado N, Milo S, Boersma E, Disco C, van Es GA, et al. Impact of body mass index on the outcome of patients with multivessel disease randomized to either coronary artery bypass grafting or stenting in the ARTS trial: The obesity paradox II? Am J Cardiol 2005; 95(4): 439-44.
17. Hoffmans MD, Kromhout D, de Lezenne Coulander C. The impact of body mass index of 78,612 18-year old Dutch men on 32-year mortality from all causes. J Clin Epidemiol 1988; 41(8): 749-56.
18. Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, et al. Body weight and mortality among women. N Engl J Med 1995; 333(11): 677-85.
19. Lissner L, Bjorkelund C, Heitmann BL, Seidell JC, Bengtsson C. Larger hip circumference independently predicts health and longevity in a Swedish female cohort. Obes Res 2001; 9(10): 644-6.
20. Okura T, Nakata Y, Yamabuki K, Tanaka K. Regional body composition changes exhibit opposing effects on coronary heart disease risk factors. Arterioscler Thromb Vasc Biol 2004; 24(5): 923-9.
21. Seidell JC, Han TS, Feskens EJ, Lean ME. Narrow hips and broad waist circumferences independently contribute to increased risk of non-insulin-dependent diabetes mellitus. J Intern Med 1997; 242(5): 401-6.
22. Snijder MB, Zimmet PZ, Visser M, Dekker JM, Seidell JC, Shaw JE. Independent and opposite associations of waist and hip circumferences with diabetes, hypertension and dyslipidemia: The AusDiab Study. Int J Obes Relat Metab Disord 2004; 28(3): 402-9.
23. Mendelsohn ME. Protective effects of estrogen on the cardiovascular system. Am J Cardiol 2002; 89(12A): 12E-7E.

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Effect of single-dose crystalloid cardioplegic agent compared to bloody cardioplegic agent in cardiac surgery in children with Tetralogy of Fallot

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Original Article

Abstract

BACKGROUND: Cardioplegia is one of the main post-operative cardiac protective factors widely used in recent decades in the form of crystalloid (St. Thomas) and bloody solutions [del Nido (DN)]. The purpose of this study was to compare the effect of a crystalloid cardioplegic agent (St. Thomas) with that of a bloody cardioplegic agent (DN) in pediatric cardiac surgery among children with Tetralogy of Fallot (TOF).

METHODS: This study was performed on 60 children with TOF, who were candidates for heart repair surgery. The participants were randomly divided into two groups of crystalloid cardioplegic agent and bloody cardioplegic agent. Operative outcomes such as required time for onset of heart arrest, duration of returning to normal heart rhythm, and cardiopulmonary bypass (CPB) time, and operative complications were compared between the two groups.

RESULTS: The duration of returning to normal heart rhythm (50.43 ± 10.93 seconds vs. 43.03 ± 16.35 seconds; P = 0.044) and duration of inotropy (80.40 ± 27.14 hours vs. 63.20 ± 26.91 hours; P = 0.017) were significantly higher in the DN group compared to the St. Thomas group. However, there were no significant differences between the two groups in terms of heart arrest time, cross-clamp time, CPB time, supplementary lasix time, duration of intubation, and intensive care unit (ICU) and hospital length of stay (LOS) (P > 0.050).

CONCLUSION: The use of St. Thomas cardioplegic solution was more effective in reducing the duration of returning to normal heart rhythm and inotropy compared with DN cardioplegic agent, and a single dose of these two cardioplegic agents can keep the mean cardiac arrest duration within the range of 50-70 minutes. It seems that the use of St. Thomas cardioplegic solution can be suggested in pediatric heart surgery.

Keywords: Cardioplegic Solutions; Tetralogy of Fallot; Cardiac Surgical Procedures; Child

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Introduction

Protection of the myocardium is one of the main factors in cardiac surgery. In the 1950s, myocardial protection against ischemia was not considered in cardiac surgeries, which led to an irreversible damage called Stone heart.[1,2] Today, there are various methods including the use of bloody or crystalloid cardioplegia, changing of the cardioplegia temperature (cold or warm), injection of single-dose or repeated cardioplegia, and addition of specific agents to the cardioplegic solution to protect the myocardium during cardiac surgery.[3]

Overall, one of the most important steps in heart protection is electromechanical arrest. The protection and management of the myocardium is influenced by various factors such as surgical technique and the surgeon's experiences and skills, trying to provide a motionless and bloodless heart for the surgical procedure, lack of necrosis during surgery, institutional equipment, and costs.[4]

Various cardioplegic solutions are used for full cardiac arrest. The main characteristics of these solutions include inducing quick and effective myocardial arrest, protection of the heart against myocardial ischemia, being reversible when the

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coronary arteries left during solvent washing, and their low toxicity.[5,6] Presently, different cardioplegic solutions are available with various concentrations; the St. Thomas and del Nido (DN) solutions can be considered as the two main cardioplegic solutions.[7]

The St. Thomas solution is an extracellular cardioplegic solution containing sodium and calcium similar to plasma, and Custodial solution is a similar intracellular solution with lower sodium and calcium that is commonly used in transplant surgery.[8]

In October 2014, following a change in cardioplegic solution from St. Thomas to DN, anecdotally, reduced rates of defibrillation was observed after cross-clamp. Therefore, it was hypothesized that a significant decrease would be observed in the rates of fibrillation after cross-clamp among all patients that received the DN solution based on the weight categories compared to the St. Thomas solution.[9]

In the DN solution, potassium chloride causes the cellular membrane to peel away and the lidocaine solution with sodium channels causes cardiac arrest in the hyperpolarized state. Its magnesium content acts as a calcium channel blocker (CCB) and prevents muscle contractility.[7,9] Single-dose DN injection has been recently used in pediatric surgery. Custodial solution contains tryptophan amino acids and its single-dose injection induces cardiac protection for up to 180 minutes.[10] Although there is yet no consensus among surgeons on single-dose usage or repetition of cardioplegia, DN is one of the most commonly used cardioplegic solutions in pediatric surgery. Various studies have been conducted with different volumes of blood/DN percentage. For example, in a study, a DN solution and blood ratio of 1 to 1 was used as a result of which patients did not need repeated cardiac injection for up to 2 hours.[11] In some other studies, the addition of various drugs and materials, such as high-concentration glucose, was evaluated.[12,13]

The use of cardioplegia in cardiac surgery, both in adults and children, is associated with numerous controversies. In this regard, many studies have been performed in adults on the type of cardioplegia, and the amount and number of repetitions of cardioplegia necessary.[9,14-16]

However, there are a limited number of studies in pediatric cardiac surgery, no study has assessed the effect of single-dose cardioplegia, and less attention has been paid to post-operative and intraoperative outcomes. For example, use of various types of cardioplegic solutions (DN, customized solutions, St. Thomas, Plegisol, Baxter, and microplegia) by surgeons has been studied in pediatric cardiac surgery and the results have indicated that DN/custodial and St. Thomas in different crystalloids or solutions with bloody forms were the most commonly used solutions. DN was the most widely used solution; however, only the types of cardioplegia have been assessed, but their postoperative outcomes and complications have not been investigated.[1]

Since injection of a cardioplegic solution is generally repeated within 15-30 minutes in adults,[15] a congenital heart disease called Tetralogy of Fallot (TOF) was selected for physiological investigation because it is less likely to have pulmonary hypertension, and has the least effect on the conductivity system and a duration of cardiac arrest of at least 50-55 minutes. Thus, the current study was carried out to evaluate the effect of a single-dose injection of a crystalloid cardioplegic agent (St. Thomas) compared with a bloody cardioplegic agent (DN) in pediatric cardiac surgery on patients with TOF.

Materials and Methods

This single-blind, randomized, clinical trial was conducted on all children with TOF who were candidates of complete heart repair surgery referred to Chamran Hospital, Isfahan, Iran, from January 2017 to June 2018. Considering the sample size formula in comparison of two groups, and a confidence level of 95%, power of 80%, error level of 0.1, and the results of previous studies regarding the rate of use of custodial (7%) and DN (38%) cardioplegic solutions,[1] the sample size was determined to be 30 patients in each group.

This study was approved by the ethics committee of Isfahan University of Medical Sciences, Isfahan, Iran, with the code IR.MUI.REC.1396.3.590. Written informed consent was obtained from the parents of the studied children for participation in the study. In addition, patients who had undergone previous primary cardiac surgery (including pulmonary artery banding or Blalock-Taussig shunt), the purpose of their surgery was not complete heart repair, or the surgeon decided against complete heart repair during the surgery based on their condition were excluded from the study. The excluded participants were replaced by other participants, so that there was no drop in the number of participants. Using convenience random sampling, 60 children with TOF were selected. They were divided into two groups using Random Allocation Software (RAS) (Figure 1).

