Original Article

Assessment of Endothelial Function in Iranian Healthy Obese Patients after Bariatric Surgery

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Abstract

Background: Endothelial function plays a critical role in cardiovascular homeostasis. Morbid obesity is associated with an enhanced risk of atherosclerosis and chronic inflammation. Bariatric surgery (BS) is a promising method used recently for weight loss; however, the number of studies that have examined the effect of BS on endothelial function is limited. This study aimed to investigate the association between endothelial function evaluated by flow-mediated dilation (FMD) and weight loss after BS.

Materials and Methods: This is a cross-sectional study conducted in Isfahan, Iran, and included 40 healthy obese individuals who underwent BS as an intervention group and 40 healthy obese patients who did not undergo BS as a control group in a 6-month follow-up duration period. FMD as an indicator of endothelial function was evaluated in these participants. FMD <7.1% is considered abnormal.

Results: There was no significant difference between control and BS groups in terms of age and body mass index (BMI) at baseline. The mean ± standard deviation (SD) of FMD in the BS group pre- and post-intervention were 12.95 ± 6.90 and 37.65 ± 13.52 respectively and the mean ± SD of FMD in the control group were 15.88 ± 6.85 and 15.85 ± 5.83. The association between significant weight loss after BS and FMD was strongly significant ($P < 0.001$).

Conclusions: According to the results of this study, it can be concluded that BS has been effective in terms of improving the FMD as an indicator of endothelial function.

Keywords: Bariatric surgery, body mass index, body weight, endothelial function, flow-mediated dilation, gastric bypass, gastric bypass, gastroplasty, lipectomy, obesity

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Introduction

Obesity is associated with vascular endothelial dysfunction, which is due to a decreased nitric oxide (NO) availability due to the increased oxidative stress production.[1] Obesity on the one hand and the obesity-related diseases such as diabetes, insulin resistance, hypertension, and sleep apnea are associated with an increased risk of cardiovascular disease. Obese people need more blood to supply their body with oxygen and nutrients, which raises blood pressure. High blood pressure is also a major cause of heart attack, which is, unfortunately, more common in obese people.[2] Obesity is the second leading cause of preventable death in the United States, causing 2.8 million deaths annually according to the World Health Organization statistics (WHO).[3]

The identification of NO as an important endothelium-derived molecule for vasodilation, and the discovery of the endothelium as more than just a link between blood and the vessel wall, has led to significant advances in vascular

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research. The endothelium maintains the balance between vasoconstriction and vasodilation and acts as the main regulator of inhibitory vascular homeostasis. The endothelium also stimulates the cell growth of smooth muscle, fibrinolysis, and thrombogenesis. When this balance is lost, endothelial dysfunction happens and causes damage to the arterial wall. Before angiographic or ultrasonic evidence of atherosclerotic plaques, endothelial dysfunction is considered a primary marker for atherosclerosis.[4,5] The endothelial function is primarily assessed by measuring the brachial artery flow-mediated dilation (FMD) method which was developed almost 20 years ago as a noninvasive.[6,7] It is widely believed that FMD reflects endothelium-dependent arterial function, largely mediated by NO, and has been used as a substitute for vascular health.[7] According to previous studies, obesity causes systemic endothelial dysfunction.[8] However, the exact mechanisms of the negative impact of obesity on vascular function are not yet fully understood.[9] Bariatric surgery (BS) promotes long-term effective weight loss and ultimately improves the obesity-related cardiovascular disease (CVD) risk factors and also endothelial dysfunction.[9,10] The rationale for performing BS is to reduce the incidence of CVDs and CVD-related all-cause mortality.[10] BS for severe obesity was defined and approved by the National Institutes of Health from 1991 for body mass index (BMI) of 40 kg/m^2 or a BMI of 35 kg/m^2 in the presence of conditions associated with a high risk of morbid obesity.[11] Follow-up of patients shows that BS significantly reduces global and cardiac mortality in these patients.[12,13]

A comprehensive meta-analysis has shown that BS is associated with a reduction in short-term mortality as well as a reduction in long-term mortality from CVDs and cancer.[14] So far, only a few studies have examined the effects of BS on endothelial function in terms of FMD, which generally shows that FMD improves after BS.[15,16] Although a meta-analysis study showed that BS improves the endothelial function and FMD scores;[16] however, heterogeneities are seen in the results of various studies and some controversial results have been reported that oppose the positive effect of BS on endothelial function.[17-19] To date, no study has been performed in Iran to evaluate the effects of weight loss after BS on endothelial function by measuring FMD in obese patients and this study is the first study in this field among obese patients in the short-term (≤6 months) in Isfahan, Iran.

