

Outcome Success in Obesity

Samuel Klein

Abstract

KLEIN, SAMUEL. Outcome success in obesity. *Obes Res.* 2001;9:354S–358S.

Intentional weight loss improves many of the medical complications associated with obesity. Moreover, many of these beneficial effects have a dose-dependent relationship with the amount of weight lost and begin after only modest weight losses of 5% to 10% of initial body weight. There is no conclusive evidence that weight loss decreases mortality in obese people. The therapeutic effect of weight loss on risk factors for cardiovascular disease (insulin resistance and diabetes, dyslipidemia, and hypertension) has received the most attention in clinical trials. The hazard of developing coronary heart disease is directly related to the concomitant burden of risk factors. Modest weight loss can affect the entire cluster of risk factors simultaneously. Both negative energy balance and weight loss improve insulin sensitivity and glycemic control in obese patients with type 2 diabetes. Most studies have found that weight loss decreases serum triglyceride, total cholesterol, and low-density lipoprotein cholesterol concentrations and increases serum high-density lipoprotein cholesterol concentration. Regain of weight leads to relapse in triglyceride and cholesterol concentrations. Weight loss, independent of sodium restriction, decreases systolic and diastolic blood pressure. Dietary intervention is the cornerstone of weight-loss therapy. Most diets proposed for losing weight vary in two principal dimensions: energy content and macronutrient composition. Manipulation of food macronutrient content, energy density, and portion size can help decrease energy intake and facilitate weight loss.

Key words: outcome, quality of life, cardiovascular disease, type 2 diabetes, medical complications

Introduction

Obesity causes a number of serious medical complications that impair health and lead to premature mortality.

Weight loss is an important goal for obese patients because it ameliorates or eliminates many of the medical illnesses associated with obesity and can prevent the development of new obesity-related diseases. This article will review the effect of weight loss on obesity-related disease and survival outcomes.

Cardiovascular Disease

Obesity is associated with several risk factors for coronary heart disease (CHD). The risk of CHD is directly proportional to the number of risk factors. Data from the Framingham Offspring Study found that modest weight loss can affect a cluster of risk factors simultaneously (1). A weight loss of ≥ 2.25 kg over 16 years was associated with a 40% to 50% reduction in the sum of risk factors (systolic blood pressure, serum triglyceride, serum total cholesterol, fasting blood glucose, and lowest quintile of high-density lipoprotein [HDL] cholesterol) in men and women. Weight loss may also decrease the progression of atherosclerosis. The progression of carotid artery intimal wall thickness, assessed by B-mode ultrasound over 4 years, was three times higher in obese subjects who maintained their body weight than in those who lost 19% of their body weight after gastric surgery (2).

Type 2 Diabetes

Acute energy restriction and weight loss have been shown to improve insulin sensitivity with respect to glucose metabolism in obese patients with type 2 diabetes. There is a considerable decrease in blood glucose and an increase in insulin-mediated glucose uptake shortly after beginning a low-calorie diet, before much weight loss has occurred (Figure 1) (3,4). Modest long-term weight loss also improves glycemic control. As little as a 5% weight loss can decrease fasting blood glucose, insulin, and hemoglobin A1c concentrations and medication requirements in obese patients with type 2 diabetes (Figure 2) (5). Greater amounts of weight loss result in greater improvement in glycemic control. In one study, >80% of obese patients with type 2 diabetes who lost $\sim 30\%$ of initial body weight after gastric bypass surgery achieved normal fasting blood glucose, insulin, and glycosylated hemoglobin concentrations (6).

Center for Human Nutrition, Washington University School of Medicine, St. Louis, Missouri.

Dr. Samuel Klein, Washington University School of Medicine, 660 South Euclid Avenue, Box 8031, St. Louis, MO 63110-1093. E-mail: sklein@imgate.wustl.edu
Copyright © 2001 NAASO

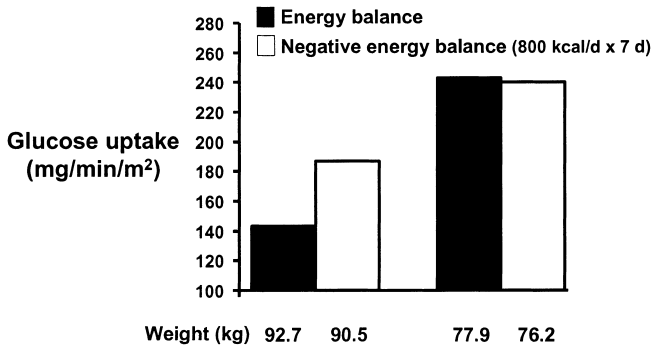


Figure 1: The effect of energy balance and weight loss on insulin sensitivity in type 2 diabetes. Adapted from Kelly et al. (4).