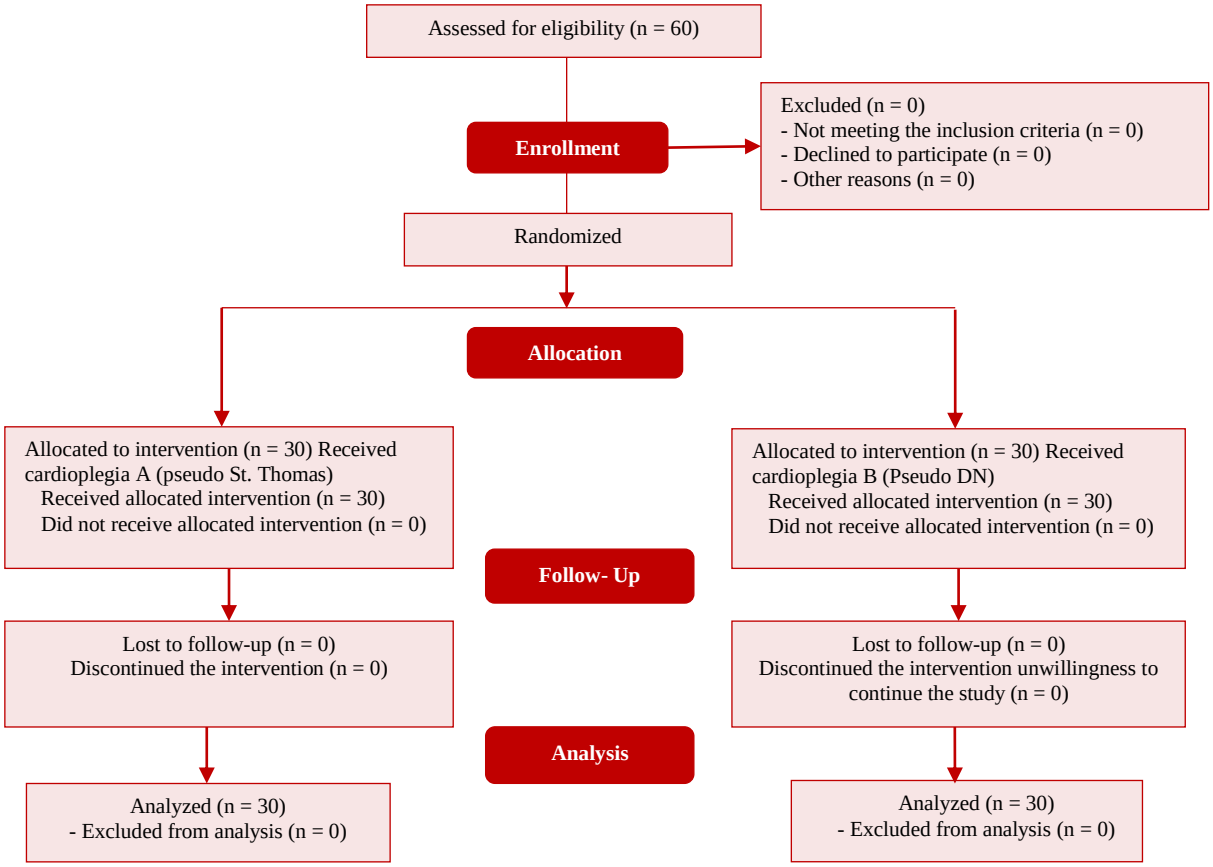

Figure 1. Flowchart Consort

Since it was not possible to use original cardioplegia in our cardiovascular center, cardioplegia with electrolyte combinations similar to DN and St. Thomas were used and the combination was prepared as follows.

To prepare cardioplegic solution A (pseudo St. Thomas), 2.5 cc magnesium sulfate electrolytes 50%, 2.5 cc lidocaine 1%, 6 cc potassium chloride (2 meq/ml), and 7.5 cc sodium bicarbonate 8.4% were dissolved in 500 cc Ringer's lactate and used as crystalloid for cardioplegia and injected at 20 cc/kg.

To prepare cardioplegic solution B (pseudo DN) 2.5 cc magnesium electrolytes 50%, 3 cc lidocaine 2%, 8 cc mannitol 20%, 6.5 cc potassium chloride (2 meq/ml), and 6.5 cc sodium bicarbonate 8.4% were mixed in a 500 cc normal saline serum and 4 units of this solution were mixed with one blood unit and injected at 20 cc/kg (Table 1).

Table 1. St. Thomas and del Nido cardioplegic solutions

ST cardioplegia	Original	P_{seudo} *
Na^+	110 mmol/l	-
K^+	16 mmol/l	6 cc (2 meq/ml)
Mg^{2+}	16 mmol/l	50%, 2.5 cc
Ca^{2+}	1.2 mmol/l	-
$NaHCO_3^-$	10 mmol/l	8.4%, 7.5 cc
Lidocaine	-	1%, 2.5 cc
DN cardioplegia	**Original**	**Pseudo** **
Mannitol	20%, 16.3 ml, 3.26 g	20%, 8 cc
Magnesium sulfate	50%, 4 ml, 2g	50%, 2.5 cc
Sodium bicarbonate	8.4%, 13 ml, 13 mEq	8.4%, 6.5 cc
Lidocaine	1%, 13 ml, 130 mg	2%, 3cc
Potassium chloride (2 mEq/ml)	13 ml, 26 mEq	6.5 cc (2 meq/ml)

*: This cardioplegic solution was solved in a 0.5 l ringer (containing 73 Eq Na^+, 2 Eq K^+, 2 Eq Ca^+, 77 Eq Cl^-); **: This cardioplegic solution was solved in a 0.5 l normal saline (containing 77 Eq Na^+, 77 Eq Cl^-)

Following preparation of cardioplegic solutions, they were tagged as code A and B and the person who gathered the data was not aware of the cardioplegic solution used to make the study single-blinded. Cardioplegia A was administered in the first group and the second group received cardioplegia B.

In addition to age, gender, and weight of the child, blood and metabolic tests were implemented before cardiopulmonary bypass (CPB) initiation, during CPB, 6 hours later, and 1 day after surgery and recorded. Operative outcomes, such as the time required for cardiac arrest, the time necessary to revert to normal heart rhythm, and CPB time, and operative complications were measured and recorded. Furthermore, the intensive care unit (ICU) length of stay (LOS), duration of hospitalization, and incidence of arrhythmia were recorded.

Finally, the collected data were entered into SPSS software (version 22; IBM Corporation, Armonk, NY, USA). Qualitative and quantitative data are demonstrated in the forms of frequency and frequency percentage, and mean and standard deviation, respectively. Fisher's exact test and chi-square test were applied to compare frequency distribution of qualitative data between the two groups. The results of Kolmogorov-Smirnov (KS) test indicated normal distribution of variables. Moreover, independent sample t-test was used to compare the means of continuous variables between the two groups and repeated measures ANOVA was used to compare the two groups at different times. Significance level was considered as less than 0.05 in all analyses.

Results

The group B participants consisted of 18 (60%) boys and 12 (40%) girls with the mean age of 19.8 ± 16.39 months and group A participants consisted of 16 (53.3%) boys and 14 (46.7%) girls with the mean age of 22.26 ± 15.62 month. There was no significant difference in the distribution of gender and age between the two groups (P> 0.050) (Table 2).

As shown in table 3, repeated measures ANOVA showed that the main effect of group was not significant on any of the blood and metabolic outcomes (P > 0.050), in fact, there was no significant difference in the mean of these variables between the two groups. Significant changes were observed in ejection fraction (EF), HCO_3, base excess (BE), lactate level, Cl, creatine phosphokinase (CPK), Na (P< 0.001), pH (P = 0.001), and calcium (P = 0.008) at the different measurement stages of the study. Moreover, there was only a significant difference in calcium with the passage of time between the groups (P = 0.025), so that group A had a higher mean than group B 6 hours after surgery.

Table 2. Demographic characteristics of patients

Characteristics		Group B (n = 30)	Group A (n = 30)	P
Sex [n (%)]	Male	18 (60)	16 (53.3)	0.602*
	Female	12 (40)	14 (46.7)	
Age (month) (mean ± SD)		19.80 ± 16.39	22.26 ± 15.62	0.553**
Weight (kg) (mean ± SD)		9.63 ± 2.87	10.60 ± 5.19	0.374**

* Use of chi-square for comparison between the groups
** Use of independent t-test for comparison between the groups
SD: Standard deviation

No significant difference was observed in the duration of heart arrest, clamp time, CPB time, and duration of supplementary lasix between the two groups (P > 0.050). However, the mean duration of time necessary to revert to normal heart rhythm was significantly higher in group B (50.43 ± 10.93 seconds) than that in group A (43.3 ± 16.35 seconds) (P = 0.044). Moreover, 96.7% of children in group B and all children in group A required inotropic agent, while the duration of inotropy in group B with the mean of 80.40 ± 27.14 hours was significantly higher than that in group A with the mean of 63.20 ± 26.91 hours (P = 0.017). It should be noted that no patient required shock in group B, but 40% of patients needed electrolyte during the pumping and 16.7% had arrhythmia in the ICU. In group A, 3.3% needed shock, 46.7% required electrolyte during pumping, and 6.7% had arrhythmia in the ICU. No significant difference was observed between the two groups in these variables (P > 0.050). In addition, intubation duration, ICU LOS, and duration of hospitalization were slightly higher in group B compared to group A (P > 0.050) (Table 4).

Discussion

Clinical research has been focused on myocardial protection in open-heart surgery for many years, but debate is still ongoing about the ultimate cardioprotective strategy and optimal cardioplegic solution. In the early 1990s, at the University of Pittsburgh, Dr. Pedro del Nido and his colleagues introduced a cardioplegic solution to show the specific requirements of immature myocardium during neonatal and pediatric cardiac surgery. It is commonly known as DN cardioplegic solution, induces a depolarizing arrest during cardiac surgery, and has been increasingly used recently.[17]

