SAGE-Hindawi Access to Research
International Journal of Hypertension
Volume 2011, Article ID 398065, 6 pages
doi:10.4061/2011/398065

Research Article

Management of Hypertension and Diabetes in Obesity: Non-Pharmacological Measures

Joseph M. Pappachan,[1] Elias C. Chacko,[2] Ganesan Arunagirinathan,[3] and Rajagopalan Sriraman[4]

[1] *Department of Medicine, Grantham and District Hospital, NG31 8DG East Midlands, UK*
[2] *Department of Medicine, Singapore General Hospital, Singapore 169608*
[3] *Department of Diabetes and Endocrinology, The Royal Infirmary of Edinburgh, Edinburgh, UK*
[4] *Department of Diabetes and Endocrinology, Lincoln County Hospital, LN2 5QY East Midlands, UK*

Correspondence should be addressed to Joseph M. Pappachan, drpappachan@yahoo.co.in

Received 20 January 2011; Accepted 24 January 2011

Academic Editor: Kazuko Masuo

Obesity has become a global epidemic over the past few decades because of unhealthy dietary habits and reduced physical activity. Hypertension and diabetes are quite common among obese individuals and there is a linear relationship between the degree of obesity and these diseases. Lifestyle interventions like dietary modifications and regular exercise are still important and safe first-line measures for treatment. Recently, bariatric surgery has emerged as an important and very effective treatment option for obese individuals especially in those with comorbidities like hypertension and diabetes. Though there are few effective drugs for the management of obesity, their efficacy is only modest, and they should always be combined with lifestyle interventions for optimal benefit. In this paper we aim to outline the non-pharmacological measures for the management of hypertension and diabetes in obesity.

1. Introduction

Hypertension, diabetes mellitus and obesity together form 24% of the global risk for mortality [1]. Cardiovascular disorders related to these life-style diseases form the major cause of morbidity and mortality among the sufferers worldwide. Obesity has become a global epidemic in the past few decades. Among the adult US population, 33.8% are obese, and another 34.2% are overweight [2]. Obesity is a risk factor for many diseases of which hypertension and type 2 diabetes mellitus are the most important.

Obese individuals (those with body mass index (BMI) more than 30 kg/m^2) were found to have higher risk for diabetes mellitus (age-adjusted odds ratio (OR) = 3.66) and hypertension (age-adjusted OR = 3.72) compared to those with normal body weight [3]. Overweight individuals also had higher risk for diabetes and hypertension (age-adjusted OR = 1.59 and 1.88, resp.) and those with morbid obesity (BMI > 40 kg/m^2) had the highest risk (age-adjusted OR = 7.37 and 6.38, resp.) [3]. As there is a significant linear relationship between body weight and these two diseases, control of excess bodyweight is important for their prevention and treatment.

Over the past few decades, a lot of effective drugs have been developed for the treatment of hypertension and diabetes. However, the pharmacotherapy of obesity is still not very promising without lifestyle modification and/or surgical intervention. Therefore, we aim to discuss the treatment options without drugs for management of hypertension and diabetes in obesity through this paper.

2. Life-Style Interventions for Treatment of Hypertension and Diabetes in Obesity

2.1. Exercise for the Obese Hypertensive. The role of physical activity for treatment of hypertension is wellknown [4–6]. Aerobic exercise has shown to be associated with reduction

of systolic blood pressure (SBP) by 3.84 mm Hg and diastolic blood pressure (DBP) by 2.58 mm Hg in a meta-analysis examining large data from 54 randomized controlled trials [4]. More profound reduction of SBP (14.77 mm Hg) and DBP (5.63 mm Hg) has been observed in a recent study among obese patients after a 12-month regular exercise program along with dietary changes [7]. Significant reduction in body weight and cardiometabolic parameters like insulin resistance and hepatic fat also have been observed among the participants in this study.

Regular exercise along with dietary modifications has shown to be associated with significantly greater reduction in both SBP (4.5 mm Hg) and DBP (2.4 mm Hg) when compared with dietary adjustments alone among hypertensive patients [8]. Reduction in body weight was also higher among the former group. Weight loss has been found to be associated with a decrease in arterial stiffness [8, 9]. Better control of blood pressure among obese hypertensives following weight loss may be partly due to the reduction in arterial stiffness. Even minor reduction in the body weight has been associated with better control of hypertension and cardiovascular risk factors [10].

