statistical power to detect an effect on clinical outcomes. Similar findings in Thailand[1] and the results of numerous epidemiologic studies confirm the importance of multivitamins in persons with HIV infection.[2] In light of the evidence accumulated to date, the next trial involving persons in the early stages of HIV disease ought to examine the role of other nutrients that were not included in our regimen, such as selenium.[3] The safety and efficacy of vitamin and mineral supplementation among persons who have more advanced disease and who are receiving antiretroviral therapy are also important issues that will need to be examined.

Wafaie W. Fawzi, M.B., B.S., Dr.P.H.

Harvard School of Public Health
Boston, MA 02115
mina@hsph.harvard.edu

Gernard I. Msamanga, M.D., Sc.D.

Muhimbili University College of Health Sciences
Dar es Salaam, Tanzania

David J. Hunter, M.B., B.S., Sc.D.

Harvard School of Public Health
Boston, MA 02115

1. Jiamton S, Pepin J, Suttent R, et al. A randomized trial of the impact of multiple micronutrient supplementation on mortality among HIV-infected individuals living in Bangkok. AIDS 2003;17:2461-9.
2. Fawzi WW. Micronutrients and human immunodeficiency virus type 1 disease progression among adults and children. Clin Infect Dis 2003;37:Suppl 2:S112-S116.
3. Baum MK, Shor-Posner G, Lai S, et al. High risk of HIV-related mortality is associated with selenium deficiency. J Acquir Immune Defic Syndr Hum Retrovirol 1997;15:370-4.

Metabolic Effects of Liposuction — Yes or No?

TO THE EDITOR: Klein and colleagues (June 17 issue)[1] report an absence of effects of abdominal liposuction on cardiovascular risk factors, inflammatory markers, and insulin resistance in obese women. We would suggest alternative explanations for their negative findings. The small number of subjects investigated (eight obese women without diabetes) and the limited length of follow-up (10 to 12 weeks) precluded the emergence of significant differences. We pooled data from our own studies[2-4] evaluating the effect of large-volume liposuction on markers of vascular inflammation and insulin resistance in 45 premenopausal obese women (mean [±SD] age, 37±4 years) who were followed for up to six months (Table 1, facing page). We selected women whose changes in body weight during the follow-up period were due only to the liposuction procedure. Only at six months was there a significant shift in inflammatory markers, which were significantly reduced, and antiinflammatory markers, which were significantly increased.

Katherine Esposito, M.D.

Second University of Naples
80021 Naples, Italy
katherine.esposito@unina2.it

Giovanni Giugliano, M.D.

University of Rome
00100 Rome, Italy

Dario Giugliano, M.D., Ph.D.

Second University of Naples
80021 Naples, Italy

1. Klein S, Fontana L, Young VL, et al. Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. N Engl J Med 2004;350:2549-57.
2. Ziccardi P, Nappo F, Giugliano G, et al. Reduction of inflammatory cytokine concentrations and improvement of endothelial functions in obese women after weight loss over one year. Circulation 2002;105:804-9.
3. Nicoletti G, Giugliano G, Pontillo A, et al. Effect of a multidisciplinary program of weight reduction on endothelial functions in obese women. J Endocrinol Invest 2003;26:RC5-RC8.
4. Giugliano G, Nicoletti G, Grella E, et al. Effect of liposuction on insulin resistance and vascular inflammatory markers in obese women. Br J Plast Surg 2004;57:190-4.

TO THE EDITOR: I do not agree with the conclusion that removal of about 10 kg of adipose-tissue mass alone fails to achieve the metabolic benefits of weight loss. It depends on what type of fat you remove.[1] My colleagues and I compared the removal of less than 1 kg of visceral fat in connection with bariatric surgery with bariatric surgery alone.[2] When the subjects were reinvestigated two years after surgery, we observed significant improvements in glucose tolerance, insulin sensitivity, and fasting plasma levels of glucose and insulin in the group receiving both visceral-fat removal and bariatric surgery, as compared with the group receiving bariatric surgery alone. Thus, it might be essential to remove visceral adipose tissue in order to obtain beneficial effects in obese patients. Visceral fat is directly connected to the liver by the portal system; therefore, the release of fatty acids and other regulatory factors to the portal vein may be decreased

after the removal of visceral fat, possibly leading to improved liver function. Such effects do not occur after the removal of subcutaneous fat.