Long-term weight loss also prevents the onset of diabetes in obese people without diabetes (7–9). During a 16-year observation period, data from the Framingham Study found that the risk of diabetes decreased by one-third in those who lost 3.7 to 6.8 kg, and by one-half in those who lost >6.8 kg (8). Weight loss achieved by gastric surgery was associated with a 5-fold decrease in the risk of diabetes during an 8-year period of observation after surgery (9).

Hypertension

Weight loss decreases systolic and diastolic blood pressure (10). Data from the Trials of Hypertension Prevention Phase II found a dose-response relationship between weight loss and blood pressure at 36 months of treatment (11). An average weight loss of 8.8 kg was associated with a reduction of 7 mm Hg systolic and 5 mm Hg diastolic blood pressure, a loss of 2.6 kg was associated with a reduction of 4.5 mm Hg systolic and 2.5 mm Hg diastolic blood pressure, and a loss of 0.1 kg was associated with an reduction of 2.0 mm Hg systolic without a change in diastolic blood pressure. However, long-term improvement in blood pressure was not achieved in subjects who achieved initial weight loss but later regained most or all of their lost weight. Marked weight loss induced by gastric surgery has been shown to improve or completely resolve hypertension in approximately two-thirds of patients (12,13). However, the results from an 8-year prospective controlled trial of surgically induced weight loss found that the beneficial effect of weight loss on blood pressure is not permanent. The decrease in blood pressure observed during the first 2 years after surgery was no longer evident by 3 years, and blood pressure continued to increase for the next 5 years (9).

Dyslipidemia

Data from most studies demonstrate that weight loss decreases serum triglyceride, total cholesterol, and low-density lipoprotein (LDL) cholesterol concentrations and increases serum HDL cholesterol concentration (14,15).

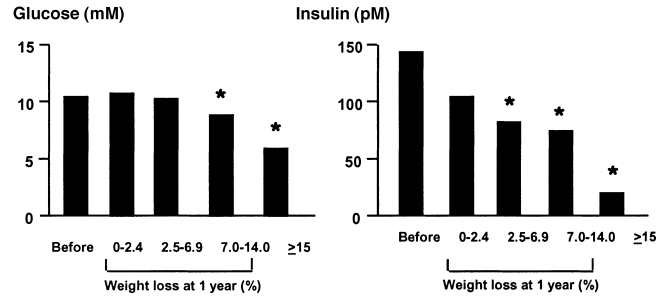


Figure 2: The relationship between weight loss and glycemic control in patients with type 2 diabetes. Adapted from Wing et al. (5). *Value is different from control value, $p < 0.01$.

The improvement in serum lipids is directly related to the amount of weight lost, and weight regain leads to increased triglyceride and cholesterol concentrations (16–19). The largest changes in serum triglyceride, total cholesterol, and LDL cholesterol concentrations tend to occur in the first 4 to 8 weeks of weight loss (16,17). Two years after initiating diet therapy, a sustained weight loss of 5% is needed to maintain the decrease in serum triglyceride concentrations, whereas serum total and LDL cholesterol revert toward baseline if at least a 10% weight loss is not maintained (16–19). Serum HDL cholesterol concentration also decreases during active weight loss but later increases once weight loss stabilizes (15).

Respiratory Disease

Many pulmonary abnormalities improve with weight loss. A modest loss of ~10% body weight decreases the respiratory disturbance index, improves sleep patterns, and decreases daytime hypersomnolence in patients with sleep apnea syndrome (20). Marked weight loss of ~30% body weight in patients with extreme obesity (body mass index ≥ 40 kg/m²) usually decreases the severity of sleep apnea and can result in complete resolution of the syndrome when the respiratory disturbance index is not markedly abnormal (21–23). It is possible that each patient has a critical threshold of weight loss that can correct sleep apnea, depending on the patient’s upper airway collapsibility (24). Bariatric surgery has also been shown to improve and resolve obesity hypoventilation syndrome (23,25).