An average weight loss of 3.0 kg through lifestyle interventions corresponded 2.5 years later with a 30% reduction in combined cardiovascular events, poorly controlled blood pressure and the need to reinitiate antihypertensive medications [11]. Reductions in total body and abdominal fat, even without significant weight loss achieved through regular exercise, were found to be associated with improved SBP, DBP and cardiovascular risk factors [12]. Diet, Exercise, and Weight Loss Intervention Trial (DEW-IT) showed that exercise-incorporated lifestyle interventions can result in significantly better BP control among patients taking pharmacotherapy for hypertension [13].

2.2. Exercise for Diabetes in Obesity. Regular exercise improves glycemic control in all forms of diabetes. Insulin resistance is the major cause for hyperglycemia in obese diabetics and physical activity is one of the best ways to reduce insulin resistance [7, 14–16]. Physical activity improves insulin resistance through various mechanisms. Hepatic lipid accumulation is one of the primary mechanisms that drive obesity-related insulin resistance and type 2 diabetes, and exercise can reduce the free fatty acid-induced hepatic insulin resistance [14]. Reversal of hepatic insulin resistance is related to the reduction in central adiposity induced by exercise. Weight loss achieved by regular exercise was found to improve hepatic insulin sensitivity better than weight loss induced through calorie restriction [16]. Exercise can also reduce hepatic glucose production and augment insulin-mediated suppression of hepatic glucose output [14, 17].

Exercise increases skeletal muscle glucose uptake and utilization. This effect is mediated by an increase in expression of glucose transporter 4 (GLUT 4, an isoform of glucose transporter) in skeletal muscle [18]. Exercise also induces an increase in muscle insulin sensitivity [19]. Through these adaptations in the muscle, physical activity improves the peripheral glucose disposal and insulin resistance, and augments the glycemic control among obese individuals with diabetes.

Aerobic exercise has been demonstrated to improve the insulin sensitivity and reduce the glycemic load, without any significant change in energy intake, among obese men and women, and exercise may have a synergistic effect to reduce insulin resistance when combined with a low glycemic diet [15]. Despite the absence of weight loss, moderate-intensity exercise was associated with significant reductions in visceral obesity (an important determinant of insulin resistance) among obese individuals with type 2 diabetes [20].

Look AHEAD (Action for Health and Diabetes) is a US National Institutes of Health-funded long-term multicentric clinical trial studying the effect of an intensive lifestyle intervention on cardiovascular disease (CVD) morbidity and mortality in overweight/obese people with type 2 diabetes. Weight loss achieved by exercise and dietary changes among the intervention group resulted in better glycemic control and CVD risk factors [21]. Reduced medication use and lower therapeutic costs were the other benefits observed among this group after one year [22].

Diabetes Prevention Program (DPP) was a prospective multi-centre randomized clinical trial examining the diabetes incidence in overweight/obese adults managed with intensive lifestyle intervention or metformin or placebo. Exercise-incorporated lifestyle intervention reduced the incidence of type 2 diabetes by 58% and metformin by 31% when compared with placebo after 2.8 years of follow up [23]. Decreased diabetes risk by lifestyle intervention observed in the DPP trial was related to reductions of body weight, BMI, and central adiposity [24]. Follow up data from the trial has shown that the cumulative incidence of diabetes remained lowest in the lifestyle intervention group even after 10 years [25].

2.3. Dietary Measures for Hypertension Management in Obesity. The Dietary Approaches to Stop Hypertension (DASH) trial was a multicenter, randomized clinical trial that examined the effects of dietary patterns on blood pressure. This landmark study showed that a diet rich in fruits, vegetables and low-fat diary products along with reduced saturated and total fat lowered systolic blood pressure by 5.5 mm Hg and diastolic blood pressure by 3.0 mm Hg more than a control diet [26]. For overweight or obese persons, the addition of exercise and weight loss to the DASH diet resulted in even larger BP reductions and cardiac risk factors [8].