Peter Arner, M.D., Ph.D.

Karolinska Institutet
SE-141 86 Stockholm, Sweden
peter.arner@medhs.ki.se

1. Arner P. Not all fat is alike. Lancet 1998;351:1301-2.
2. Thorne A, Lonnqvist F, Apelman J, Hellers G, Arner P. A pilot study of long-term effects of a novel obesity treatment: omentectomy in connection with adjustable gastric banding. Int J Obes Relat Metab Disord 2002;26:193-9.

TO THE EDITOR: Klein et al. report that abdominal liposuction in 15 overweight women did not produce any significant change in metabolic abnormalities associated with obesity. We analyzed the metabolic effects of ultrasound-assisted megalipoplasty in eight premenopausal obese women (mean [±SD] body-mass index [the weight in kilograms divided by the square of the height in meters], 42.0±7.0). Measurements of body composition with dual-energy x-ray absorptiometry, insulin resistance (with the homeostasis-model assessment method),[1] leptin, C-reactive protein, interleukin-6, resistin, and adiponectin were taken before and 1, 3, 28, and 180 days after ultrasound-assisted megalipoplasty.

Ultrasound-assisted megalipoplasty reduced fat mass from 48.9±10.2 kg to 41.0±8.1 kg at day 3,

Table 1. Effects of Large-Volume Liposuction on Body Weight, Insulin Resistance, Blood Lipid Levels, and Cytokine Levels in 45 Premenopausal Obese Women.*

Characteristic	Baseline	Change at 3 Mo (95% CI)	Change at 6 Mo (95% CI)	P Value at 6 Mo
Weight (kg)	91.3±8.2	−4.5 (−6.1 to −3.5)	−4.8 (−6.7 to −2.8)	0.003
Body-mass index	35.1±2.9	−1.8 (−2.6 to −1.1)	−1.9 (−2.7 to −1.2)	0.01
Waist (cm)	100.3±9.2	−6.1 (−8.5 to −3.4)	−6.0 (−8.7 to −2.2)	0.01
HOMA	4.5±0.7	−1.2 (−2.1 to −0.4)	−1.3 (−2.2 to −0.5)	0.01
Total cholesterol (mg/dl)	195±29	−14 (−25 to −3)	−16 (−30 to −2)	0.045
Triglycerides (mg/dl)	159±57	−24 (−40 to −7)	−27 (−49 to −5)	0.04
Inflammatory markers				
C-reactive protein (mg/liter)				
Median	3.1	−0.4 (−0.9 to 0.3)	−0.6 (−1.0 to −0.2)	0.045
Interquartile range	1.5 to 8.1	—	—	
Tumor necrosis factor α (pg/ml)				
Median	5.3	−0.6 (−1.2 to 0)	−0.9 (−1.7 to 0.2)	0.04
Interquartile range	2.1 to 10.2	—	—	
Interleukin-6 (pg/ml)				
Median	4.2	−0.4 (−1.2 to 0.5)	−0.7 (−1.3 to 0.1)	0.05
Interquartile range	1.5 to 8.4	—	—	
Interleukin-18 (pg/ml)				
Median	240	−17 (−35 to 2)	−29 (−52 to −6)	0.04
Interquartile range	168 to 295	—	—	
Antiinflammatory markers				
Adiponectin (μg/ml)	5.3±2.1	0.4 (−0.2 to 1.0)	0.9 (0.2 to 1.8)	0.04
Interleukin 10 (pg/ml)				
Median	2.0	0.5 (−0.4 to 1.9)	0.9 (0.2 to 1.6)	0.045
Interquartile range	0.5 to 4.5	—	—	

* Plus–minus values are means ±SD. CI denotes confidence interval, and HOMA homeostasis-model assessment of insulin sensitivity (plasma glucose, in millimoles per liter, times serum insulin, in microunits per milliliter, divided by 25). Dashes denote not applicable. The body-mass index is the weight in kilograms divided by the square of the height in meters. To convert the values for cholesterol to millimoles per liter, multiply by 0.0259. To convert the values for triglycerides to millimoles per liter, multiply by 0.0113.