Table 3. Blood and metabolic outcomes before and after surgery

Blood and metabolic outcomes	Time of surgery	Group B (n = 30)	Group A (n = 30)	P^*_{time}	P^*_{group}	$P^*_{time \times group}$
EF	Before	70.63 ± 5.18	70.53 ± 4.71	< 0.001	0.645	0.162
	1 day after	64.57 ± 4.57	63.83 ± 4.04			
	1 week after	64.57 ± 4.56	63.80 ± 4.02			
CO_2	Before	33.92 ± 7.23	34.03 ± 8.97	0.124	0.354	0.744
	During the pump	32.42 ± 5.96	33.23 ± 6.51			
	End	31.55 ± 5.90	32.07 ± 5.28			
	6 hours after	32.60 ± 5.50	34.88 ± 5.50			
pH (n)	Before	7.38 ± 0.08	7.35 ± 0.09	0.001	0.109	0.704
	During the pump	7.47 ± 0.07	7.44 ± 0.09			
	End	7.43 ± 0.08	7.43 ± 0.09			
	6 hours after	7.41 ± 0.09	7.38 ± 0.08			
HCO_3	Before	20.40 ± 3.36	20.01 ± 4.18	< 0.001	0.182	0.851
	During the pump	24.68 ± 2.98	24.19 ± 4.39			
	End	27.20 ± 0.28	25.84 ± 2.82			
	6 hours after	27.69 ± 3.98	27.23 ± 3.03			
Lactate level (n)	Before	1.09 ± 0.40	1.16 ± 0.45	< 0.001	0.743	0.305
	During the pump	3.38 ± 1.13	3.35 ± 1.72			
	End	3.06 ± 1.02	3.53 ± 1.64			
	6 hours after	2.73 ± 1.34	2.45 ± 0.91			
BE (mmol/l)	Before	-4.00 ± 2.71	-4.32 ± 2.57	< 0.001	0.341	0.415
	During the pump	0.97 ± 3.10	-0.55 ± 2.86			
	End	4.90 ± 4.25	4.47 ± 3.88			
	6 hours after	4.49 ± 3.54	4.67 ± 2.53			
Calcium	Before	4.08 ± 0.36	4.00 ± 0.58	0.008	0.537	0.025
	During the pump	3.99 ± 0.21	4.04 ± 0.37			
	End	3.89 ± 0.22	3.91 ± 0.30			
	6 hours after	3.79 ± 0.26	3.92 ± 0.43			
Cl	Before	103.53 ± 2.40	104.13 ± 1.89	< 0.001	0.669	0.174
	During the pump	102.77 ± 3.51	102.50 ± 2.73			
	End	101.13 ± 2.85	102.20 ± 2.52			
	6 hours after	104.40 ± 3.76	103.90 ± 2.02			
CPK	Before	36.37 ± 23.95	36.17 ± 11.12	< 0.001	0.593	0.555
	End	184.57 ± 43.42	177.43 ± 23.13			
	6 hours after	144.93 ± 41.39	142.40 ± 20.49			
Na	Before	132.77 ± 3.88	134.72 ± 2.83	< 0.001	0.871	0.641
	During the pump	133.50 ± 2.74	132.45 ± 3.01			
	End	135.92 ± 6.11	135.85 ± 3.93			
	6 hours after	142.43 ± 7.09	142.00 ± 6.37			
K	Before	3.74 ± 0.51	3.57 ± 0.39	0.797	0.406	0.266
	During the pump	3.51 ± 0.64	3.68 ± 0.82			
	End	3.78 ± 0.85	3.51 ± 0.74			
	6 hours after	3.57 ± 0.57	3.56 ± 0.59			

* Use of repeated measures ANOVA; BE: Base excess; EF: Ejection fraction; CPK: Creatine phosphokinase

It is an improvised form of cardioplegia, which includes the beneficial effect of crystalloid cardioplegia, as well as blood components.

The current study aimed to compare the effect of single-dose crystalloid cardioplegic agent (pseudo St. Thomas) with blood cardioplegic solution (pseudo Del Nido) in pediatrics cardiac surgery. It was performed on 60 children with TOF that were divided into two groups (n = 30) of stimulated crystalloid cardioplegia and bloody cardioplegia. A statistically significant difference was not observed between the two groups in terms of age and gender. The results of metabolic and blood changes before, during, and after surgery showed EF and acidity reduction, and increased sodium ion and BE in both groups.

Table 4. Intraoperative and postoperative outcomes

Outcomes	Group B (n = 30)	Group A (n = 30)	P
Arrest duration (second) (mean ± SD)	46.30 ± 13.58	42.47 ± 13.11	0.271*
Cardiopulmonary bypass time (minute) (mean ± SD)	98.33 ± 13.76	92.87 ± 11.84	0.105*
Aortic cross-clamp time (minute) (mean ± SD)	71.33 ± 13.12	67.47 ± 9.07	0.190*
return to normal heart rhythm (second) (mean ± SD)	50.43 ± 10.93	43.03 ± 16.35	0.044*
Supplementary lasix duration (hour) (mean ± SD)	57.10 ± 25.18	49.30 ± 26.20	0.249*
Inotropic time (hour) (mean ± SD)	80.40 ± 27.14	63.20 ± 26.91	0.017*
Duration of intubation (hour) (mean ± SD)	63.20 ± 27.65	51.33 ± 29.69	0.115*
ICU LOS (day) (mean ± SD)	5.23 ± 1.07	4.77 ± 1.13	0.107*
Total hospital LOS (day) (mean ± SD)	10.53 ± 1.59	10.03 ± 1.50	0.215*
Arrhythmias [n (%)]	5 (16.7)	2 (6.7)	0.212***
Need for supplementary electrolyte during CPB [n (%)]	12 (40.0)	14 (46.7)	0.397**
Inotropic requirement [n (%)]	29 (96.7)	30 (100)	0.999**
Delayed sternal closure [n (%)]	0 (0)	0 (0)	-
Need for intraoperative DC shocks [n (%)]	0 (0)	1 (3.3)	0.999***

SD: Standard deviation; ICU: Intensive care unit; LOS: Length of stay; CPB: Cardiopulmonary bypass; DC: Direct current

* Use of independent sample t-test for comparison of mean variables between the two groups

** Use of chi-square test for comparison of variables' frequency distribution between the groups

*** Use of Fisher's exact test for comparison of variables' frequency distribution between the groups

In the present study, the crystalloid and bloody cardiopelgic solutions used were similar to the original solutions, but it should be noted that we solved crystalloid St. Thomas in a 0.5 l ringer (including 73 Eq Na^+, 2 Eq K^+, 2 Eq Ca^+, and 77 Eq Cl^-) and bloody DN in 0.5 l normal saline (including 77 Eq Na^+, and 77 Eq Cl^-).

Different components in cardioplegia play different roles, for instance potassium plays the role of arresting agent, glucose acts as substrate, bicarbonate as buffer, mannitol as oncotic agent and free radical scavenger, and magnesium and lidocaine as membrane stabilizers, and only traces of calcium are seen. Addition of magnesium and lidocaine increases the potassium content and magnesium helps to counteract the effects of calcium and lidocaine by blocking the sodium channels. It causes a decrease in the adverse effects of prolonged membrane depolarization and prevents cellular edema. Use of lidocaine in the DN cardioplegia prolongs the heart arrest duration through its effect on the cell membrane.[3,18]

O'Brien et al. conducted the first clinical study on DN cardioplegia in Halifax in 2009.[19] Their results approved DN cardioplegia effects on lower troponin T and improvement of calcium management in pediatric patients.[19] A clinical investigation was carried out by Charette et al. on 34 children with a cross-clamp time of longer than 90 minutes and single-dose of DN cardioplegia or modified multi-dose of cardioplegia solution.[11] They observed no significant differences in the risk of congenital heart surgery, CPB times, aortic cross-clamp time, weight, or number of intraoperative exogenous blood units. However, they reported significant differences in cardioplegic solution doses and perioperative glucose levels.[11]

A survey among pediatric cardiothoracic surgeons in North America showed that regardless of cross-clamp time a single shot of DN cardioplegic solution is the most commonly used cardioprotective method (38%).[1] In a randomized trial on 100 patients of younger than 12 years who had undergone elective repair of ventricular septal defects (VSD) and TOF, a single-dose DN solution or repeated doses of St. Thomas solution at 30-minute intervals were used.[20] Electron microscopic ultrastructural alterations were assessed through myocardial biopsy. The results showed that the cardiac index was higher in the DN group than the St. Thomas group at 2, 6, and 24 hours. Mechanical ventilation, and ICU and hospital LOS were significantly lower in the DN group and there was lower troponin I release at the 24-hour interval. Electron microscopic studies illustrated more myofibrillar disarray in the St. Thomas solution group.[20]

Cardioplegic solutions have an important role in protecting the heart from myocardial injury during open-heart surgery and in pediatric cardiac surgery; DN solution has been successfully used to his end.[21]

Among the suggested benefits of this solution, the decreased need for repetition of several doses of standard cardioplegia that results in shorter cross-

clamp time, and lower postoperative complications and mortality rate can be mentioned, but the reported differences were not statistically significant.[22]

Accelerated accumulation of intracellular Ca^{2+} can mediate the occurrence of reperfusion injury during cardiac surgery in myocardial ischemia. The myocardial cell prevents the accumulation of these high intracellular ions through energy consuming active transport mechanisms, and ultimately, introducing accelerated accumulation of intracellular Ca^{2+} as myocardial dysfunction upon reperfusion.[23] The DN solution contains lidocaine, a membrane-stabilizing agent that increases Na^{+} channel blockade and lowers the potential of Na^{+}. In addition, Mg^{2+} acts as a Ca^{2+} antagonist that is a suggested mechanism of myocardium protection against high rate of intracellular Ca^{2+}.[24]

It can be stated that reduced cellular acidity caused the activation of the hydrogen-sodium pump (Na^{+}-H^{+}) and sodium-calcium pump (Na^{+}-Ca^{2+}) for removing the hydrogen ion, which led to increased intercellular calcium and sodium ions. In addition, it should be noted that in the case of acidity reduction, patients under electrolyte during pumping (group B: 40%, group Z: 46.7%) are controlled. Thus, the changes therapy in pH were not considered as significant.

Some previous studies have shown superior cardiac index values in the DN group indicating better myocardial protection that in part can be associated with the lidocaine content. It abolishes all electrical activity, reduces the incidence of arrhythmias, and prevents intracellular calcium accumulation. This action results in the prevention of cell injury and probably safeguards the cells from the harmful effects of intracellular calcium accumulation thus providing better myocardial protection.[25] It has also been hypothesized that single-dose cardioplegia offers better myocardial protection than multiple-dose cardioplegia.[26] The DN solution leads to prolonged heart arrest that allows the surgeon to complete most of the routine procedures with a single dose. Although some studies have suggested the provision of a better ultrastructural preservation by multiple doses assigned to metabolic end products,[27] the results of the present study and some previous studies have shown better functional recovery with long-acting single-dose DN cardioplegia.[28,29]

In a randomized control trial, the DN cardioplegia and modified St. Thomas cardioplegia were compared in terms of the inflammatory cytokine response and cardiac troponin I changes in patients undergoing TOF surgery and there were no significant differences in Tumor necrosis factor-alpha (TNF-α), Interleukin 6 (IL-6), or Interleukin-8 (IL-8)cytokine levels.[17] A moderately significant increase was seen in IL-10 level in the St. Thomas group, postoperative lactate level was significantly higher in the DN group, and no differences were detected in troponin levels. It was finally concluded that anti-inflammatory cytokine response in the St. Thomas solution group was significantly better than the DN group, which may be due to the shorter intervals of St. Thomas solution administration.[17]

In the current study, the level of lactate increased from the beginning until the end of surgery, but it again decreased after 6 hours. The level of CPK increased immediately and 6 hours after surgery compared with preoperative CPK.