Dietary sodium restriction (to <3 grams/day) is an important component of management of any patient with hypertension. Overweight/obese hypertensives were found to have higher salt sensitivity in observational studies [27, 28]. Obese subjects were also found to have an enhanced rate of renal tubular sodium reabsorption [29]. Animal studies showed that obesity is associated with salt retention by the kidney through reduction of natriuresis (increased clearance of atrial natriuretic peptide by adipose cells), increased sympathetic activity and activation of renin angiotensin-aldosterone system (and high blood pressure as

a consequence) [30]. Hence, the beneficial effect of salt restriction would be more profound among obese hypertensives. A recent large population-based study reported from China adds evidence to this concept [31].

A long-term dietary intervention trial with a nutrient-fortified prepared meal plan (approximately 22% energy from fat, 58% from carbohydrate and 20% from protein) was found to be associated with better control of BP among obese/overweight hypertensives than with the usual care diet [32]. The dietary intervention group in this study also achieved better weight loss and improved cardiovascular risk factors. Combining a daily fish meal with a weight-loss diet has an additive effect on blood pressure among overweight hypertensives [33].

A systematic review to determine the long-term effects of weight loss on hypertension through dietary interventions versus pharmacologic treatment showed that the former approach resulted in greater weight loss and BP reductions than the latter [34]. The American Dietetic Association recommends the application of medical nutrition therapy (MNT) and lifestyle counseling as an integral component of the medical treatment for management of specific disease states and conditions (including hypertension and obesity) and should be the initial step in the management of these situations [35]. When pharmacotherapy becomes necessary for control, MNT may complement or enhance its therapeutic effectiveness, thereby reducing or eliminating the need for multiple medications.

Excess alcohol consumption is well known to raise the blood pressure in human beings. However, social drinking may not be very hazardous. According to the European Society of Hypertension and Cardiology recommendation, alcohol consumption in hypertensive subjects who drink alcohol should be limited to no more than 20 to 30 gm of ethanol per day for men and no more than 10 to 20 gm for women [36]. In obese hypertensives, low levels of drinking may help to reduce calorie consumption and thus may facilitate weight reduction.

Overall, weight reduction achieved through lifestyle interventions like dietary modification and regular exercise programs (at least 30 minutes/day on most days) help obese individuals with hypertension to obtain better BP control and reduce complications related to uncontrolled hypertension.

2.4. Dietary Measures to Treat Diabetes in Obesity. Nutritional intervention is of paramount importance in preventing diabetes, managing existing diabetes and preventing/slowing diabetic complications. Total calorie intake can be distributed as follows in a type 2 diabetic: 45–65% of total calorie intake as carbohydrate, 10–30% as proteins and less than 30% as total fat (<7% saturated fat) with <300 mg/day of cholesterol [37]. Total calorie intake must be appropriate to weight management goals of the individual. Macronutrient intake should be tailored according to the metabolic status of the patient (e.g., lipid profile). Similarly, there is no evidence-based recommendation for generalization of micronutrient supplements.

For obese diabetic, a weight losing diet containing either low-carbohydrate or low-fat calorie-restricted diet may be effective in the short term (up to 1 year) [37]. Standard weight loss diets provide 500–1,000 fewer calories than estimated to be necessary for weight maintenance. Up to 10% of weight loss can be achieved in 6 months with such diets. Lipid profiles, renal function and protein intake (in those with nephropathy) of patients on low-carbohydrate-diets should be monitored and adjustments of hypoglycemic drug therapy should be made to avoid the risk of hypoglycemia. Maintenance of weight loss after one year usually depends on the adherence to lifestyle interventions.

Intensive individualized dietary advice (according to the nutritional recommendations of the European Association for the Study of Diabetes) for six months has shown to reduce HbA1c by 0.4%, body weight by 1.3 Kg, BMI by 0.5 kg/M^2 and waist circumference by 1.6 cm when compared to controls, among overweight/obese diabetics on optimal medical treatment without adequate glycemic control [38].

A carbohydrate intake of 130 grams/day is recommended for patients as this provides adequate glucose for the central nervous system, without reliance on glucose production from ingested protein or fat, for its fuel needs [39]. Long-term metabolic effects of very-low-carbohydrate diets on brain are unclear (though brain may function even on lower carbohydrate diets) and such diets may result in imbalance of energy, fiber, vitamins and minerals, and may not be palatable.

