

Letters

RESEARCH LETTER

Thromboxane-Dependent Platelet Activation After Gastric Banding for Obesity

Laparoscopic adjustable gastric banding (LAGB) is associated with persistent weight reduction but variable health outcomes.¹ The molecular heterogeneity of obesity may lead to substantial variability among its specific subtypes.² In severe obesity, bariatric surgery is the only treatment that results in considerable, persistent weight loss. Compared with usual care, bariatric surgery reduced cardiovascular events among obese adults.³ We demonstrated in vivo platelet activation in obese women free from other cardiovascular risk factors.⁴ Moreover, visceral obesity was characterized by systemic inflammation and enhanced lipid peroxidation. A substantial reduc-

tion of this mechanistic chain of events was achieved with a successful weight loss program.⁴ Our study investigated whether platelet activation and oxidative stress were persistently modulated by LAGB in nondiabetic, normotensive obese participants.

Methods | Thirteen consecutive obese patients who were 18 years of age or older and scheduled to undergo LAGB were enrolled. Exclusion criteria were clinical evidence of cardiovascular disease, cancer, or altered liver or renal function, as well as treatment with lipid-lowering, antidiabetic, anti-inflammatory, antioxidant, or antithrombotic drugs. Patients were evaluated at baseline and after 3, 6, and 12 months. Overnight urine samples were obtained immediately before obtaining blood samples. Urinary 8-iso-prostaglandin F_{2α} (PGF_{2α})

Table. Clinical and Laboratory Characteristics of 13 Severely Obese Patients Before LAGB and 3, 6, and 12 Months After LAGB^a

Variable	Before LAGB	3 mo After LAGB	6 mo After LAGB	12 mo After LAGB	P Value ^b
Body weight, kg	118 (102-132)	111 (95-125)	104 (90-114)	96 (86-109)	<.001
BMI	43.6 (39.6-44.2)	41.4 (36.2-42.3)	36.8 (35.3-41)	35.2 (33.2-36.8)	<.001
Body fat, %	45 (41-46)	NA	42 (40-45)	40 (38-44)	.04
Excess weight, kg	49.1 (38.6-56.4)	45.2 (33.3-50.2)	32.7 (28.4-43.4)	26.8 (22.0-35.2)	<.001
Excess weight loss, %	NA	10.8 (9.3-28.2)	24.4 (15.3-36.6)	32.2 (25.0-48.3)	<.001
Waist, cm	128 (113-131)	124 (110-126)	115 (109-132)	113 (102-117)	<.001
Blood pressure, mm Hg					
Systolic	140 (130-150)	130 (120-140)	120 (115-140)	110 (110-120)	<.001
Diastolic	90 (80-95)	80 (80-85)	80 (80-80)	70 (70-80)	<.001
Cholesterol, mg/dL					
Total	184 (174-197)	NA	178 (170-187)	160 (150-170)	<.001
HDL	43 (39-46)	NA	48 (40-55)	50 (48-57)	.002
LDL	110 (101-118)	NA	106 (91-112)	93 (78-103)	<.001
Triglycerides, mg/dL	170 (113-196)	NA	110 (89-150)	80 (73-110)	<.001
Plasma glucose, mg/dL					
Fasting	109 (92-119)	NA	98 (88-105)	92 (80-100)	<.001
Postprandial	133 (112-193)	NA	118 (110-120)	112 (110-120)	.04
Impaired glucose tolerance, No. (%)	3 (23.1)	NA	1 (7.7)	1 (7.7)	.99
Type 2 diabetes mellitus, No. (%)	3 (23.1)	NA	1 (7.7)	0 (0.0)	.99
HOMA-IR index	4.9 (4.0-8.3)	NA	3.9 (3.1-5.9)	3.5 (2.2-4.4)	<.001
Basal metabolic rate, kcal/d	2134 (1858-2417)	NA	1815 (1680-2045)	1804 (1784-1971)	.009
C-reactive protein, mg/dL	2.3 (1.8-2.4)	1.8 (1.5-2)	1.8 (1.4-1.9)	1.6 (1.2-1.8)	<.001
Excretion rate, pg/mg of creatinine					
U-8-iso-PGF _{2α}	893 (776-927)	718 (657-798)	604 (508-683)	485 (442-505)	<.001
U-11-dehydro-TXB ₂	1447 (1113-1791)	959 (760-1124)	674 (547-996)	571 (427-707)	<.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL, high-density lipoprotein; LAGB, laparoscopic adjustable gastric banding; LDL, low-density lipoprotein; NA, not available; HOMA-IR, homeostatic model assessment of insulin resistance; U-8-iso-PGF_{2α}, urinary 8-iso-prostaglandin F_{2α}; U-11-dehydro-TXB₂, urinary 11-dehydro-thromboxane B₂.