and no further changes were seen. The greatest amounts of fat were removed from the lower limbs. The changes in insulin resistance and cytokine levels after the procedure are depicted in Figure 1. An acute reduction in insulin sensitivity occurred postoperatively, with related changes in the adipocytokines involved in insulin action. In the recovery phase, we observed improvement in insulin resis-

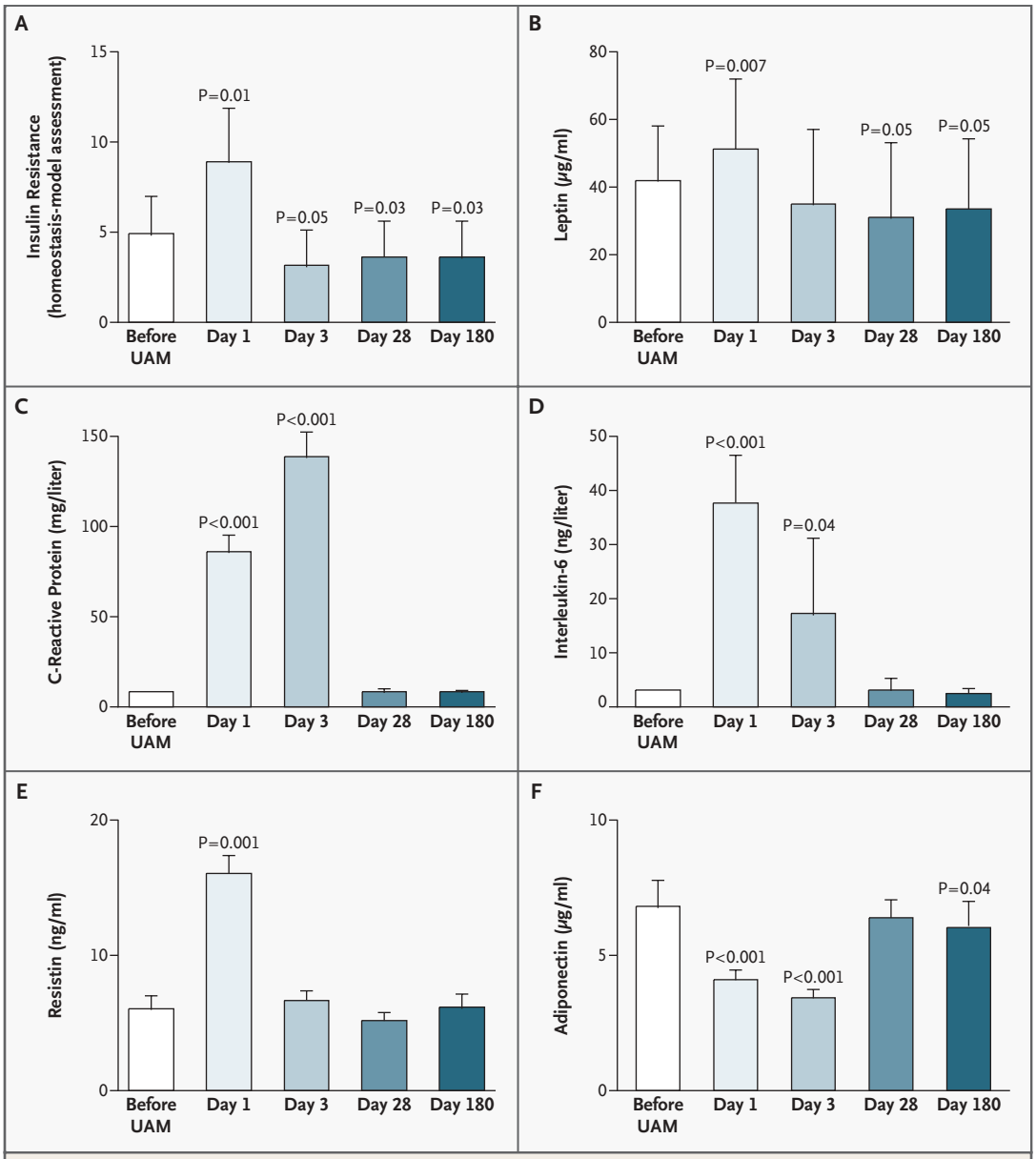

Figure 1. Insulin Resistance and Cytokine Levels in Eight Premenopausal Obese Women with Peripheral Fat Distribution, before and after Ultrasound-Assisted Megalipoplasty (UAM).