Materials and Methods

Subjects

Our study included 40 BS subjects (36 females and 4 males), with a confirmed diagnosis of morbid obesity according to the guidelines of the WHO. All the patients admitted to the BS unit of our hospital at Isfahan University of Medical Sciences for BS intervention and approved to participate in this study. Ethics Committee of Isfahan University of Medical Sciences approved all steps of the study. The control group included 40 subjects (30 females and 10 males) and was selected nonrandomly of people with a confirmed morbid obesity diagnosis who decided not to undergo BS and were comparable with the intervention group in terms of age. Both BS and control groups were excluded if they had any history of diabetes, hypertension, cancer, asthma, and CVDs. Both groups did not receive any treatment for nutritional or medical obesity.

Protocol

All participants (control and BS) underwent assessment of FMD at baseline. FMD assessment was again repeated 6-month after BS in the intervention group and at 6-month follow-up in the control group. All research was performed in the early afternoon hours (3–4 pm) and the fasting state.

Flow-mediated dilation

Brachial artery ultrasound to assess FMD was performed by the same expert operator according to the standard protocol,[20] using a high-resolution GE Vivid 3 ultrasound device and a 10 MHz linear probe to measure the FMD. The following formula was used to estimate the FMD:

$$FMD\ (\%) = ([POD - BBD]/BBD) \times 100$$

Subjects were placed in a warm, quiet room (22–24°C) for at least 10 min before the experiment. Basal brachial diameter (BBD) is evaluated in resting position, and postocclusion diameter (POD) is evaluated 30 s before and 90 s after cuff evacuation (cuff pressure is raised up to 300 mmHg for 5 min before evacuation). Caffeine, high-fat foods, and Vitamin C were banned for 8–10 h before the examination. The size of the brachial artery was measured at rest, then the artery was occluded using a blood pressure measuring cuff, 50 mm Hg above systolic blood pressure for 5 min, and then the cuff was emptied and the diameter of the brachial artery was measured again.[21] The cutoff value for normal endothelial function assessed by FMD of the brachial artery was considered as 7.1%.[21]

Statistical analysis

Fisher's exact test was applied to calculate the statistical significance difference of variables. *t*-test or Mann–Whitney test was used to compare the means of variables between the BS and control groups. Linear regression was used to determine the relationship between quantitative data of variables. All data analysis was performed using SPSS version 20.0, Inc., Chicago, IL, USA for MS Windows ($P < 0.05$ was considered statistically significant).

Results

Eighty participants were enrolled in this study, 40 as intervention (BS) group and 40 as the control group. Of them were 14 were male and 66 were female. FMD was carried out for all of them. The demographic characteristics of participants are shown in Table 1.

The mean ± standard deviation (SD) of age in the BS group was 38.78 ± 9.17, and the mean ± SD of age in the control was 37.20 ± 9.24 and there was no significant difference between control and BS groups in terms of age ($P = 0.45$). Mean ± SD of BMI in the BS group was 43.57 ± 4.74 kg/m^2 and in the control group was 44.07 ± 5.17 kg/m^2 and there were no significant differences between the two groups in terms of BMI ($P = 0.65$). Mean ± SD of height in the BS group was 162.65 ± 9.96 and in the control group was 168.50 ± 8.51, so the mean ± SD of height in the control group was significantly different and was higher ($P = 0.006$). Mean ± SD of weight in the BS group was 115.55 ± 19.01 which was significantly lower than the control group (125.83 ± 22.68) ($P = 0.02$).