Liver Disease

Obesity is associated with a spectrum of liver diseases, known as nonalcoholic fatty liver disease (26). Losing 10% or more of body weight can correct abnormal liver chemistries, decrease liver fat content, and improve features of steatohepatitis (27–29). Rapid weight loss that occurs after gastric surgery (30), very-low-calorie diets (31), or fasting

(32) will decrease hepatic fat content but can induce hepatic inflammation and exacerbate steatohepatitis.

Reproductive and Urinary Tract Function in Women

Marked weight loss after gastric bypass surgery has been shown to correct urinary overflow incontinence (33). In addition, marked weight loss can produce normal menses in previously amenorrheic women and can improve fertility.

Physical Function and Quality of Life

Weight loss can improve physical function and quality of life. Moreover, improvements in physical function and health-related quality of life are directly correlated with the amount of weight lost. In obese patients with osteoarthritis, weight loss leads to improvement in symptoms, an increase in pain-free range of motion, and a decrease in analgesic use (34). In most patients, marked weight loss due to obesity surgery results in pain relief in one or more joints (35). Improvements in health-related quality of life, measured by the Short-Form 36 (SF-36) Health Survey and by other instruments that evaluated social interaction, anxiety and depression, mood, perceived health, and daily activities, have been demonstrated after modest diet-induced weight loss of 8.6 kg (36) and surgery-induced weight loss (37). In addition, patients who had gastric surgery for obesity had less sick days and disability pension days than did the control group who did not lose weight (38).

Mortality

Although weight loss in obese persons has a beneficial effect on obesity-related medical complications, there is no conclusive evidence that weight loss increases survival. Three studies reported data from different population subgroups of the American Cancer Society's Cancer Prevention Study I (39–41). This large epidemiological study obtained baseline data between 1959 and 1960 and followed the participants for an average of 12 years. In one study of women, any intentional weight loss in women with obesity-related illnesses was associated with a 20% reduction in all-cause mortality (39). There was no overall relationship between intentional weight loss and mortality in women who did not have a preexisting illness. In a second study of men, intentional weight loss in those with obesity-related illnesses did not affect survival, but cancer-related deaths increased in those who had lost ≥ 20 lb (40). In men who did not have a preexisting illness, intentional weight loss was not associated with total, cardiovascular or cancer mortality, but diabetes-associated mortality was increased in those who lost ≥ 20 lb. Overweight and obese men and women who had diabetes were evaluated in the third study (41). Intentional weight loss was associated with a 25% reduction

in total mortality and a 28% reduction in cardiovascular disease and diabetes-related mortality. A retrospective analysis of patients with type 2 diabetes found that survival was directly correlated with weight loss during the patient's first year of diabetes therapy (42). The results from these studies suggest that intentional weight loss may improve survival in overweight and obese persons who have an obesity-related illness, particularly type 2 diabetes. However, these data do not prove a causal relationship, and long-term prospective studies are needed to determine the true effect of weight loss on mortality.

Patients' Expected Outcome

Obese persons often want and expect to lose more weight than is achieved by therapy. In one study, obese women who were beginning a nonsurgical weight loss program indicated that they wanted to lose 38% of their body weight but would be happy with a loss of 31%, satisfied with a loss of 25%, and disappointed with a loss of 17% of initial weight (43). After 48 weeks of diet and exercise therapy, these subjects lost an average of 16% of their initial weight. Patients who seek bariatric surgery also often have unrealistically high weight loss expectations (44). Therefore, there is often a large discrepancy between a realistic and clinically beneficial weight loss response to treatment and the patient's expected weight loss.

Conclusions

Intentional weight loss improves many of the existing medical complications associated with obesity and can prevent the development of new obesity-related diseases. Many of these beneficial effects are directly related to the amount of weight that is lost and become noticeable after only modest weight losses of 5% to 10% of initial body weight. It is important to inform patients about the beneficial effects of modest and achievable weight loss to avoid disappointment with treatment outcome.

Acknowledgments

This work was supported by a grant from Roche Laboratories and National Institute for Health grants RR-00036 (General Clinical Research Center) and DK-56341 (Clinical Nutrition Research Unit). The authors thank Renata J. Braudy and Jennifer C. McCrea for assistance in subject recruitment, the nursing staff of the General Clinical Research Center for their help in performing the studies, and Steven Block for his technical assistance.

References

1. Wilson PW, Kannel WB, Silbershatz H, D'Agostino RB. Clustering of metabolic factors and coronary heart disease. *Arch Intern Med.* 1999;159:1104–9.