Generally, it should be noted that none of these metabolic and blood changes were significant in the two groups. Evaluating intraoperative and postoperative outcomes showed that although cardiac arrest duration, CBP, and aortic cross-clamp were higher in group B than group A, this difference was not significant. It has also been showed that returning to normal heart rhythm was significantly higher in group B than group A. In addition, the need for inotropy in groups A and B was 100 and 96.7%, respectively, but the duration of inotropy was higher in group B than group A. It should be noted that these two factors were also dependent upon the child's weight, as the duration of returning to normal heart rhythm and need for inotropy increased with weight.

The findings of some previous studies are in agreement with that of the present study, there is evidence regarding the advantages of single-dose DN compared with multi-dose cardioplegia in terms of mechanical ventilation time, cross-clamp time, and pumping time.[18,19,29-31]

Charette et al. reported no significant differences in cross-clamp and CPB times between DN and multi-dose cardioplegia groups and revealed that multiple doses of cardioplegia could not significantly increase the duration of cross-clamp;[11] this finding was in accordance with that of Kim et al. in adults undergoing CPB.[25]

Moreover, significant differences were not observed in these variables between the DN and St. Thomas groups in the present study. Considering the variable complexity of repairing TOF, the slightly longer, but not significant cross-clamp time in the DN group may be due to the complexity of the defect and the related reparative operation.

Mishra et al. reported lower rates of immediate postoperative complications and mortality with DN usage, but the differences were not significant.[15]

In the current study, no death or arrhythmia in the ICU occurred in the groups. There were also no significant differences in the need and duration of intubation and shock, length of hospitalization, and ICU LOS between the two groups.

One of the limitations of this study was that only one type of disease (TOF) was evaluated, but some studies have evaluated various types of heart disorders. The evaluation of single-dose cardioplegia in children can be considered as the advantage of this study. To the researchers' knowledge, there are very few studies in this field, so it is a very important topic in countries such as Iran due to some deprivations and their economic conditions, and further studies are needed in this area. It should be noted that we had no hospital mortality cases and this can be considered as the most important advantage of this study.

Conclusion

The present study results indicate that a single dose of a routine cardioplegic agent can be used in children and a cardiac arrest time of 50-70 minutes be achieved. Considering that the duration of returning to normal heart rhythm and need for inotropy were lower in the St. Thomas group compared to the DN group, the St. Thomas cardioplegic solution can be suggested for children within the age group under the age of 5 years. However, further studies with larger sample sizes and different types of cardiac diseases are needed.

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Conflict of Interests

Authors have no conflict of interests.

References

1. Kotani Y, Tweddell J, Gruber P, Pizarro C, Austin EH 3rd, Woods RK, et al. Current cardioplegia practice in pediatric cardiac surgery: A North American multiinstitutional survey. Ann Thorac Surg 2013; 96(3): 923-9.
2. Cooley DA, Reul GJ, Wukasch DC. Ischemic contracture of the heart: "stone heart". Am J Cardiol 1972; 29(4): 575-7.
3. Yamamoto H, Yamamoto F. Myocardial protection in cardiac surgery: A historical review from the beginning to the current topics. Gen Thorac Cardiovasc Surg 2013; 61(9): 485-96.
4. Kouchoukos NT, Blackstone EH, Hanley FL, Kirklin JK. Kirklin/Barratt-Boyes Cardiac Surgery E-Book. Philadelphia, PA: Elsevier Health Sciences; 2012.
5. Feindel CM, Tait GA, Wilson GJ, Klement P, MacGregor DC. Multidose blood versus crystalloid cardioplegia. Comparison by quantitative assessment of irreversible myocardial injury. J Thorac Cardiovasc Surg 1984; 87(4): 585-95.
6. Fallouh HB, Kentish JC, Chambers DJ. Targeting for cardioplegia: Arresting agents and their safety. Curr Opin Pharmacol 2009; 9(2): 220-6.
7. Buckberg GD. Antegrade/retrograde blood cardioplegia to ensure cardioplegic distribution: Operative techniques and objectives. J Card Surg 1989; 4(3): 216-38.
8. Jonas RA. Myocardial protection. In: Jonas R, Editor. Comprehensive Surgical Management of Congenital Heart Disease. Boca Raton, FL: CRC Press; 2004. p. 175-84.
9. Buel ST, Striker CW, O'Brien JE. del Nido versus St. Thomas cardioplegia solutions: A single-center retrospective analysis of post cross-clamp defibrillation rates. J Extra Corpor Technol 2016; 48(2): 67-70.
10. Liu J, Feng Z, Zhao J, Li B, Long C. The myocardial protection of HTK cardioplegic solution on the long-term ischemic period in pediatric heart surgery. ASAIO J 2008; 54(5): 470-3.
11. Charette K, Gerrah R, Quaegebeur J, Chen J, Riley D, Mongero L, et al. Single dose myocardial protection technique utilizing del Nido cardioplegia solution during congenital heart surgery procedures. Perfusion 2012; 27(2): 98-103.
12. Mimic B, Ilic S, Vulicevic I, Milovanovic V, Tomic D, Mimic A, et al. Comparison of high glucose concentration blood and crystalloid cardioplegia in paediatric cardiac surgery: A randomized clinical trial. Interact Cardiovasc Thorac Surg 2016; 22(5): 553-60.
13. Fazelifar S, Bigdelian H. Effect of esmolol on myocardial protection in pediatrics congenital heart defects. Adv Biomed Res 2015; 4: 246.
14. Kim K, Ball C, Grady P, Mick S. Use of del nido cardioplegia for adult cardiac surgery at the cleveland clinic: Perfusion implications. J Extra Corpor Technol 2014; 46(4): 317-23.
15. Mishra P, Jadhav RB, Mohapatra CK, Khandekar J, Raut C, Ammannaya GK, et al. Comparison of del Nido cardioplegia and St. Thomas Hospital

solution-two types of cardioplegia in adult cardiac surgery. Kardiochir Torakochirurgia Pol 2016; 13(4): 295-9.
16. Gorjipour F, Dehaki MG, Totonchi Z, Hajimiresmaiel SJ, Azarfarin R, Pazoki-Toroudi H, et al. Inflammatory cytokine response and cardiac troponin I changes in cardiopulmonary bypass using two cardioplegia solutions; del Nido and modified St. Thomas':A randomized controlled trial. Perfusion 2017; 32(5): 394-402.
17. Matte GS, del Nido PJ. History and use of del Nido cardioplegia solution at Boston Children's Hospital. J Extra Corpor Technol 2012; 44(3): 98-103.
18. Sorabella RA, Akashi H, Yerebakan H, Najjar M, Mannan A, Williams MR, et al. Myocardial protection using del nido cardioplegia solution in adult reoperative aortic valve surgery. J Card Surg 2014; 29(4): 445-9.
19. O'Brien JD, Howlett SE, Burton HJ, O'Blenes SB, Litz DS, Friesen CL. Pediatric cardioplegia strategy results in enhanced calcium metabolism and lower serum troponin T. Ann Thorac Surg 2009; 87(5): 1517-23.
20. Talwar S, Bhoje A, Sreenivas V, Makhija N, Aarav S, Choudhary SK, et al. Comparison of del Nido and St Thomas Cardioplegia Solutions in Pediatric Patients: A Prospective Randomized Clinical Trial. Semin Thorac Cardiovasc Surg 2017; 29(3): 366-74.
21. Suleiman MS, Hancock M, Shukla R, Rajakaruna C, Angelini GD. Cardioplegic strategies to protect the hypertrophic heart during cardiac surgery. Perfusion 2011; 26(Suppl 1): 48-56.
22. Valooran GJ, Nair SK, Chandrasekharan K, Simon R, Dominic C. del Nido cardioplegia in adult cardiac surgery - scopes and concerns. Perfusion 2016; 31(1): 6-14.
23. Tsukube T, McCully JD, Federman M, Krukenkamp IB, Levitsky S. Developmental differences in cytosolic calcium accumulation associated with surgically induced global ischemia: Optimization of cardioplegic protection and mechanism of action. J Thorac Cardiovasc Surg 1996; 112(1): 175-84.
24. O'Blenes SB, Friesen CH, Ali A, Howlett S. Protecting the aged heart during cardiac surgery: The potential benefits of del Nido cardioplegia. J Thorac Cardiovasc Surg 2011; 141(3): 762-70.
25. Kim JS, Jeong JH, Moon SJ, Ahn H, Hwang HY. Sufficient myocardial protection of del Nido cardioplegia regardless of ventricular mass and myocardial ischemic time in adult cardiac surgical patients. J Thorac Dis 2016; 8(8): 2004-10.
26. Pourmoghadam KK, Ruzmetov M, O'Brien MC, Piggott KD, Plancher G, Narasimhulu SS, et al. Comparing del Nido and Conventional Cardioplegia in Infants and Neonates in Congenital Heart Surgery. Ann Thorac Surg 2017; 103(5): 1550-6.
27. Ramanathan R, Parrish DW, Armour TK, Brinster DR. Use of del Nido Cardioplegia in Adult Cardiac Surgery. Thorac Cardiovasc Surg 2015; 63(7): 624-7.
28. Smigla G, Jaquiss R, Walczak R, Bonadonna D, Kaemmer D, Schwimer C, et al. Assessing the safety of del Nido cardioplegia solution in adult congenital cases. Perfusion 2014; 29(6): 554-8.
29. Mick SL, Robich MP, Houghtaling PL, Gillinov AM, Soltesz EG, Johnston DR, et al. del Nido versus Buckberg cardioplegia in adult isolated valve surgery. J Thorac Cardiovasc Surg 2015; 149(2): 626-34.
30. Ota T, Yerebakan H, Neely RC, Mongero L, George I, Takayama H, et al. Short-term outcomes in adult cardiac surgery in the use of del Nido cardioplegia solution. Perfusion 2016; 31(1): 27-33.
31. Yerebakan H, Sorabella RA, Najjar M, Castillero E, Mongero L, Beck J, et al. Del Nido Cardioplegia can be safely administered in high-risk coronary artery bypass grafting surgery after acute myocardial infarction: A propensity matched comparison. J Cardiothorac Surg 2014; 9: 141.