3. Bariatric Surgery for Management of Obese Individuals with Hypertension and Diabetes

Few surgical procedures in the upper gastrointestinal tract, collectively termed as bariatric surgery, have emerged as important therapeutic options for management of obesity in the recent years. They are classified as purely restrictive (limiting the stomach volume) and primarily malabsorptive [40]. Restrictive procedures commonly used now are laparoscopic adjustable gastric banding and laparoscopic vertical sleeve gastrectomy. The main malabsorptive procedure in use now is Roux-en-Y gastric bypass.

Calorie restriction may be through three mechanisms in bariatric surgery: (1) mechanical limiting of volume of the gastric pouch and reduction of its outlet (2) modulation of satiety by postprandial induction of neuro-hormonal signals (e.g., peptide YY, an anorexiant) and (3) restriction of calorie intake spontaneously adopted by patients to limit the burden of postprandial dumping syndrome [41]. Weight loss is achieved mainly through restriction of calorie intake. Significant weight loss following the surgery usually results in improvement of diabetes and hypertension.

A recent meta-analysis that included 621 studies with 888 treatment arms and 135,246 patients has shown that the weight loss overall was 38.5 kg or 55.9% excess body weight loss [42]. Overall, 78.1% of diabetic patients had complete resolution and diabetes was improved or resolved in 86.6% of patients. Improvement of diabetes usually occurs days after surgery even before significant weight loss is achieved.

Apart from calorie restriction obtained through the procedure, improvement of insulin resistance and insulin sensitivity (mainly related to weight loss) also contributes to better glycemic control among obese diabetic patients undergoing bariatric surgery. Other proposed mechanisms are through release of gut hormones like glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide (the incretin effect) and increase in the beta-cell mass [41].

Hypertension was resolved in 61.7% and resolved or improved in 78.5% of patients undergoing bariatric procedures [43]. The improvement in hypertension is mainly related to weight loss. In general, one percent reduction in body weight will decrease systolic blood pressure by 1 mm Hg and diastolic blood pressure by 2 mm Hg [43]. Reduction in salt sensitivity and alteration of renal hemodynamics brought about by weight loss may be the contributing factors for improvement of hypertension following bariatric surgery. A 14 mm Hg reduction in SBP and 12 mm Hg reduction in DBP was observed among obese hypertensives undergoing bariatric surgery in a recent clinical trial [44]. Discontinuation/ reduction of dose of antihypertensive medication can be achieved in many patients following bariatric surgery.

A recent study showed the distinct advantages of bariatric surgery over lifestyle interventions for treatment of obesity and related diseases like hypertension and diabetes [44]. The mean weight loss at one year was 30% and 8% in the surgical and lifestyle intervention groups, respectively. Remission rates of type 2 diabetes and hypertension were significantly higher in the surgery group than in the lifestyle intervention group (70 versus 33% and 49 versus 23%).

Bariatric surgery is a relatively safe (perioperative mortality rate 0.3%) procedure with only a few adverse consequences (4.3%) [45]. The most frequent and severe adverse events in the immediate postprocedure period are anastomotic leaks, hemorrhage and thromboembolic events. Long-term hazards are vitamin deficiencies, malnutrition, osteoporosis, psychiatric disorders and a slightly higher risk of accidental death [41, 46]. However, a Swedish study showed significantly reduced 10-year mortality risk with bariatric surgery when compared to nonsurgical treatment of obesity, making this treatment option a promise for many [47].

The Scottish Intercollegiate Guidelines Network (SIGN) recommends that bariatric surgery may be considered for patients with all three of the following: (a) BMI of 35 or more, (b) one or more severe comorbidities that are expected to have a meaningful clinical improvement with weight reduction (e.g., severe mobility problems, arthritis, type 2 diabetes), and (c) evidence of completion of a structured weight management program that covered diet, physical activity, and psychological and drug interventions but did not result in significant and sustained improvement in co-morbidities [48]. The most recent Diabetes Surgery Summit consensus conference recommends bariatric surgery for type 2 diabetic patients with severe obesity (BMI > 35 kg/m^2) as well as in carefully selected, moderately obese patients (BMI: 30–35 kg/m^2) who are inadequately controlled by conventional medical and behavioral therapies [49].

