1.15 (1.08 to 1.22), 1.53 (1.42 to 1.64), and 1.40 (1.33 to 1.48), respectively. In the multivariate model adjusted for age, sex, comorbid risk, and concomitant diuretics and beta-blockers, statin therapy was independently associated with the risk of diabetes occurrence (hazard ratio: 1.13 [95% confidence interval: 1.07 to 1.20], $p < 0.001$).

Statin therapy has been associated with excessive occurrence of diabetes in subjects with unfavorable metabolic profiles (4,5). Beyond that, it is particularly important to investigate whether the risk would be further amplified by the concomitant treatment targeting those factors to decide the treatment matrix for future patients.

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REFERENCES

1. Wang KL, Liu CJ, Chao TF, et al. Statins, risk of diabetes, and implications on outcomes in the general population. J Am Coll Cardiol 2012;60:1231–8.
2. Taylor EN, Hu FB, Curhan GC. Antihypertensive medications and the risk of incident type 2 diabetes. Diabetes Care 2006;29:1065–70.
3. Mancia G, Grassi G, Zanchetti A. New-onset diabetes and antihypertensive drugs. J Hypertens 2006;24:3–10.
4. Waters DD, Ho JE, DeMicco DA, et al. Predictors of new-onset diabetes in patients treated with atorvastatin: results from 3 large randomized clinical trials. J Am Coll Cardiol 2011;57:1535–45.
5. Ridker PM, Pradhan A, MacFadyen JG, Libby P, Glynn RJ. Cardiovascular benefits and diabetes risks of statin therapy in primary prevention: an analysis from the JUPITER trial. Lancet 2012;380:565–71.

Slimming the Heart With Bariatric Surgery

We read with interest the paper by Gaborit et al. (1) describing the effects of bariatric surgery on epicardial fat and myocardial triglyceride content (MTGC). One of the authors' main conclusions is that a reduction in epicardial fat may be partially responsible for the decrease in cardiac mortality observed after successful weight-loss surgery because ectopic cardiac fat releases inflammatory mediators and free fatty acids into the vasculature (1). The study also demonstrates a decrease in systemic insulin resistance and improvement in diastolic function after bariatric surgery. We have made similar observations (2–4) and wish to offer a somewhat different interpretation, which should complement the authors' well-designed study. In patients with clinically severe obesity and insulin resistance, we observed a negative association between the plasma levels of long-chain free fatty acids and diastolic function and suggest that excess free fatty acids exert lipotoxic effects on the heart, leading to impairment in intracellular calcium cycling and cardiac function (2). Thus, one may reasonably conclude that the improvement in cardiac function after bariatric surgery is directly related to a decrease in lipotoxicity. However, no considerable change in MTGC was appreciated in the authors' study through the use of magnetic resonance spectroscopy despite a statistically significant decrease in epicardial fat and serum triglyceride levels. One plausible explanation involves the modality used in the measurement of MTGC. The practical method used to determine MTGC is a conventional technique known as voxel positioning in the ventricular septum to avoid contamination from epicardial fat and lessen the degree of artifact from cardiac motion. Nonetheless, the distribution of triglycerides in the human heart is heterogeneous in nature; thus, the conventional approach does not correlate well with overall cardiac steatosis (5).

After successful bariatric surgery, our studies also show a remarkable decrease in increased plasma free fatty acid levels, as well as improved derangements in muscle metabolism and cardiac function (3). Moreover, even as other hallmarks of obesity, such as insulin resistance, free fatty acid levels, body composition, and body mass index, have a tendency to plateau postoperatively, the benefits of successful weight-loss surgery on left ventricular mass are sustained and show a linear decrease over a 2-year period (4).

In short, our earlier work adds to the authors' remarkable study on the effects of weight loss after bariatric surgery on cardiac function. We propose that by targeting the source of excess energy, weight-loss surgery reduces left ventricular mass and improves overall cardiac function by limiting the substrate supply to a metabolically overloaded heart (6). The decrease in epicardial fat volume after weight loss likely plays a key role in decreasing fatty acid fuel to the heart, further reducing lipotoxicity. There is much more to be gained from this fascinating area of research.

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REFERENCES

1. Gaborit B, Jacquier A, Kober F, et al. Effects of bariatric surgery on cardiac ectopic fat: lesser decrease in epicardial fat compared to visceral fat loss and no change in myocardial triglyceride content. J Am Coll Cardiol 2012;60:1381–9.
2. Leichman JG, Aguilar D, King TM, Vlada A, Reyes M, Taegtmeyer H. Association of plasma free fatty acids and left ventricular diastolic function in patients with clinically severe obesity. Am J Clin Nutr 2006;84:336–41.
3. Leichman JG, Wilson EB, Scarborough T, et al. Dramatic reversal of derangements in muscle metabolism and diastolic left ventricular function after bariatric surgery. Am J Med 2008;121:966–73.
4. Algahim MF, Lux TR, Leichman JG, et al. Progressive regression of left ventricular hypertrophy two years after bariatric surgery: an unexpected dissociation with the body mass index. Am J Med 2010;123:549–55.
5. Liu C, Redheuil1 A, Steenbergen C, et al. Measurement of myocardial triglyceride content by magnetic resonance spectroscopy in transplant native heart autopsies. J Cardivasc Mag Reson 2010;12 Suppl 1:P125.