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The transulnar approach in the patients with ipsilateral radial artery occlusion

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Original Article

Abstract

BACKGROUND: Transulnar approach (TUA) has been classified as an appropriate surrogate for the transradial approach (TRA), but the safety of TUA in the presence of ipsilateral radial artery occlusion (RAO) is not well studied. In this article, we aimed to assess the feasibility and occurrence of complications of this approach in Iranian individuals with ipsilateral RAO.

METHODS: In this prospective double-center study, a total number of 70 participants from July 2017 to November 2018 with coexisting ipsilateral RAO due to prior RA angiography, severe arterial spasm, prominent vascular anomalies, or arterial harvesting for hemodialysis or graft procedures were enrolled and underwent TUA. Incidence of probable complications including pain, hematoma, arteriovenous fistula (AVF), pseudoaneurysm formation, any adverse events requiring immediate vascular surgery, life-threatening hand ischemia, infection, ulnar nerve palsy, major adverse cardiac events (MACE) including death, myocardial infarction (MI), or stroke plus ulnar artery (UA) obstruction and narrowing was evaluated both before discharge time and one month afterward.

RESULTS: The mean age of the study population was 68.2 ± 12.8 years [men number: 41 (58.5%)]. Our success rate was 98.6% and 37.1% of subjects underwent further coronary intervention. No aforementioned adverse outcomes were reported in any individual except for pain (11.4%) and minor hematoma (grade I) (5.7%) as well as MACE (1.4%). Follow-up assessment revealed asymptomatic UA occlusion (UAO) and severe narrowing in 2.8% and 1.4% of participants, respectively.

CONCLUSION: Our outcomes suggested that due to high safety and low complication rates, TUA could be tried safely in patients with concurrent ipsilateral RAO. Other appropriate cohort studies are required for assessing the incidence of TUA complications.

Keywords: Ulnar Artery; Radial Artery; Percutaneous Coronary Intervention; Coronary Angiography

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Introduction

One of the cornerstone points in coronary artery diseases (CADs) diagnosis improving remarkably is coronary angiography (CAG). Since the first execution of this method in 1929, this procedure has become one of the most common modalities done to either diagnose or treat all related CADs. Despite the old method of transfemoral approach (TFA) remaining the standard therapeutic modality, which was associated with higher rates of complications, other novel options have been introduced based on raised equipment technology.[1] The transradial approach (TRA) for CAG first announced in 1989 was the initiation of a new era in this regard.[2]

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Lower complication and mortality rates plus faster discharge period and patient convenience and early ambulation, as well as declining management costs, were some potential advantages of the modality as mentioned above, making this approach to be considered as an appropriate surrogate to TFA.[3-8] However, smaller radial artery (RA) diameter, anatomical abnormalities, arterial spasms, or needing the desired artery for coronary artery bypass graft (CABG) surgery were reported to be some difficulties attributable to TRA.[9-11] Another option first introduced by Terashima et al. in 2001 providing a better alternative modality especially in terms of TRA failure, was CAG with a transulnar approach (TUA).[12] Although most studies revealed a similar efficacy of TUA in comparison to TRA as well as easier approach way plus less anatomical variations as well as arterial vasospasm rates, Roghani-Dehkordi et al.[13] Dahal et al.[14] revealed that TUA was associated with higher rates of puncture attempts and cross-over to other current diagnosis and therapeutic modalities. Also, the deep location of the ulnar artery (UA) near the ulnar nerve might play an essential role in incidence of complications.[15] By the way, TUA safety in terms of ipsilateral radial artery occlusion (RAO)[5] is less frequently investigated in literature with findings from as mild as minor hematoma to as significant as UA obstruction.[16,17] On the other hand, this approach has been proved to be efficacious even in terms of visceral diagnostic and therapeutic angiographic procedures.[18]

In this article, we aimed to evaluate the feasibility and occurrence of probable complications with TUA in patients with ipsilateral RAO.

Materials and Methods

This prospective double-center study was designed to be performed in two governmental heart centers located in Isfahan City, Iran (Shahid Chamran and Khorshid Hospitals). Any individual more than 18 years old eligible for CAG or angioplasty without right RA pulsation due to previous coronary interventions with TRA, prior history of arterial surgery for arteriovenous fistula (AVF) or graft procedures, and vascular anomalies or severe arterial spasm was recruited in our study from July 2017 to November 2018. Presence of carpal tunnel, Guyon's canal or hypothenar hammer syndrome (HHS), elective TFA, motor or sensory deficits along the median or ulnar nerve route, medial wrist bone fracture, severe hand deformity or chronic tenosynovitis, as well as osteomyelitis (OM) was defined as exclusion criteria. Before the initiation of the procedure, all research aims were explained to each individual and the coordinator entirely answered probable questions. After that, each participant was asked to sign an informed consent form. After collection of all appropriate information, 70 individuals met our predefined inclusion criteria. The Ethics Committee of Isfahan University of Medical Sciences approved this study (No. 398101).

After proper preparation of patients for the procedure, approximately 2 cm above ulnar hand bone was marked, and 1.5 ml of lidocaine (2%) was injected subcutaneously. Afterward, 5-6 French hydrophilic sheath (Merit Medical, Utah, USA) was used concurrently with a spasmolytic cocktail consisting of 2.5 mg of verapamil plus 250 µg of nitroglycerine as well as 2500 international unit (IU) of unfractionated heparin (UFH) (Figure 1). In terms of CAG, 6 inches right and left Judkins (Medtronic, Minneapolis, MN, USA) or Tiger (Terumo Interventional Systems, Somerset, NJ, USA) catheters were used. In need of coronary angioplasty, 6 inches right/left Judkins and extra backup catheters were utilized. After complementation of process, hemostasis was done with right wrist hyperextension and local pressure for 5-10 minutes, followed by ulnar TR band compression afterward.

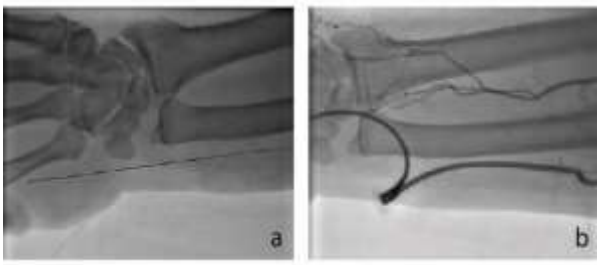

Figure 1. Angiographic view of ulnar artery (UA) access (a) and radial artery occlusion (RAO) in transulnar approach (TUA) contrast injection (b)

We used each participant's medical form to gather information about age, gender, body mass index (BMI), smoking status, and family history of CADs as well as past medical history data including hypertension (HTN), diabetes mellitus (DM), hyperlipidemia, and myocardial infarction (MI).

Access time was defined from the initiation of lidocaine injection to the time of sheath insertion. Any correct UA cannulation was considered a successful procedure. Moreover, fluoroscopy and procedure time, as well as contrast volume consumption, were assessed during the procedure

implementation. Presence or absence of complications including pain, ulnar nerve palsy, infection, hematoma [≤ 5 cm, ≤ 10 cm, and > 10 cm in diameter just below the elbow for grade I, II, and III, respectively, expanding hematoma above the elbow (grade IV) and any place with limb ischemia threads (grade V)], life-threatening hand ischemia, AVF, pseudoaneurysm formation, UA narrowing or occlusion as well as any adverse events requiring vascular surgery plus major adverse cardiac events (MACE) including death, MI, and stroke was assessed at discharge date and follow-up duration after one month as primary endpoints.

Categorical and continuous variables were reported as frequency (percentage) and mean ± standard deviation (SD), respectively. All analyses were done with the SPSS software (version 20, IBM Corporation, Armonk, NY, USA).

Results

The mean age of patients who underwent TUA was 68.2 ± 12.8 years. Male participants were the dominant contributor to our study sample [n = 41, (58.5%)]. The most prevalent metabolic abnormality found in the study population was hyperlipidemia (54.2%), followed by DM (44.2%) and HTN (40.0%) (Table 1).

Table 1. Basic characteristics of patients undergoing a transulnar approach (TUA)

Variables		TUA
Age (year)		68.2 ± 12.8
BMI (kg/m^2)		26.4 ± 3.8
Male gender		41 (58.5)
Current smoker		24 (34.2)
HTN		28 (40.0)
DM		31 (44.2)
Hyperlipidemia		38 (54.2)
Previous MI		12 (17.1)
Positive family history of CADs		18 (25.7)
Procedure	CAG	44 (62.9)
	PCI	26 (37.1)

Data are presented as frequency (percentage) and mean ± standard deviation (SD)
TUA: Transulnar approach; BMI: Body mass index; HTN: Hypertension; DM: Diabetes mellitus; MI: Myocardial infarction; CAD: Coronary artery disease; CAG: Coronary angiography; PCI: Percutaneous coronary intervention

The detailed information of the TUA procedure is represented in table 2. On 69 patients, TUA was done successfully, and our success rate was estimated to be 98.6%. We had to cross over to TFA in just one person due to the tortuosity of the UA. In addition to CAG done for all participants, 26 of them (37.1%) underwent coronary angioplasty. The mean access time was 9.7 ± 2.3 minutes. Angiography and angioplasty fluoroscopy duration was 5.3 ± 1.4 minutes and 11.2 ± 2.2 minutes, respectively.

Table 2. Transulnar approach (TUA) procedural characteristics in study participants

Procedure characteristics		TUA
Cannulation rate	Successful	69 (98.6)
	Cross-over	1 (1.4)
Access time (minute)		9.7 ± 2.3
Fluoroscopy time (minute)	CAG	5.3 ± 1.4
	PCI	11.2 ± 2.2
Contrast volume (ml)	CAG	144.0 ± 24.0
	PCI	253.0 ± 32.0
Procedure time (minute)	CAG	18.2 ± 4.6
	PCI	34.8 ± 7.9

Data are presented as frequency (percentage) and mean ± standard deviation (SD)
TUA: Transulnar approach; CAG: Coronary angiography; PCI: Percutaneous coronary intervention

Contrast volume used in angioplasty and angiography procedures was 253 ± 32 and 144 ± 24 ml, respectively. Moreover, the time needed for trans-ulnar angioplasty and the diagnostic procedure was 34.8 ± 7.9 and 18.2 ± 4.6 minutes, respectively. Data on our major endpoints which were defined as complication occurrence rates after the procedure and one month afterward are provided in table 3.

