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RESEARCH LETTER

Long-term effects of bariatric surgery on peripheral endothelial function and coronary microvascular function

KEYWORDS
Obesity;
Bariatric surgery;
Endothelial function;
Coronary microvascular function

Summary
Background: We previously demonstrated that bariatric surgery (BS) leads to a short-term significant improvement of endothelial function and coronary microvascular function. In this study we assessed whether BS maintains its beneficial effect at long-term follow up.
Design: We studied 19 morbidly obese patients (age 43 ± 9 years, 12 women) without any evidence of cardiovascular disease who underwent BS. Patients were studied before BS, at 3 months and at 4.0 ± 1.5 years follow up.
Methods: Peripheral vascular function was assessed by flow-mediated dilation (FMD) and nitrate-mediated dilation (NMD), i.e., brachial artery diameter changes in response to post-ischemic forearm hyperhaemia and to nitroglycerin administration, respectively. Coronary microvascular function was assessed by measuring coronary blood flow (CBF) response to intravenous adenosine and to cold pressor test (CPT) in the left anterior descending coronary artery.
Results: Together with improvement of anthropometric and metabolic profile, at long-term follow-up patients showed a significant improvement of FMD (6.43 ± 2.88 vs. 8.21 ± 1.73%, $p = 0.018$), and CBF response to both adenosine (1.73 ± 0.48 vs. 2.58 ± 0.54; $p < 0.01$) and CPT (1.43 ± 0.30 vs. 2.23 ± 0.48; $p < 0.01$), compared to basal values. No differences in vascular end-points were shown at 3-month and 4-year follow-up after BS.
Conclusions: Our data show that, in morbidly obese patients, BS exerts beneficial and long lasting effects on peripheral endothelial function and on coronary microvascular dilator function.

Obesity is associated with increased cardiovascular mortality and morbidity [1]. Besides its association with several cardiovascular risk factors [2], obesity also results in endothelial dysfunction, a key factor in the development of atherosclerosis [3—5], and coronary microvascular dysfunction [6]. In people with severe obesity, bariatric surgery (BS) is effective in obtaining weight loss and has been shown to reduce cardiovascular events [7,8]. We previously showed that BS improves endothelial and coronary microvascular function at short-term follow-up [3]. In this study we investigated whether these effects are maintained at long term.

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Table 1 Main clinical findings at baseline and at follow-up of the 19 patients included in the study.

	Baseline	3-month FU	4-year FU	P
Hypertension	5 (26%)	3 (16%)°	4 (21%)	0.73
Hypercholesterolemia	5 (26%)	4 (21%)°	1 (10%)	0.21
Active smoking	7 (36%)	5 (26%)°	6 (31%)	0.78
Anthropometric variables				
Weight (kg)	129.3 ± 27	101.1 ± 23.8*	81.5 ± 21*,°	<0.001
Body mass index (kg/m^2)	47.7 ± 6.2	37.11 ± 5.7*	29.7 ± 6.3*,°	<0.001
Drug therapy				
Beta blockers	1 (5%)	0	0	0.36
Calcium antagonists	1 (5%)	1 (5%)°	1 (5%)°	1.0
ACE-inhibitors/ARBs	4 (21%)	3 (16%)°	2 (10%)°	0.67
Diuretics	4 (21%)	2 (10%)°	2 (10%)°	0.56

ACE = angiotensin converting enzyme; ARBs = angiotensin receptor blockers.
* $p < 0.01$ vs. baseline.
° $p < 0.01$ vs. 3 months.

Fifty people with severe obesity (38 ± 9 years, 37 females), undergoing BS (Roux-en-Y gastric bypass in 45, biliopancreatic diversion in 3), were originally enrolled in our study [3]. Patients had no evidence of cardiovascular or other relevant disease, including diabetes, and were studied at baseline and 3 months after BS. All patients were invited to participate in the present follow-up study, and, in those who agreed, clinical conditions were reassessed and vascular tests performed after appropriate pharmacological washout.

Endothelium-dependent and endothelium-independent dilator function was assessed by flow-mediated dilation (FMD) and nitrate-mediated dilation (NMD), respectively [3,9]. After at least 10 min of rest in supine position, the right brachial artery was imaged by a 10 MHz multi-frequency linear array probe attached to a high-resolution ultrasound machine (Acuson Sequoia, Siemens S.p.A., Milan, Italy). After obtaining baseline images, a forearm cuff was inflated to 250 mmHg and released after 5 min to induce reactive hyperhaemia. Brachial artery diameter was measured using an automated edge-detection software system. FMD was calculated as the maximum percent change of the artery diameter during hyperhaemia compared to baseline. After recovery to baseline, sublingual glyceryl trinitrate (25 μg) was administered and NMD calculated as the maximum percent change of the brachial artery diameter compared to baseline.

Endothelium-independent and endothelium-dependent coronary microvascular function was assessed by coronary blood flow (CBF) response to adenosine and cold pressor test (CPT), respectively. Subjects were positioned in left lateral decubitus; the left anterior descending coronary artery was imaged by a 7 MHz transducer connected to an echocardiographic machine (Acuson Sequoia, Siemens S.p.A., Milan, Italy) and blood flow was interrogated using color-Doppler mapping. After obtaining basal CBF velocity, intravenous adenosine (140 μg/kg/min) was given for 90 s and CBF velocity was measured at peak infusion. After 15 min, a new basal CBF velocity was obtained and CPT (patient's left hand in ice for 120 s) was performed; CBF velocity was measured at the end of the test. Coronary microvascular dilation was measured as the ratio of CBF velocity at peak of each test to the respective basal value [10].

Continuous variables were compared by repeated measure analysis of variance and proportions by chi-square test. Multiple comparisons were done by paired t-test and McNemar test, respectively, and results corrected with Bonferroni rule. Correlations were assessed by Pearson test. Data are reported as mean ± standard deviation. Statistical significance was considered for $p < 0.05$.

Of 50 patients enrolled in the original study [3], 19 (38%) agreed to undergo follow-up investigation at 4 ± 1.5 years from BS (40 ± 8 years, 17 females). A Roux-en-Y gastric bypass and a bilipopancreatic diversion had been performed in 18 and 1 patients, respectively. There were no significant differences in clinical characteristics and vascular test results between patients who agreed to participate and those who declined (data not shown).

Table 1 shows the main characteristics of patients at baseline and follow-up. Compared to baseline, during follow-up there was a sustained weight reduction and improvement of cardiovascular risk profile. The results of vascular tests are summarised in Table 2. FMD and CBF response to adenosine and CPT showed sustained improvement