2. **Karason K, Wikstrand J, Sjöström L, Wendelhag I.** Weight loss and progression of early atherosclerosis in the carotid artery: a four-year controlled study of obese subjects. *Int J Obes Relat Metab Disord.* 1999;23:948–56.
3. **Henry RR, Scheaffer L, Olefsky JM.** Glycemic effects of intensive caloric restriction and isocaloric refeeding in noninsulin-dependent diabetes mellitus. *J Clin Endocrinol Metab.* 1985;61:917–25.
4. **Kelly DE, Wing R, Buonocore C, Sturis J, Polonsky K, Fitzimmons M.** Relative effects of calorie restriction and weight loss in noninsulin-dependent diabetes mellitus. *J Clin Endocrinol Metab.* 1993;77:1287–93.
5. **Wing RR, Koeske R, Epstein LH, Nowalk MP, Gooding W, Becker D.** Long-term effects of modest weight loss in type II diabetic patients. *Arch Intern Med.* 1987;147:1749–53.
6. **Pories WJ, Swanson MS, MacDonald KG, et al.** Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. *Ann Surg.* 1995;222:339–50.
7. **Pan XR, Li GW, Hu YH, et al.** Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care.* 1997;20:537–44.
8. **Moore LL, Visoni AJ, Wilson PW, D'Agostino RB, Finkle WD, Ellison RC.** Can sustained weight loss in overweight individuals reduce the risk of diabetes mellitus? *Epidemiology.* 2000;11:269–73.
9. **Sjöström CD, Peltonen M, Wedel H, Sjöström L.** Differentiated long-term effects of intentional weight loss on diabetes and hypertension. *Hypertension.* 2000;36:20–5.
10. **The Trials of Hypertension Prevention Collaborative Research Group.** Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure: the trials of hypertension prevention, phase II. *Arch Intern Med.* 1997;157:657–67.
11. **Stevens VJ, Obarzanek E, Cook NR, et al.** Long-term weight loss and changes in blood pressure: results of the trials of hypertension prevention, phase II. *Ann Intern Med.* 2001;134:1–11.
12. **Foley EF, Benotti PN, Borlase BC, Hollingshead J, Blackburn GL.** Impact of gastric restrictive surgery on hypertension in the morbidly obese. *Am J Surg.* 1992;163:294–7.
13. **Carson JL, Ruddy ME, Duff AE, Holmes NJ, Cody RP, Brolin RE.** The effect of gastric bypass surgery on hypertension in morbidly obese patients. *Arch Intern Med.* 1994;154:193–200.
14. **National Institutes of Health, National Heart, Lung, and Blood Institute.** Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. *Obes Res.* 1998;6(suppl 2):51S–209.
15. **Dattilo AM, Kris-Etherton PM.** Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *Am J Clin Nutr.* 1992;56:320–8.
16. **Wadden TA, Anderson DA, Foster GD.** Two-year changes in lipids and lipoproteins associated with the maintenance of a 5% to 10% reduction in initial weight: some findings and some questions. *Obes Res.* 1999;7:170–8.
17. **Rössner S, Sjöström L, Noack R, Meinders AE, Nosedá G.** Weight loss, weight maintenance, and improved cardiovascular risk factors after 2 years treatment with orlistat for obesity. *Obes Res.* 2000;8:49–61.
18. **Rössner S, Bjorvell H.** Early and late effects of weight loss on lipoprotein metabolism in severe obesity. *Atherosclerosis.* 1987;64:125–30.
19. **Ryttig KR, Flaten H, Rössner S.** Long-term effects of a very low calorie diet (Nutrilett) in obesity treatment: a prospective, randomized, comparison between VLCD and a hypocaloric diet + behavior modification and their combination. *Int J Obes Relat Metab Disord.* 1997;21:574–9.
20. **Smith PL, Gold AR, Meyers DA, Haponik EF, Bleecker ER.** Weight loss in mildly to moderately obese patients with obstructive sleep apnea. *Ann Intern Med.* 1985;103:850–5.
21. **Sugerman HJ, Fairman RP, Sood RK, Engle K, Wolfe L, Kellum JM.** Long-term effects of gastric surgery for treating respiratory insufficiency of obesity. *Am J Clin Nutr.* 1992;55:597S–601.
22. **Barvaux VA, Aubert G, Rodenstein DO.** Weight loss as a treatment for obstructive sleep apnea. *Sleep Med Rev.* 2000;4:435–52.
23. **Charuzi I, Ovnat A, Peiser J, Saltz H, Weitzman S, Lavie P.** The effect of surgical weight reduction on sleep quality in obesity-related sleep apnea syndrome. *Surgery.* 1985;97:535–8.
24. **Schwartz AR, Gold AR, Schubert N, et al.** Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis.* 1991;144:494–8.
25. **Sugerman HJ, Baron PL, Fairman RP, Evans CR, Vetrovek GW.** Hemodynamic dysfunction in obesity hypoventilation syndrome and the effects of treatment with surgically induced weight loss. *Ann Surg.* 1988;207:604–13.
26. **Matteoni C, Younossi ZM, McCullough A.** Nonalcoholic fatty liver disease: a spectrum of clinical pathological severity. *Gastroenterology.* 1999;116:1413–9.
27. **Palmer M, Schaffner F.** Effect of weight reduction on hepatic abnormalities in overweight patients. *Gastroenterology.* 1990;99:1408–13.
28. **Eriksson S, Eriksson KF, Bondesson L.** Nonalcoholic steatohepatitis in obesity: a reversible condition. *Acta Med Scand.* 1986;220:83–8.
29. **Ranlov I, Hardt F.** Regression of liver steatosis following gastroplasty or gastric bypass for morbid obesity. *Digestion.* 1990;47:208–14.
30. **Luyckx FH, Desai C, Thiry A, et al.** Liver abnormalities in severely obese subjects: effect of a drastic weight loss after gastroplasty. *Int J Obes Relat Metab Disord.* 1998;22:222–6.
31. **Andersen T, Gluud C, Franzmann MB, Christoffersen P.** Hepatic effects of dietary weight loss in morbidly obese subjects. *J Hepatol.* 1991;12:224–6.
32. **Capron JP, Delamarre J, Dupas JL, Braillon A, Degott C, Quenum C.** Fasting in obesity: another cause of liver injury with alcoholic hyaline? *Dig Dis Sci.* 1982;27:265–8.
33. **Bump RC, Sugerman HJ, Fantl JA, McClish DK.** Obesity and lower urinary tract function in women: effect of surgically induced weight loss. *Am J Obstet Gynecol.* 1992;167:392–9.
34. **Williams RA, Foulsham BM.** Weight reduction in osteoarthritis using phentermine. *Practitioner.* 1981;225:231–2.