Table 3. Incidence of complications with the transulnar approach (TUA)

Complications		TUA (n = 70)
Hematoma	I	4 (5.7)
	II, III, IV, V	0 (0)
Pain		8 (11.4)
MACE		1 (1.4)
Follow-up assessment	Asymptomatic UAO	2 (2.8)
	Asymptomatic UA narrowing	1 (1.4)

Data are presented as frequency (percentage)
TUA: Transulnar approach; MACE: Major adverse cardiac events; UAO: Ulnar artery occlusion; UA: Ulnar artery

Pain controlled by pain-relieving agents had been reported in 8 individuals (11.4%). 5.7% of cases experienced minor hematoma (grade I) which was managed conservatively. No other adverse outcomes in terms of life-threatening hand ischemia, infection, ulnar nerve palsy, AVF, and pseudoaneurysm formation, as well as complications needing immediate vascular surgery, had been reported. One individual who underwent percutaneous coronary intervention (PCI) experienced MACE including transient ischemic attack (TIA), which relieved entirely within 24 hours.

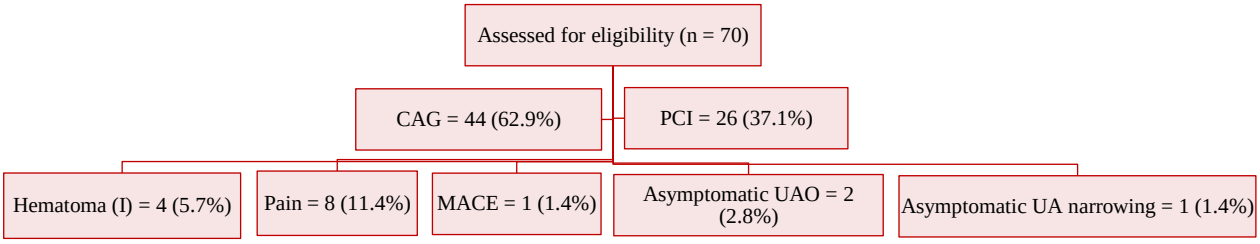

Figure 2. Flow diagram of study design and complication occurrence in study participants
CAG: Coronary angiography; PCI: Percutaneous coronary intervention; MACE: Major adverse cardiac events; UA: Ulnar artery

During one month after intervention, asymptomatic ulnar artery occlusion (UAO) and severe narrowing were reported in 2 patients (2.8%) and 1 patient (1.4%), respectively, that was confirmed by duplex ultrasonography. None of them had clinical signs and symptoms of hand ischemia during the follow-up period. A brief explanation of the study design and complication incidence was illustrated in figure 2.

Discussion

We constructed the current study to evaluate the feasibility and occurrence of complications in patients with ipsilateral RAO who underwent TUA. Our findings revealed that except for a few cases experiencing minor hematoma, controllable pain, and MACE managed conservatively as well as asymptomatic UAO and severe narrowing in the next month of follow-up duration in just 3 cases, we had a 98.6% success rate and no other previous pre-defined complications occurred at all. While TRA has been classified as a usual coronary diagnostic and therapeutic modality in most centers, low incidence of complications as well as high successful rates could categorize TUA as an appropriate alternative procedure compared to TRA, especially in individuals who did not have a patent RA. Concerning this point that TUA in the presence of RAO has been less studied in the literature, few studies were performed with similar findings. Hsueh et al. retrospectively investigated 87 patients who underwent TUA due to the inability to perform ipsilateral TRA because of multiple reasons like arteriovenous anastomosis for hemodialysis, RA harvest for CABG, weak pulse, and failed puncture attempts to evaluate possible complications incidence. The mean access and total procedural times were 5.0 ± 5.7 minutes and 72.6 ± 43.6 minutes, respectively. Their success rate of cannulation was reported to be 98.9%. Follow-up duration both during hospitalization and 32.2 ± 24.0 months afterward revealed that in spite of hematoma (2.3%), repeated revascularization (1.1%), and acute or chronic thrombosis (1.1%), no other adverse outcomes including UA obstruction, pseudoaneurysm or AVF formation, neurologic problems, hand ischemia, any complications requiring vascular surgery or blood transfusion and stroke, as well as death, happened in any participants.[15] Likewise, 476 individuals who underwent TUA were studied from March 2011 to February 2013 in Kedev et al.'s study. Their further survey showed that 240 of them also had ipsilateral RAO. Data analysis announced that during a follow-up of one month, no major vascular adverse outcomes and UAO were reported. By the way, 7% of participants experienced a clinical spasm of UA and the prevalence of grades 1, 2, 3, and 4 of hematoma was 3.7%, 2.0%, 1.6%, and 0.4%, respectively.[19] Also, 17 patients with a mean age of 77 years requiring CAG or intervention underwent TUA in the presence of ipsilateral RAO and were followed for 30 days for assessment of the probable incidence of post-procedural complications. In addition to a 100% successful procedure rate and no ulnar nerve injury or hand ischemia occurrence, both hematoma and UA spasm were observed in just two cases.

Moreover, follow-up investigation failed to report UA obstruction on days 1, 7, or 30 after initiation of the procedure.[20] Even more, this desirable safety index has been reported in TUA for non-coronary diagnostic and therapeutic interventions. Zybulewski et al. recruited 14 participants with a mean age of 60 years for visceral intervention with simultaneous contraindication for TRA. They reported a successful cannulated rate of 94.1% (16 successful attempts out of 17 ones) and did not report any major adverse events including access site bleeding or hemorrhagic complications. Only two individuals experienced minor hematoma in the access site.[18]

Although it might have appeared that TUA in the presence of ipsilateral RAO could cause life-threatening hand ischemia and might be considered a contraindication in performing this modality, anterior interosseous artery would play a pivotal role in preventing these adverse outcomes.[15,17] An experienced interventional cardiologist performed all procedures and clinical follow-up visits in this regard. However, some limitations could be considered for our study including non-randomized study design plus a quite small sample size. Moreover, a short pre-defined follow-up duration disabled us to perform a thorough assessment of probable complications. Finally, the inability to compare our outcomes with individuals who underwent TUA without RAO for better deduction might affect our results.

Conclusion

This study suggested that TUA could appropriately be considered as an alternative modality in patients suffering from ipsilateral RAO due to its high safety and feasibility as well as low complication rates.

Acknowledgments

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Conflict of Interests

Authors have no conflict of interests.

References

1. Al-Azizi KM, Lotfi AS. The distal left radial artery access for coronary angiography and intervention: A new era. Cardiovasc Revasc Med 2018; 19(8S): 35-40.
2. Campeau L. Percutaneous radial artery approach for coronary angiography. Cathet Cardiovasc Diagn 1989; 16(1): 3-7.
3. Brzezinski M, Luisetti T, London MJ. Radial artery cannulation: A comprehensive review of recent anatomic and physiologic investigations. Anesth Analg 2009; 109(6): 1763-81.
4. Hetherington SL, Adam Z, Morley R, de Belder MA, Hall JA, Muir DF, et al. Primary percutaneous coronary intervention for acute ST-segment elevation myocardial infarction: Changing patterns of vascular access, radial versus femoral artery. Heart 2009; 95(19): 1612-8.
5. Jolly SS, Yusuf S, Cairns J, Niemela K, Xavier D, Widimsky P, et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): A randomised, parallel group, multicentre trial. Lancet 2011; 377(9775): 1409-20.
6. Gokhroo R, Bisht D, Padmanabhan D, Gupta S, Kishor K, Ranwa B. Feasibility of ulnar artery for cardiac catheterization: AJmer ULnar ARtery (AJULAR) catheterization study. Catheter Cardiovasc Interv 2015; 86(1): 42-8.
7. Roghani F, Tajik MN, Khosravi A. Compare complication of classic versus patent hemostasis in transradial coronary angiography. Adv Biomed Res 2017; 6: 159.
8. Roghani F, Shirani B, Hashemifard O. The effect of low dose versus standard dose of arterial heparin on vascular complications following transradial coronary angiography: Randomized controlled clinical trial. ARYA Atheroscler 2016; 12(1): 10-7.
9. Valsecchi O, Vassileva A, Musumeci G, Rossini R, Tespili M, Guagliumi G, et al. Failure of transradial approach during coronary interventions: Anatomic considerations. Catheter Cardiovasc Interv 2006; 67(6): 870-8.
10. Dehghani P, Mohammad A, Bajaj R, Hong T, Suen CM, Sharieff W, et al. Mechanism and predictors of failed transradial approach for percutaneous coronary interventions. JACC Cardiovasc Interv 2009; 2(11): 1057-64.
11. Roghani-Dehkordi F, Hashemifard O, Sadeghi M, Mansouri R, Akbarzadeh M, Dehghani A, et al. Distal accesses in the hand (two novel techniques) for percutaneous coronary angiography and intervention. ARYA Atheroscler 2018; 14(2): 95-100.
12. Terashima M, Meguro T, Takeda H, Endoh N, Ito Y, Mitsuoka M, et al. Percutaneous ulnar artery approach for coronary angiography: A preliminary report in nine patients. Catheter Cardiovasc Interv 2001; 53(3): 410-4.
13. Roghani-Dehkordi F, Hadizadeh M, Hadizadeh F. Percutaneous trans-ulnar artery approach for coronary angiography and angioplasty; A case series study. ARYA Atheroscler 2015; 11(5): 305-9.
14. Dahal K, Rijal J, Lee J, Korr KS, Azrin M. Transulnar versus transradial access for coronary angiography or percutaneous coronary intervention: A meta-analysis of randomized controlled trials. Catheter Cardiovasc Interv 2016; 87(5): 857-65.
15. Hsueh SK, Cheng CI, Fang HY, Omran MM, Liu WH, Chung WJ, et al. Feasibility and safety of transulnar catheterization in ipsilateral radial artery occlusion. Int Heart J 2017; 58(3): 313-9.
16. Andrade PB, Tebet MA, Andrade MV, Labrunie A, Mattos LA. Primary percutaneous coronary intervention through transulnar approach: Safety

and effectiveness. Arq Bras Cardiol 2008; 91(4): e49-4.
17. Koutouzis M, Maniotis C, Agelaki M, Tzifos V, Matsoukis I, Lazaris E. Transulnar approach for coronary catheterization in patients with a harvested ipsilateral radial artery: A case series. Cardiovasc Revasc Med 2017; 18(5): 364-6.
18. Zybulewski A, Edwards M, Kim E, Nowakowski FS, Patel R, Tabori N, et al. Transulnar approach as an alternative to transradial approach in non-coronary intervention: Safety, feasibility and technical factors. J Vasc Access 2017; 18(3): 250-4.
19. Kedev S, Zafirovska B, Dharma S, Petkoska D. Safety and feasibility of transulnar catheterization when ipsilateral radial access is not available. Catheter Cardiovasc Interv 2014; 83(1): E51-E60.
20. Kwan TW, Ratcliffe JA, Chaudhry M, Huang Y, Wong S, Zhou X, et al. Transulnar catheterization in patients with ipsilateral radial artery occlusion. Catheter Cardiovasc Interv 2013; 82(7): E849-E855.