SI conversion factors: To convert total, HDL, and LDL cholesterol to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter,

multiply by 0.0113; to convert fasting and postprandial plasma glucose to millimoles per liter, multiply by 0.0555; and to convert C-reactive protein to nanomoles per liter, multiply by 9.524.

^a Data are median (interquartile range) values, unless otherwise indicated. There were 7 male and 6 female patients.

^b Determined by use of the Friedman test.

and 11-dehydro-thromboxane B₂ (TXB₂) excretion rates were measured as previously described.⁴ The study protocol was approved by the local ethics committee, and patients provided written informed consent.

The effects of LAGB surgery were assessed using Friedman and Wilcoxon tests for paired samples. The Spearman rank correlation test and stepwise multiple linear regression analysis (using log-transformed data) were performed to assess variables associated with urinary 11-dehydro-TXB₂ excretion rates. Two-sided *P* values of less than .05 were considered to be statistically significant.

Results | The clinical and laboratory characteristics of the participants are shown in the **Table**. Lipid peroxidation (8-iso-PGF_{2α}) and platelet activation (11-dehydro-TXB₂), as well as C-reactive protein levels, progressively decrease at any time point following LAGB, with significant correlation among the 3 variables (*P* = .001). By pooling data from each time point after LAGB, we found that changes in urinary 8-iso-PGF_{2α} and 11-dehydro-TXB₂ excretion were significantly correlated ($\rho = 0.67$, *P* < .001). Moreover, both changes were significantly related to the amount of weight lost and to changes in body mass index, waist circumference, fasting plasma glucose level, and high-density lipoprotein cholesterol level. Changes in the homeostatic model assessment of insulin resistance (HOMA-IR) index correlated with changes in 11-dehydro-TXB₂ ($\rho = 0.466$, *P* = .02).

A multiple regression analysis of pooled data from baseline and 6 and 12 months after LAGB indicates that only the 8-iso-PGF_{2α} excretion rate ($\beta = 0.611$, *t* = 6.03, *P* < .001) and the HOMA-IR index ($\beta = 0.385$, *t* = 3.81, *P* = .001) can predict the rate of 11-dehydro-TXB₂ excretion, independent of body mass index, waist circumference, serum lipid levels, fasting plasma glucose levels, postprandial plasma glucose levels, fat mass, and C-reactive protein levels (adjusted *R*² = 0.665, *P* = .001).

Discussion | We previously identified a novel mechanism through which obesity may affect cardiovascular morbidity and mortality (namely, thromboxane-dependent platelet activation).⁵ Moreover, we established that isoprostanes may be a link between obesity and platelet activation. Notably, a 10% reduction in body weight, obtained through a successful diet-induced weight loss program, was associated with more than a 50% reduction in thromboxane biosynthesis.⁴

In our study, the rates of 8-iso-PGF_{2α} and 11-dehydro-TXB₂ excretion were significantly reduced 12 months after LAGB (by approximately 45% and approximately 60%, respectively), correlated with an approximately 18% decrease in body weight and with a concomitant decrease (~30%) in the level of C-reactive protein, a marker of systemic inflammation. However, because severe obesity is characterized by a very high rate of thromboxane biosynthesis, all but 4 values of thromboxane metabolite excretion did not return to the normal range 12 months after LAGB.

Moreover, weight loss following the surgical procedure significantly affected the fasting plasma glucose level, the postprandial plasma glucose level, and insulin sensitivity in our

obese participants. Thus, the HOMA-IR index and the 8-iso-PGF_{2α} excretion rate were the only predictors of the rate of thromboxane biosynthesis.

In conclusion, LAGB ameliorates the vicious cycle of inflammation, oxidative stress, and thromboxane-dependent platelet activation in obesity. However, the incomplete normalization of thromboxane biosynthesis in the majority of the obese participants may support the concept that different genotypic/phenotypic subtypes of obesity may exist.

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ASSOCIATION OF VA SURGEONS

Ultrasonography-Guided Identification With Methylene Blue Tattooing of the Ilioinguinal Nerve for Neurectomy for Chronic Pain: A Case Series

Chronic ilioinguinal pain is a common but morbid complication of inguinal herniorrhaphy for 12% to 62% of patients.¹ Although pharmacologic options exist (such as nerve blocks), long-term pain relief is inferior to surgical neurectomy.^{2,3} We present our experience in ilioinguinal neurectomy with preoperative ultrasonography-guided identification and perineural injection of methylene blue to tattoo the nerve.