4. Conclusions

Weight loss achieved through lifestyle interventions like dietary adjustments and regular physical activity are safe and moderately effective measures for management of hypertension and diabetes in obesity. They also help to reduce the treatment costs related to pharmacotherapy and also to reduce the pill burden. Even when drug therapy is considered, lifestyle interventions should continue, to obtain the desired effects of medications. Bariatric surgery is more effective than lifestyle interventions for treatment and is remarkably safe in selected patient groups. These non-pharmacological interventions should be the first-line management option and should also be combined with pharmacotherapy for scientific treatment of these diseases.

References

[1] World Health Organization, "Global health risks: mortality and burden of disease attributable to selected major risks," December 2010, http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf.

[2] K. M. Flegal, M. D. Carroll, C. L. Ogden, and L. R. Curtin, "Prevalence and trends in obesity among US adults, 1999–2008," *Journal of the American Medical Association*, vol. 303, no. 3, pp. 235–241, 2010.

[3] A. H. Mokdad, E. S. Ford, B. A. Bowman et al., "Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001," *Journal of the American Medical Association*, vol. 289, no. 1, pp. 76–79, 2003.

[4] S. P. Whelton, A. Chin, X. Xin, and J. He, "Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials," *Annals of Internal Medicine*, vol. 136, no. 7, pp. 493–503, 2002.

[5] N. A. Khan, B. Hemmelgarn, R. J. Herman et al., "The 2009 Canadian hypertension education program recommendations for the management of hypertension: part 2—therapy," *Canadian Journal of Cardiology*, vol. 25, no. 5, pp. 287–298, 2009.

[6] J. Redon, R. Cifkova, S. Laurent et al., "The metabolic syndrome in hypertension: European society of hypertension position statement," *Journal of Hypertension*, vol. 26, no. 10, pp. 1891–1900, 2008.

[7] B. H. Goodpaster, J. P. DeLany, A. D. Otto et al., "Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: a randomized trial," *Journal of the American Medical Association*, vol. 304, no. 16, pp. 1795–1802, 2010.

[8] J. A. Blumenthal, M. A. Babyak, A. Hinderliter et al., "Effects of the DASH diet alone and in combination with exercise and weight loss on blood pressure and cardiovascular biomarkers in men and women with high blood pressure: the ENCORE study," *Archives of Internal Medicine*, vol. 170, no. 2, pp. 126–135, 2010.

[9] A. L. Dengo, E. A. Dennis, J. S. Orr et al., "Arterial destiffening with weight loss in overweight and obese middle-aged and older adults," *Hypertension*, vol. 55, no. 4, pp. 855–861, 2010.

[10] J. M. Pascual, E. Rodilla, J. A. Costa et al., "Body weight variation and control of cardiovascular risk factors in essential hypertension," *Blood Pressure*, vol. 18, no. 5, pp. 247–254, 2009.

[11] K. M. McTigue, R. Hess, and J. Ziouras, "Obesity in older adults: a systematic review of the evidence for diagnosis and treatment," *Obesity*, vol. 14, no. 9, pp. 1485–1497, 2006.

[12] K. J. Stewart, A. C. Bacher, K. Turner et al., "Exercise and risk factors associated with metabolic syndrome in older adults," *American Journal of Preventive Medicine*, vol. 28, no. 1, pp. 9–18, 2005.

[13] E. R. Miller 3rd, T. P. Erlinger, D. R. Young et al., "Results of the diet, exercise, and weight loss intervention trial (DEW-IT)," *Hypertension*, vol. 40, no. 5, pp. 612–618, 2002.

[14] J. M. Haus, T. P. J. Solomon, C. M. Marchetti, J. M. Edmison, F. González, and J. P. Kirwan, "Free fatty acid-induced hepatic insulin resistance is attenuated following lifestyle intervention in obese individuals with impaired glucose tolerance," *Journal of Clinical Endocrinology and Metabolism*, vol. 95, no. 1, pp. 323–327, 2010.

[15] J. P. Kirwan, H. Barkoukis, L. M. Brooks, C. M. Marchetti, B. P. Stetzer, and F. Gonzalez, "Exercise training and dietary glycemic load may have synergistic effects on insulin resistance in older obese adults," *Annals of Nutrition and Metabolism*, vol. 55, no. 4, pp. 326–333, 2009.