The mean ± SD of FMD in the BS group pre- and post-intervention (at baseline and after 6 months follow-up) were 12.95 ± 6.90 and 37.65 ± 13.52, respectively. The mean ± SD of FMD in the control group at baseline and after 6 months were 15.88 ± 6.85 and 15.85 ± 5.83 respectively [Figure 1 and Table 2]. The difference between the pre and postintervention in the BS group was strongly significant compared to the control group ($P < 0.001$) [Figure 2 and Table 3]. Tables 2 and 3 show the mean ± SD of FMD in both groups and their related *P* value. Figure 2 shows the brachial Doppler ultrasound image before and after BS.

Discussion

In this study, the association of FMD (as endothelial function indication) followed by significant weight loss after BS has been evaluated. We found that FMD was significantly improved after BS. Our results confirm the association between weight loss and endothelium function improvement. Conversely, FMD did not change in obese patients who had not undergone BS.

Obesity is an increasingly common global major health concern of adults, teenagers, children, and especially women in both developed and developing countries and is reported as one of the main predictors of CVDs, type 2 diabetes, dyslipidemia, and hypertension.[22-27] Traditional weight-loss interventions such as food, lifestyle, and behavioral therapy have been found to be ineffective in morbidly obese patients (BMI >40 kg/m^2).[28] "People who underwent weight-loss surgery have a better chance of beating the odds and living longer, better, and healthier lives." While diet and exercise by themselves are more difficult to maintain over time, lifestyle improvements combined with weight loss surgery appear to have the best overall outcome. An experimental study showed that subjects activity experienced improved level of physical activity (73%) followed BS versus 18% by diet, less hunger 76% followed BS versus diet 18%, improved appearance 94% surgery followed BS versus 50% by diet, and fewer social limitations 69% followed BS versus 27% followed by diet.[29,30] BS is a proven and reliable method to achieve significant long-term weight loss in morbidly obese individuals and has been associated with a significantly

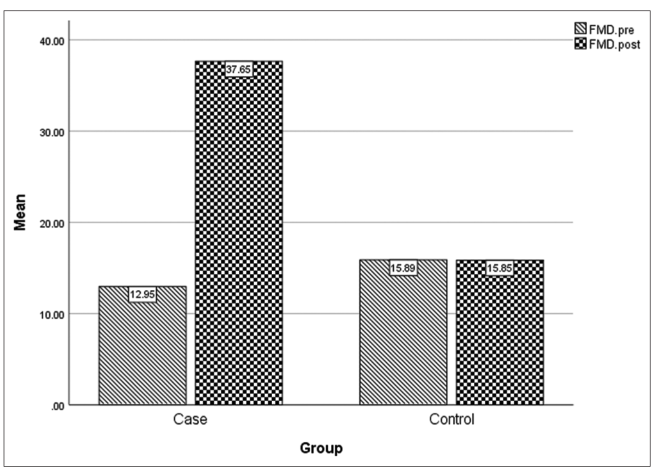

Figure 1: Mean of flow mediated dilation pre and post intervention in the control and case (bariatric surgery) groups

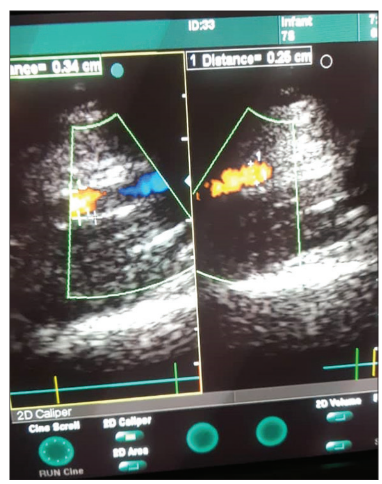

Figure 2: Brachial Doppler ultrasound image before and after bariatric surgery

Table 1: Demographic characteristics of participants in bariatric surgery and control groups

	Total population (*n*=80)	BS (*n*=40)	Control (*n*=40)	*P*
Age (mean±SD)	37.99±9.18	38.78±9.17	37.20±9.24	0.45[a]
Height (mean±SD)	165.58±9.66	162.65±9.96	168.50±8.51	0.006[a]
Weight (mean±SD)	120.69±21.43	115.55±19.01	125.83±22.68	0.02[b]
BMI (mean±SD)	43.82±4.94	43.57±4.74	44.07±5.17	0.65[a]
Sex, *n* (%)				0.14[c]
Male	14 (17.5)	4 (10)	10 (25)	
Female	66 (82.5)	36 (90)	30 (75)	