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The association between anthropometric parameters and cardiovascular risk indicators in women with polycystic ovarian syndrome

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Short Communication

Abstract

BACKGROUND: In patients with polycystic ovarian syndrome (PCOS), this is now hypothesized that whether increased risk for cardiovascular disorders is related more to obesity than PCOS per se. This study aimed to compare cardiovascular risk factors between the lean and obese women with PCOS.

METHODS: This case-control study was conducted on 86 (43 obese and 43 lean) women with PCOS. The presence of overweight and obesity was defined based on the body mass index (BMI) (> 25 kg/m²). The study objectives were first to compare mean levels of cardiovascular laboratory parameters between lean and obese patients with PCOS and then to assess the relationship between obesity indices and these laboratory parameters.

RESULTS: Compared to the lean group, the obese group had significantly higher mean fasting blood sugar (FBS) (89.40 ± 10.73 versus 84.09 ± 7.87 mg/dl, P = 0.011), higher mean serum triglyceride (TG) (119.09 ± 60.66 versus 96.86 ± 27.23 mg/dl, P = 0.032), higher mean total cholesterol (147.70 ± 57.38 versus 126.79 ± 35.95 mg/dl, P = 0.045), and also higher mean low-density lipoprotein (LDL) (92.30 ± 13.53 versus 83.77 ± 17.61 mg/dl, P = 0.014). Using the Pearson's correlation test, positive correlations were found between BMI and waist circumference (WC) indices and study parameters including FBS, serum TG, serum total cholesterol, serum LDL, and also blood pressure (BP).

CONCLUSION: Because of higher concentrations of FBS and lipid profiles in obese patients with PCOS and considering obesity as a more important risk factor for coronary artery disease (CAD) than PCOS, it is recommended to assess and monitor cardiovascular risk factors in these population to reduce the risk for cardiovascular disorders and metabolic syndrome. Also, by reducing body weight and normalizing BMI value, the cardiovascular and metabolic risk factors can be modified and prevented.

Keywords: Obesity; Cardiac; Risk Factors; Polycystic Ovarian Syndrome

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Introduction

In addition to inherited pattern of polycystic ovarian syndrome (PCOS), its related endocrinological aspects have been also well determined. Even, this syndrome has been identified as the most common endocrinopathy in women within the childbearing period with an overall prevalence range of 4% to 12%.[1,2] The metabolic aspect of PCOS is frequently based on the reduced insulin sensitivity, leading to increased risk for progressive diabetes mellitus (DM) and its complications. Furthermore, obesity, hyperlipidemia, and systolic hypertension (HTN) are well-known comorbidities among women with PCOS with higher prevalence than the general population.[3]

In fact, higher prevalence of these risk components predisposes patients with PCOS to coronary atherosclerosis and thus coronary atherogenesis is an early event predictable in these patients.[3]

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In total, various studies could demonstrate lower high-density lipoprotein (HDL) cholesterol, as well as higher serum levels of triglycerides (TGs), low-density lipoprotein (LDL) cholesterol, and homocysteine.[4] Moreover, endothelial dysfunction and also increased carotid intima-media thickness (CIMT) are more prevalent in patients with PCOS compared to age-matched controls.[5-8] All of these risk profiles increase the risk for myocardial infarction (MI) in patients with PCOS.[9-11]

As previously pointed, special metabolic manifestations of PCOS include fasting hyperinsulinemia, peripheral insulin resistance, and dyslipidemia. In fact, this syndrome is now identified as a major cause of DM, so the prevalence of glucose tolerance test and diabetes in obese women with PCOS is 11% and 38%, respectively,[12] and thus, it seems that the occurrence of metabolic disturbances and also cardiovascular risk factors can be associated with the simultaneous presence of obesity in these patients.

In this regard, it is now hypothesized that the increased risk for cardiovascular disorders may be related to obesity in the patients with PCOS. Therefore, the present study aimed to compare cardiovascular risk factors between the lean and obese women with PCOS.

Materials and Methods

This case-control study was conducted on 86 women with PCOS (43 obese and 43 lean women) who referred to Shariati Hospital in Isfahan, Iran, in 2014. The presence of PCOS in the subjects was confirmed based on the meeting two of the following three criteria: presence of oligo-ovulation or anovulation, clinical or biochemical signs of hyperandrogenism (not due to pituitary, adrenal, or tumor-related causes), and presence of polycystic ovaries by ultrasound.[13]

The presence of overweight and obesity was defined based on the body mass index (BMI) measures as BMI higher than 25 kg/m^2. Patient selection was based on their reference to our clinic and then everybody who met inclusion criteria was included and obese and lean patients, based on criteria, were divided to two groups.

The two groups were matched for three parameters of age, present medication, and history of smoking. The exclusion criteria were unwillingness to participate in the project, history of kidney disease, DM type I, and BMI lower than 19 kg/m^2.

This study was approved by the Research and Ethics Committees of Islamic Azad University, Najafabad Branch, Isfahan, Iran.

After explaining the study aims to participants and also receiving written informed consent, baseline characteristics and medical data were collected by reviewing.

In all participants, body weight was measured using the same calibrated digital scale and height was also measured by a standard stadiometer with the participant wearing no shoes. BMI was calculated using the most recent weight (kilograms) documented in the medical record divided by the height (meters squared).[13] Waist circumference (WC) was measured using flexible tapes on a horizontal plane, midway between the lower border of the ribs and the iliac crest. Blood pressure (BP) was measured by a physician in all participants. Laboratory parameters including fasting blood sugar (FBS) and lipid profiles were also measured by especial laboratory techniques. The study objectives were first to compare mean levels of cardiovascular laboratory parameters between lean and obese patients with PCOS and then to assess the relationship between obesity indices (BMI and WC) and these laboratory parameters.

For the statistical analysis, SPSS statistical software (version 16, SPSS Inc., Chicago, IL, USA) was used. Kolmogorov–Smirnov test (K-S test) was used for checking normality of distribution of variables. Data were expressed as mean ± standard deviation (SD) and absolute number by percent for quantitative and categorical variables, respectively.

Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed.

Quantitative variables were also compared using t-test or Mann-Whitney U test. The correlation between quantitative variables was assessed using the Pearson's correlation coefficient test.

P-value of less than 0.050 was considered statistically significant.

Results

In total, 43 patients in obese group and 43 in lean group were included into the study.

The mean age of the participants in obese and lean groups was 24.26 ± 3.32 and 25.21 ± 2.23 years, respectively, with no difference (P = 0.122).

The mean BMI was 28.27 ± 2.41 kg/m^2 in the obese and 21.99 ± 1.89 kg/m^2 in the lean group (P < 0.001) with the mean WC of 95.23 ± 5.91 and 82.37 ± 6.68 cm, respectively (P < 0.001).

Table 1. Clinical and laboratory parameters in obese and lean groups

Item	Lean group (n = 43)	Obese group (n = 43)	P
FBS (mg/dl)	84.09 ± 7.87	89.40 ± 10.73	0.011
TG (mg/dl)	96.86 ± 27.23	119.09 ± 60.66	0.032
Cholesterol (mg/dl)	126.79 ± 35.95	147.70 ± 57.38	0.045
LDL (mg/dl)	83.77 ± 17.61	92.30 ± 13.53	0.014
HDL (mg/dl)	41.37 ± 12.04	34.49 ± 12.64	0.429
SBP (mmHg)	112.56 ± 11.20	116.05 ± 12.56	0.178
DBP (mmHg)	72.09 ± 7.89	74.42 ± 6.29	0.134

P-value < 0.050 is significant
Statistical analysis is based on dependent t-test
FBS: Fasting blood sugar; TG: Triglyceride; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

Comparing clinical and laboratory parameters between the two study groups (Table 1) showed that compared to the lean group, the obese group had significantly higher mean FBS (P = 0.011), higher mean serum TG (P = 0.032), higher mean total cholesterol (P = 0.045), and also higher mean LDL (P = 0.014), but there was no difference between the two groups in terms of mean serum HDL level (P = 0.429) as well as in mean systolic BP (SBP) (P = 0.178) and diastolic BP (DBP) (P = 0.134). Using the Pearson's correlation test (Table 2), positive correlations were found between BMI index and all study laboratory parameters including FBS (P < 0.001), serum TG (P = 0.001), serum total cholesterol (P = 0.002), serum LDL (P = 0.002), and also SBP (P = 0.031) and DBP (P = 0.002). Also, the positive association was revealed between WC and the indicators of FBS (P = 0.001), serum TG (P = 0.001), serum total cholesterol (P = 0.011), serum LDL (P = 0.038), and also SBP (P = 0.003) and DBP (P = 0.001).

Discussion

The present study concluded important points. It was demonstrated that the obese women with PCOS had higher levels of lipid profiles, including serum TG (P = 0.032), total cholesterol (P = 0.045), and serum LDL (P = 0.014) as well as higher FBS (P = 0.011). In fact, these women were posed in higher risk for glucose and lipid metabolism impairment; however, these patients had similar SBP and DBP compared to those lean women with PCOS and therefore, obese women with PCOS may have normal BP and no increased risk for HTN.