[16] R. H. Coker, R. H. Williams, S. E. Yeo et al., "The impact of exercise training compared to caloric restriction on hepatic and peripheral insulin resistance in obesity," *Journal of Clinical Endocrinology and Metabolism*, vol. 94, no. 11, pp. 4258–4266, 2009.

[17] J. P. Kirwan, T. P. J. Solomon, D. M. Wojta, M. A. Staten, and J. O. Holloszy, "Effects of 7 days of exercise training on insulin sensitivity and responsiveness in type 2 diabetes mellitus," *American Journal of Physiology—Endocrinology and Metabolism*, vol. 297, no. 1, pp. E151–E156, 2009.

[18] J. O. Holloszy, "A forty-year memoir of research on the regulation of glucose transport into muscle," *American Journal of Physiology—Endocrinology and Metabolism*, vol. 284, no. 3, pp. E453–E467, 2003.

[19] J. O. Holloszy, "Invited review: exercise-induced increase in muscle insulin sensitivity," *Journal of Applied Physiology*, vol. 99, no. 1, pp. 338–343, 2005.

[20] S. Lee, J. L. Kuk, L. E. Davidson et al., "Exercise without weight loss is an effective strategy for obesity reduction in obese individuals with and without Type 2 diabetes," *Journal of Applied Physiology*, vol. 99, no. 3, pp. 1220–1225, 2005.

[21] X. Pi-Sunyer, G. Blackburn, F. L. Brancati et al., "Reduction in weight and cardiovascular disease risk factors in individuals with Type 2 diabetes one-year results of the look AHEAD trial," *Diabetes Care*, vol. 30, no. 6, pp. 1374–1383, 2007.

[22] J. B. Redmon, A. G. Bertoni, S. Connelly et al., "Effect of the Look AHEAD study intervention on medication use and related cost to treat cardiovascular disease risk factors in individuals with type 2 diabetes," *Diabetes Care*, vol. 33, no. 6, pp. 1153–1158, 2010.

[23] W. C. Knowler, E. Barrett-Connor, S. E. Fowler et al., "Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin," *New England Journal of Medicine*, vol. 346, no. 6, pp. 393–403, 2002.

[24] W. Y. Fujimoto, K. A. Jablonski, G. A. Bray et al., "Body size and shape changes and the risk of diabetes in the diabetes prevention program," *Diabetes*, vol. 56, no. 6, pp. 1680–1685, 2007.

[25] W. C. Knowler, S. E. Fowler, R. F. Hamman et al., "10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study," *Lancet*, vol. 374, no. 9702, pp. 1677–1686, 2009.

[26] L. J. Appel, T. J. Moore, E. Obarzanek et al., "A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group," *New England Journal of Medicine*, vol. 336, no. 16, pp. 1117–1124, 1997.

[27] T. Uzu, G. Kimura, A. Yamauchi et al., "Enhanced sodium sensitivity and disturbed circadian rhythm of blood pressure in essential hypertension," *Journal of Hypertension*, vol. 24, no. 8, pp. 1627–1632, 2006.

[28] I. S. Hoffmann and L. X. Cubeddu, "Increased blood pressure reactivity to dietary salt in patients with the metabolic syndrome," *Journal of Human Hypertension*, vol. 21, no. 6, pp. 438–444, 2007.

[29] P. Strazzullo, G. Barba, F. P. Cappuccio et al., "Altered renal sodium handling in men with abdominal adiposity: a link to hypertension," *Journal of Hypertension*, vol. 19, no. 12, pp. 2157–2164, 2001.

[30] J. E. Hall, "Mechanisms of abnormal renal sodium handling in obesity hypertension," *American Journal of Hypertension*, vol. 10, no. 5, part 2, pp. 49S–55S, 1997.

[31] J. Chen, D. Gu, J. Huang et al., "Metabolic syndrome and salt sensitivity of blood pressure in non-diabetic people in China: a dietary intervention study," *Lancet*, vol. 373, no. 9666, pp. 829–835, 2009.

[32] J. A. Metz, J. S. Stern, P. Kris-Etherton et al., "A randomized trial of improved weight loss with a prepared meal plan in overweight and obese patients impact on cardiovascular risk reduction," *Archives of Internal Medicine*, vol. 160, no. 14, pp. 2150–2158, 2000.