6. Algahim MF, Sen S, Taegtmeyer H. Bariatric surgery to unload the stressed heart: a metabolic hypothesis. Am J Physiol Heart Circ Physiol 2012;302:H1539–45.

Reply

We read with interest the letter by Drs. Khalaf and Taegtmeyer (1), which nicely emphasizes the importance of research on thinning the heart with bariatric surgery (BS). Improvement of cardiac function after BS has been widely described, but Taegtmeyer's group (2) has remarkably shown that left ventricular (LV) mass continues to improve 24 months after surgery, whereas body mass index (BMI) and metabolic parameters have started to plateau. We agree that the regression of cardiac abnormalities after BS is complex, sequential, and of a multifactorial nature. The chronological sequence of events after BS is thus crucial to examine. We and others (3) have previously shown that one of the first events after surgery is the improvement of the adipose tissue inflammatory pattern, which in turn may contribute to reduced muscular and heart insulin resistance. This decrease in low-grade inflammation could be partly linked to the rapid adaptation of gut microbiota to starvation and weight loss (4). This rapid decrease in inflammation and insulin resistance is associated 3 months after surgery with a favorable change in LV function, whereas BMI is still very high (5). The increase in incretin levels and particularly glucagon-like peptide 1 may also participate in the improvement of endothelial function and cardiac parameters. Although the metabolic and hormonal shifts are very sudden, the impact of weight loss on sympathetic tone and sleep apnea is more gradual and may be involved in the sustained recovery of cardiac function. We agree that the lack of a decrease in myocardial triglyceride content (MTGC) 6 months after surgery was unexpected, which suggests that MTGC is not the sole mediator of cardiac function recovery. As the imbalance between fatty acid uptake and oxidation leads to accumulation of intramyocellular triglycerides, one should reasonably expect that the decrease in free fatty acid (FFA) supply would lead to a decrease in MTGC. However, according to the "starvation theory," a persistent lack of FFA supply in a previously overloaded heart may initially trigger mechanisms of energy preservation, protecting the heart against a lack of energy substrate and preventing it from removing intracellular lipid storage. An alternative explanation would be that a more prolonged weight loss is required to change MTGC to a measurable extent and that our assessment was too early. Indeed, the decrease in intramuscular lipid content was previously shown to occur at later time points and reach significance only after 9 months (5). Regarding the heterogeneity of cardiac steatosis proposed by Khalaf et al. and the position of the voxel used in our study (interventricular septum), we intentionally chose this location because it is distant from epicardial fat. Moreover, Liu et al. (6), as cited by Khalaf et al. (1), recently demonstrated that septal fat is representative of a mean myocardial fat percentage.

To summarize, further cinetic studies with long-term follow-up are needed to evaluate the sequence of ectopic fat storage and removal after bariatric surgery.

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REFERENCES

1. Gaborit B, Jacquier A, Kober F, et al. Effects of bariatric surgery on cardiac ectopic fat: lesser decrease in epicardial fat compared to visceral fat loss and no change in myocardial triglyceride content. J Am Coll Cardiol 2012;60.1381–9.
2. Algahim MF, Lux TR, Leichman JG, et al. Progressive regression of left ventricular hypertrophy two years after bariatric surgery: an unexpected dissociation with the body mass index. Am J Med 2010;123:549–55.
3. Cancello R, Henegar C, Viguerie N, et al. Reduction of macrophage infiltration and chemoattractant gene expression changes in white adipose tissue of morbidly obese subjects after surgery-induced weight loss. Diabetes 2005;54:2277–86.
4. Furet JP, Kong LC, Tap J, et al. Differential adaptation of human gut microbiota to bariatric surgery-induced weight loss: links with metabolic and low-grade inflammation markers. Diabetes 2010;59:3049–57.
5. Leichman JG, Wilson EB, Scarborough T, et al. Dramatic reversal of derangements in muscle metabolism and diastolic left ventricular function after bariatric surgery. Am J Med 2008;121:966–73.
6. Liu CY, Liu YC, Venkatesh BA, et al. Heterogeneous distribution of myocardial steatosis–an ex vivo evaluation. Magn Reson Med 2012;68:1–7.