[a]Obtained by independent *t*-test, [b]Obtained by Mann-Whitney test, [c]Obtained by Fisher's exact test. BS: Bariatric surgery, BMI: Body mass index, SD: Standard deviation

Table 2: Mean±standard deviation of flow mediated dilation in bariatric surgery and control groups before and after intervention (at baseline and after 6 months follow-up)

	Case (*n*=40)			Control (*n*=40)		
	Pre	Post	*P**	Pre	Post	*P**
FMD (mean±SD)	12.95±6.90	37.65±13.52	<0.0001	15.88±6.85	15.85±5.83	0.96

*Obtained by paired *t*-test. SD: Standard deviation, FMD: Flow mediated dilation

Table 3: Mean±standard deviation of flow mediated dilation changes in bariatric surgery and control groups

	Case	Control	*P**
FMD (post-pre) (mean±SD)	24.69±12.55	−0.04±5.04	<0.0001

*Obtained by independent-*t*-test. SD: Standard deviation, FMD: Flow mediated dilation

reduced cardiovascular-related mortality, according to the studies; however, results on the effects of BS on endothelial function in terms of FMD are inconsistent.[16-19] A study on 19 obese people with BMI = 43.8 ± 3.1 kg/m^2 showed that FMD did not change significantly after BS although a weight loss of 30% after 1 year was achieved, our study on obese people with BMI 43.57 ± 4.74 kg/m^2 in the BS group showed that FMD improved significantly after BS.[17] A prospective study on 33 hypertensive obese subjects showed that after BS weight loss was associated with significant improvements in BP, metabolic, and inflammatory markers, although FMD did not improve.[18,19] Also reported a significant reduction in the mean of BMI and 51.7% weight loss ($P < 0.001$) with no meaningful changes in endothelial function. Despite these studies, which oppose the positive effect of BS on improving endothelial function, most studies show that this surgery has a significant positive effect on improving endothelial function.[16]

One study showed that both endothelium-dependent and endothelial-independent coronary artery function significantly improved in obese patients after BS without any signs or evidence of CVD.[9] Bigornia *et al*.[31] investigated the effect of BS and long-term weight loss on FMD and as a control group, selected obese people who did not manage to lose significant weight. They found that sustained weight loss, improved the FMD from 6.8% ± 4.2% to 10.0% ± 4.7%, but remained stagnant in patients without significant weight loss.[31] They found that successful BS and weight loss were associated with a reduced glucose level, total cholesterol, and low-density lipoprotein cholesterol, high-sensitivity C-reactive protein, and hemoglobin A1c levels.[31] Bigornia *et al*. showed that sustained weight loss, improved FMD regardless of the type of intervention method;[31] however, Borzì *et al*. found that weight loss and BMI reduction followed by medical nutrition treatment was not as effective in improving endothelial function as BS.[15] Mingrone *et al*. in a single-center, nonblinded, randomized, controlled trial on type 2 diabetic patients with severe obesity found that BS resulted in better glucose control than medical treatment, although weight loss was seen in both groups.[32] Albaugh *et al*. also found that BS is more effective in terms of improving CVD risk factors compared to nonsurgical obesity treatments.[33]

In our study, unlike many studies,[32-34] the presence of diabetes and blood pressure was considered as exclusion criteria and the study population was healthy obese people. However, our results similar to the results of others showed a positive effect of BS on FMD. Many studies on the effect of this method have evaluated long-term results (after 1 year),[35,36] but our study considered a short-term (≤6 months) follow-up duration. Our results agree with[9] that evaluated FMD after a short duration (3-month follow-up) and it can be seen that the positive effect of this method on improving endothelial function can be achieved even at the beginning after BS.

Conclusion

According to the results of our study and other studies, it can be concluded that BS has been effective in terms of improving the FMD as an indicator of endothelial function. There is a fact that reversing endothelial dysfunction and restoring arterial homeostasis is possible as a result of weight loss through BS.

This study has several limitations. Although sufficient for the whole group, the sample size was relatively small, and we did not perform subgroup analysis and comparison in people who underwent BS or diet intervention/medical nutrition treatment. This study was observational and will have all the limitations of this category of study.

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Conflicts of interest

There are no conflicts of interest.

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