[33] T. A. Mori, D. Q. Bao, V. Burke, I. B. Puddey, G. F. Watts, and L. J. Beilin, "Dietary fish as a major component of a weight-loss diet: effect on serum lipids, glucose, and insulin metabolism in overweight hypertensive subjects," *American Journal of Clinical Nutrition*, vol. 70, no. 5, pp. 817–825, 1999.

[34] K. Horvath, K. Jeitler, U. Siering et al., "Long-term effects of weight-reducing interventions in hypertensive patients: systematic review and meta-analysis," *Archives of Internal Medicine*, vol. 168, no. 6, pp. 571–580, 2008.

[35] J. McCaffree, "Position of the American Dietetic Association: integration of medical nutrition therapy and pharmacotherapy," *Journal of the American Dietetic Association*, vol. 103, no. 10, pp. 1363–1370, 2003.

[36] G. Mancia, G. de Backer, A. Dominiczak et al., "2007 guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)," *Journal of Hypertension*, vol. 25, no. 6, pp. 1105–1187, 2007.

[37] J. P. Bantle, J. Wylie-Rosett, A. L. Albright et al., "Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association," *Diabetes Care*, vol. 31, supplement 1, pp. S61–S78, 2008.

[38] K. J. Coppell, M. Kataoka, S. M. Williams, A. W. Chisholm, S. M. Vorgers, and J. I. Mann, "Nutritional intervention in patients with type 2 diabetes who are hyperglycaemic despite optimised drug treatment—lifestyle Over and Above Drugs in Diabetes (LOADD) study: randomised controlled trial," *British Medical Journal*, vol. 341, p. c3337, 2010.

[39] Institute of Medicine, *Dietary Reference Intakes: Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*, National Academies Press, Washington, DC, USA, 2002.

[40] G. Rao, "Office-based strategies for the management of obesity," *American Family Physician*, vol. 81, no. 12, pp. 1429–1449, 2010.

[41] R. Caiazzo, C. Zerrweck, R. Verhaeghe, T. Hubert, L. Arnalsteen, and F. Pattou, "Gastric bypass and glucose metabolism," *Diabetes and Metabolism*, vol. 35, no. 6, part 2, pp. 528–531, 2009.

[42] H. Buchwald, R. Estok, K. Fahrbach et al., "Weight and Type 2 diabetes after bariatric surgery: systematic review and meta-analysis," *American Journal of Medicine*, vol. 122, no. 3, pp. 248.e5–256.e5, 2009.

[43] H. Buchwald, Y. Avidor, E. Braunwald et al., "Bariatric surgery: a systematic review and meta-analysis," *Journal of the American Medical Association*, vol. 292, no. 14, pp. 1724–1737, 2004.

[44] D. Hofsø, N. Nordstrand, L. K. Johnson et al., "Obesity-related cardiovascular risk factors after weight loss: a clinical trial comparing gastric bypass surgery and intensive lifestyle intervention," *European Journal of Endocrinology*, vol. 163, no. 5, pp. 735–745, 2010.

[45] D. R. Flum, S. H. Belle, W. C. King et al., "Perioperative safety in the longitudinal assessment of bariatric surgery," *New England Journal of Medicine*, vol. 361, no. 5, pp. 445–454, 2009.

[46] T. D. Adams, R. E. Gress, S. C. Smith et al., "Long-term mortality after gastric bypass surgery," *New England Journal of Medicine*, vol. 357, no. 8, pp. 753–761, 2007.

[47] L. Sjöström, K. Narbro, C. D. Sjöström et al., "Effects of bariatric surgery on mortality in Swedish obese subjects," *New England Journal of Medicine*, vol. 357, no. 8, pp. 741–752, 2007.

[48] J. Logue, L. Thompson, F. Romanes, D. C. Wilson, J. Thompson, and N. Sattar, "Management of obesity: summary of SIGN guideline.," *British Medical Journal*, vol. 340, p. c154, 2010.

[49] F. Rubino, L. M. Kaplan, P. R. Schauer, and D. E. Cummings, "The diabetes surgery summit consensus conference: recommendations for the evaluation and use of gastrointestinal surgery to treat type 2 diabetes mellitus," *Annals of Surgery*, vol. 251, no. 3, pp. 399–405, 2010.