P values were determined with the use of the paired Student's t-test and are for the comparisons with the values before the megalipoplasty procedure. I bars indicate standard deviations.

tance in association with a reduction in leptin levels, consistent with loss of fat mass, as reported by others.[2] We suggest that the metabolic effects of ultrasound-assisted megalipoplasty may be influenced by fat distribution and the length of follow-up.

Luca Busetto, M.D.
Franco Bassetto, M.D.
University of Padua
35128 Padua, Italy
luca.busetto@unipd.it
Maria L. Nolli, M.D.
University Hospital of Padua
35128 Padua, Italy

1. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-9.
2. Giugliano G, Nicoletti G, Grella E, et al. Effect of liposuction on insulin resistance and vascular inflammatory markers in obese women. Br J Plast Surg 2004;57:190-4.

DR. KLEIN REPLIES: Dr. Arner proposes that the removal of visceral fat should improve insulin sensitivity because visceral fat releases fatty acids into the portal vein, delivering them directly to the liver and perhaps inhibiting insulin action.[1] However, visceral fat is probably not a major factor in the pathogenesis of insulin resistance, because the proportion of fatty acids in the portal vein that are derived from lipolysis of visceral fat (about 20 percent) is much less than the proportion derived from subcutaneous fat (about 80 percent) in obese persons.[2,3] Moreover, few fatty acids released from visceral fat (about 14 percent) are ever "seen" by skeletal muscle, because they are metabolized by the liver and do not enter the systemic circulation. In the elegant study conducted by Dr. Arner and his colleagues,[4] greater weight loss, rather than the removal of visceral fat, may have been responsible for most of the differences in insulin sensitivity observed between the groups after bariatric surgery; patients who underwent omentectomy plus gastric banding lost about 9 kg more than those who underwent gastric banding alone.

Dr. Esposito and colleagues suggest that our follow-up studies may have been conducted too soon after liposuction to detect metabolic benefits. However, most of the beneficial metabolic effects observed in their patients were already present three months after liposuction, which is the same time our studies were performed. In addition, we found that liposuction did not improve glucose metabolism six months after surgery. Plasma glucose and insulin concentrations during an oral glucose-tolerance test performed six months after liposuction were the same as those before liposuction (unpublished data). Therefore, the timing of our follow-up studies does not explain why we did not see metabolic benefits. We made a considerable effort to prevent changes in lifestyle that often occur when patients become "motivated" after liposuction, because even small changes in diet and activity can improve insulin sensitivity.

Most of the data presented by Dr. Busetto and colleagues at 180 days after liposuction, such as plasma leptin, C-reactive protein, and interleukin-6 concentrations, are consistent with our results. Surprisingly, insulin resistance, determined by the homeostasis-model assessment of insulin sensitivity, decreased within three days after liposuction in their patients, despite an increase in inflammatory markers and a decrease in plasma adiponectin concentration, changes that are normally associated with an increase in insulin resistance. However, the homeostasis-model assessment is not as reliable a measure of insulin sensitivity as is the euglycemic–hyperinsulinemic clamp procedure performed in our study.

Samuel Klein, M.D.
Washington University School of Medicine
St. Louis, MO 63110

1. Boden G. Role of fatty acids in the pathogenesis of insulin resistance and NIDDM. Diabetes 1997;46:3-10. [Erratum, Diabetes 1997;46:536.]
2. Nielsen S, Guo ZK, Johnson CM, Hensrud DD, Jensen MD. Splanchnic lipolysis in human obesity. J Clin Invest 2004;113:1582-8.
3. Klein S. The case of visceral fat: argument for the defense. J Clin Invest 2004;113:1530-2.
4. Thorne A, Lonnqvist F, Apelman J, Hellers G, Arner P. A pilot study of long-term effects of a novel obesity treatment: omentectomy in connection with adjustable gastric banding. Int J Obes Relat Metab Disord 2002;26:193-9.