In this regard, it seems that the PCOS patients with obesity may be more in danger of cardiovascular disorders as well as metabolic syndrome when compared to non-obese women with PCOS. A new viewpoint to PCOS that we recommend is: 'PCOS by itself is not an important risk factor for coronary artery disease (CAD)." Indeed, accompanying obesity is a strong risk factor for CAD and should be managed optimally which is concomitant with PCOS in these patients. In a similar study by Conway et al.,[13] obese women with PCOS were found to have higher SBP, serum TG, and plasma glucose concentration than lean women with PCOS group. In another study by Holte et al.,[14] plasma concentrations of free fatty acids and TGs, and also total and LDL cholesterol were markedly higher in obese than in non-obese women with PCOS. They also showed higher levels of fasting insulin levels than non-obese ones. Similar to our finding that was shown in patients with PCOS, obesity was associated with blood sugar and lipid profiles impairment. In fact, the mechanisms of occurring obesity in women with PCOS may be associated with the lipid metabolism pathways and vice versa.

Table 2. Correlation between anthropometric indices and laboratory parameters in obese and lean groups

Index	Pearson value	FBS	TG	Cholesterol	LDL	HDL	SBP	DBP
BMI	R coefficient	0.393	0.349	0.330	0.335	0.072	0.232	0.326
	P	< 0.001	< 0.001	< 0.001	< 0.001	0.509	0.031	< 0.001
WC	R coefficient	0.340	0.347	0.271	0.224	0.047	0.321	0.343
	P	< 0.001	< 0.001	0.011	0.038	0.667	0.003	< 0.001

BMI: Body mass index; WC: Waist circumference; FBS: Fasting blood sugar; TG: Triglyceride; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

Similarly, Pirwany et al.[15] showed an important relationship between lipids and lipoprotein sub-fractions and metabolic and endocrine parameters in women with PCOS; they figured out that independent predictor of plasma TG and lipase activity was fat distribution which was assessed by WC and fasting insulin concentration. In an important survey by Elting et al.,[16] not only FBS and lipid profiles were more impaired in obese women with PCOS than in non-obese ones, but also it was demonstrated that the influence of obesity on hyperinsulinemia, dyslipidemia, and HTN was stronger than major indicators including menstrual cycle pattern or follicle size. In another study by Roa et al.,[17] women with PCOS showed significantly higher values of the TG/HDL ratio which is closely related to WC and insulin resistance and sensitivity indexes, with the highest values being observed in obese patients.

Conclusion

The findings in the present study lead to two final conclusion. First, because of higher concentrations of FBS and lipid profiles in obese patients with PCOS, the assessing and monitoring of cardiovascular risk factors is advisable in these population to reduce the risk of cardiovascular disorders and metabolic syndrome. Second, because of the association between overweight and obesity and these risk factors, it seems that by reducing body weight and normalizing BMI value, the cardiovascular and metabolic risk factors can be modified and their risks will be prevented.

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Conflict of Interests

Authors have no conflict of interests.

References

1. Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. Am J Obstet Gynecol 1935; 29(2): 181-91.
2. Broekmans FJ, Knauff EA, Valkenburg O, Laven JS, Eijkemans MJ, Fauser BC. PCOS according to the Rotterdam consensus criteria: Change in prevalence among WHO-II anovulation and association with metabolic factors. BJOG 2006; 113(10): 1210-7.
3. Bajuk Studen K, Jensterle Sever M, Pfeifer M. Cardiovascular risk and subclinical cardiovascular disease in polycystic ovary syndrome. Front Horm Res 2013; 40: 64-82.
4. Talbott EO, Zborowski JV, Sutton-Tyrrell K, McHugh-Pemu KP, Guzick DS. Cardiovascular risk in women with polycystic ovary syndrome. Obstet Gynecol Clin North Am 2001; 28(1): 111-33, vii.
5. Wild RA. Long-term health consequences of PCOS. Hum Reprod Update 2002; 8(3): 231-41.
6. Christian RC, Dumesic DA, Behrenbeck T, Oberg AL, Sheedy PF, Fitzpatrick LA. Prevalence and predictors of coronary artery calcification in women with polycystic ovary syndrome. J Clin Endocrinol Metab 2003; 88(6): 2562-8.
7. Guzick DS, Talbott EO, Sutton-Tyrrell K, Herzog HC, Kuller LH, Wolfson SK Jr. Carotid atherosclerosis in women with polycystic ovary syndrome: Initial results from a case-control study. Am J Obstet Gynecol 1996; 174(4): 1224-9.
8. Talbott EO, Guzick DS, Sutton-Tyrrell K, McHugh-Pemu KP, Zborowski JV, Remsberg KE, et al. Evidence for association between polycystic ovary syndrome and premature carotid atherosclerosis in middle-aged women. Arterioscler Thromb Vasc Biol 2000; 20(11): 2414-21.
9. Dahlgren E, Janson PO. Polycystic ovary syndrome-long-term metabolic consequences. Int J Gynaecol Obstet 1994; 44(1): 3-8.
10. Pierpoint T, McKeigue PM, Isaacs AJ, Wild SH, Jacobs HS. Mortality of women with polycystic ovary syndrome at long-term follow-up. J Clin Epidemiol 1998; 51(7): 581-6.
11. Wild S, Pierpoint T, McKeigue P, Jacobs H. Cardiovascular disease in women with polycystic ovary syndrome at long-term follow-up: A retrospective cohort study. Clin Endocrinol (Oxf) 2000; 52(5): 595-600.
12. Antuna-Puente B, Feve B, Fellahi S, Bastard JP. Adipokines: The missing link between insulin resistance and obesity. Diabetes Metab 2008; 34(1): 2-11.
13. Conway GS, Agrawal R, Betteridge DJ, Jacobs HS. Risk factors for coronary artery disease in lean and obese women with the polycystic ovary syndrome. Clin Endocrinol (Oxf) 1992; 37(2): 119-25.
14. Holte J, Bergh T, Berne C, Lithell H. Serum lipoprotein lipid profile in women with the polycystic ovary syndrome: Relation to anthropometric, endocrine and metabolic variables. Clin Endocrinol (Oxf) 1994; 41(4): 463-71.
15. Pirwany IR, Fleming R, Greer IA, Packard CJ, Sattar N. Lipids and lipoprotein subfractions in women with PCOS: relationship to metabolic and endocrine parameters. Clin Endocrinol (Oxf) 2001;

54(4): 447-53.

16. Elting MW, Korsen TJ, Schoemaker J. Obesity, rather than menstrual cycle pattern or follicle cohort size, determines hyperinsulinaemia, dyslipidaemia and hypertension in ageing women with polycystic ovary syndrome. Clin Endocrinol (Oxf) 2001; 55(6): 767-76.

17. Roa MB, Arata-Bellabarba G, Valeri L, Velaķzquez-Maldonado E. Relationship between the triglyceride/high-density lipoprotein-cholesterol ratio, insulin resistance index and cardiometabolic risk factors in women with polycystic ovary syndrome. Endocrinol Nutr 2009; 56(2): 59-65.

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Chronic rheumatic mitral regurgitation with normal atrial size and pulmonary artery pressure

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Letter to Editor

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Dear Editor

Chronic rheumatic mitral regurgitation (MR) is identified by enlargement of left atrium (LA) size as a pathophysiologic response to volume overload and establishment of LA pressure hemostasis, and to maintain pulmonary artery pressure (PAP) within normal limits; but in our country, we have observed some cases with severe rheumatic MR with normal atrial size and normal PAP. Therefore, the LA size could not be performed using measurement of atrial size in this subgroup of rheumatic mitral diseases.

Rheumatic mitral disease is common in developing countries.[1] Basically, the entity of chronic rheumatic MR has been jointed with enlargement of LA size as a pathophysiologic response to volume overload and establishment of LA pressure hemostasis.[2] LA size at the time of diagnosis has a major predictive role for long-term outcomes, risk-stratification protocols, and life expectancy.[3] Thus, measurement of LA size, as a marker of cardiac remodeling, is a guideline-based advice. The superiority of LA volume measurement to diameter has been demonstrated, and is a guideline-based approach.[4] Indeed, LA enlargement is an adaptive response in severe MR to maintain PAP within normal limits, and avoid pulmonary artery hypertension. The progression of MR severity is usually in parallel with eventual development of pulmonary artery hypertension. Nevertheless, in cases with normal size LA, PAP is usually elevated due to sudden pulmonary congestion.[5]

As physicians working in developing country, we have observed some cases with severe rheumatic MR with normal atrial size and normal PAP. Severe MR with normal atrial size and normal PAP is not a usual finding in rheumatic mitral valve diseases, and there are very limited reports with very old references.[6] In these cases, both LA area and 3-dimentional (3D) volume are within normal limits. Since the LA size is an indirect measure of atrial remodeling, assessment of atrial remodeling could not be performed using measurement of atrial size in this subgroup of rheumatic mitral diseases, and novel measures for LA remodeling are needed.

Conflict of Interests

Authors have no conflict of interests.

References

1. Mvondo CM, Pugliese M, Giamberti A, Chelo D, Kuate LM, Boombhi J, et al. Surgery for rheumatic mitral valve disease in sub-saharan African countries: Why valve repair is still the best surgical option. Pan Afr Med J 2016; 24: 307.
2. Cameli M, Incampo E, Mondillo S. Left atrial deformation: Useful index for early detection of cardiac damage in chronic mitral regurgitation. Int J Cardiol Heart Vasc 2017; 17: 17-22.
3. Le Tourneau T, Messika-Zeitoun D, Russo A, Detaint D, Topilsky Y, Mahoney DW, et al. Impact of left atrial volume on clinical outcome in organic mitral regurgitation. J Am Coll Cardiol 2010; 56(7): 570-8.

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4. Perez de I, Feltes G, Moreno J, Martinez W, Saltijeral A, de Agustin JA, et al. Quantification of left atrial volumes using three-dimensional wall motion tracking echocardiographic technology: Comparison with cardiac magnetic resonance. Eur Heart J Cardiovasc Imaging 2014; 15(7): 793-9.
5. Ratanasit N, Karaketklang K, Krittayaphong R. Left atrial volume index as an independent determinant of pulmonary hypertension in patients with chronic organic mitral regurgitation. BMC Cardiovasc Disord 2016; 16: 141.
6. Gould L, Reddy R. Severe mitral regurgitation with a normal-sized left atrium. Angiology 1978; 29(2): 174-8.