35. **McGoey BV, Deitel M, Saplys RJ, Kliman ME.** Effect of weight loss on musculoskeletal pain in the morbidly obese. *J Bone Joint Surg.* 1990;72:322–3.
36. **Fontaine KR, Barofsky I, Andersen RE, et al.** Impact of weight loss on health-related quality of life. *Qual Life Res.* 1999;8:275–7.
37. **Karlsson J, Sjöström L, Sullivan M.** Swedish Obese Subjects (SOS)—an intervention study of obesity: two-year follow-up of health-related quality of life (HRQL) and eating behavior after gastric surgery for severe obesity. *Int J Obes Relat Metab Disord.* 1998;22:113–26.
38. **Narbro K, Agren G, Jonsson E, et al.** Sick leave and disability pension before and after treatment for obesity: a report from the Swedish Obese Subjects (SOS) study. *Int J Obes Relat Metab Disord.* 1999;23:619–24.
39. **Williamson DF, Pamuk E, Thun M, Flanders D, Byers T, Heath C.** Prospective study of intentional weight loss and mortality in never-smoking overweight U. S. white women aged 40–64years. *Am J Epidemiol.* 1995;141:1128–41.
40. **Williamson DF, Pamuk E, Thun M, Flanders D, Byers T, Heath C.** Prospective study of intentional weight loss and mortality in overweight white women aged 40–64 years. *Am J Epidemiol.* 1999;149:491–503.
41. **Williamson DF, Thompson TJ, Thun M, Flanders D, Pamuk E, Byers T.** Intentional weight loss and mortality among overweight individuals with diabetes. *Diabetes Care.* 2000;23:1499–1504.
42. **Lean MEJ, Powrie JK, Anderson AS, Garthwaite PH.** Obesity, weight loss and prognosis in type 2 diabetes. *Diabet Med.* 1990;7:228–33.
43. **Foster GD, Wadden TA, Vogt RA, Brewer G.** What is a reasonable weight loss? Patients' expectations and evaluations of obesity treatment outcomes. *J Consult Clin Psychol.* 1997; 65:79–85.
44. **Rabner JG, Greenstein RJ.** Obesity surgery: expectations and reality. *Int J Obes Relat Metab Disord.* 1991;15: 841–55.