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Effect of Bariatric Surgery on Primary Hypertension in Morbidly Obese Patients: Possible Mechanisms

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Abstract
Obesity has become a serious threat to the human health and is considered as a major non-communicable disease. Bariatric surgery has proved to be the most competent in the treatment of morbid obesity and its related metabolic comorbidities like type 2 diabetes, hypertension, obstructive sleep apnea, coronary heart disease and hyperlipidemia. The chances of developing primary hypertension increases with an increase in weight and even notable gain in weight in this group are accompanied with the higher chances for acquiring primary hypertension. Bariatric surgery has proven to be a landmark in the resolution of obesity along with the improvement or complete resolution of hypertension in hypertensive obese patients. The adipose tissues in obese patients, not only store energy, but also secret various adipokines. These adipokines such as adiponectin, leptin and resistin have shown to have a vital role in the pathophysiology of essential hypertension. Studies have shown a marked reduction in blood pressure in hypertensive obese patients undergoing Bariatric surgery. The renin-angiotensin-aldosterone system activation, the sympathetic nervous system disorders and endothelial dysfunction seems to play a major role between the obesity and hypertension. Currently, there has not been any independent study showing the relation between the Bariatric surgeries having a role in relieving primary hypertension or the mechanism by which Bariatric surgery decreases blood pressure. Thus, in this review, we discussed the possible causes of primary hypertension in the obese patients along with the role of Bariatric surgery in hypertensive obese patients, with its possible mechanisms involved in decreasing the blood pressure.
Keywords Bariatric surgery, obesity, primary hypertension, relationship.

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Introduction

With the improvement of lifestyle and people's eating habits, the prevalence of obesity worldwide is rising at a dramatic rate. By 2015, The World Health Organization projects 2.3 billion of the world's population to be overweight with more than 700 million to be under obesity line [1]. Obesity is often accompanied with the increase in risk of developing comorbidities like type 2 diabetes, hypertension, obstructive sleep apnea, hyperlipidemia and coronary heart diseases [2]. To date, Bariatric surgery has proved to be the most competent in the treatment of morbid obesity and its related metabolic comorbidities. Among the different comorbidities, one of the most common comorbidity associated with obesity is hypertension. It is seen that in obese patients, the chances of possessing primary hypertension increases with an increase in weight and even notable gain in weight in this group are accompanied with the higher chances of acquiring primary hypertension [3-5]. Studies have shown that the excess gain in weight may contribute to about 65%-75% chances of developing primary hypertension [6]. Currently, the treatment of essential hypertension includes lifestyle improvement, taking B-blockers and other antihypertensive drugs; however, to treat obesity, especially morbid obesity there is no truly effective pharmaceutical agents available. Studies have shown that Bariatric surgery has proven to be landmark in a long-term resolution of obesity along with the improvement or complete resolution of hypertension [7]. Currently, there has not been any independent study showing the relation between the Bariatric surgeries having a role in relieving primary hypertension or the mechanism by which Bariatric surgery decreases blood pressure. In this review, we have discussed the possible causes of primary hypertension in the obese patients along with the role of Bariatric surgery in hypertensive obese patients, with its possible mechanisms involved in decreasing the blood pressure.

Relation between obesity and hypertension

Obesity has become a serious threat to the human health and is considered as a major non-communicable disease. At present, the research on obesity and primary hypertension has made a significant progress. Juharri et al. [8] in his study

showed a consistent link between adiposity and hypertension relating that an increase in blood pressure is closely associated with the increase in weight. The body of obese patients contains a lot of adipose tissue. These adipose tissues not only store energy, but also secret various types of adipokines. These adipokines such as adiponectin, leptin and resistin have shown to have a vital role in the pathophysiology of essential hypertension [9]. Yatagi et al. [10] in his studies showed that in obese patients, adiponectin levels are associated with visceral fat, but irrelevant to the subcutaneous fat content and has an inverse relation to the weight gain. At the same time, lower serum adiponectin can induce insulin resistance (IR). Chou et al. [11] proposed an assumption that showed low adiponectin levels to have a vital role in the development of primary hypertension. An experiment done on rats has shown that rats injected with adiponectin tend to improve IR [12]. In obese patients without IR, low serum adiponectin may be the main cause of essential hypertension mechanism as systolic and diastolic blood pressure are in negative correlation with the serum adiponectin levels [13]. Luo et al. [14] in their studies have demonstrated leptin to be closely related in increasing blood pressure. Higher level of leptin is seen among hypertensive patients compared to the normotensive patients. *In vitro* experiments of Quehenberger et al. [15] confirmed leptin induced endothelin-1 to be a potent vasoconstrictor in human umbilical vein endothelial cells. Rosmond et al. [16] studied on the diversity of the leptin receptor gene, showing the association of leptin with blood pressure through leptin receptor, having different degrees of impact on blood pressure when certain protein mutates on certain leptin receptor loci. Moreover, the renin-angiotensin-aldosterone system (RAAS) activation [17], endothelial dysfunction [18] and the sympathetic nervous system disorders [19] are also playing a major role between the obesity and hypertension.

Bariatric surgery as a treatment of primary hypertension

Bariatric surgery has become a boon for the obese patients with metabolic syndromes (MS). It not only decreases the body mass index (BMI), but also helps in the improvement of their MS and quality of life [20, 21]. At present days, usually three kinds of Bariatric surgical procedures (laparoscopic sleeve gastrectomy (LSG), Roux-en-Y gastric bypass (RYGBP) and gastric binding) are performed and they all have varying degree of effects on essential hypertension. Kourosh et al. [21] did a systematic review of 33 studies, including 3997 cases of obese patients with essential hypertension having undergone LSG. Their mean BMI was 49.1±7.5kg/m^2 and the average time for their follow-up was 16.9±9.8 months. Their mean postoperative BMI was 36±7kg/m^2 with about 75% of patients having complete remission or improvement in their blood pressure.

Marcelo et al. [22] did an analysis of 95 morbidly obese patients with documented hypertension and were under antihypertensive medications and underwent laparoscopic RYGBP. Their preoperative mean BMI was 47±8 kg/m^2. After surgery, their mean excess body weight loss after one month was 23%-66% after one year. Along with this weight loss, a significant reduction in mean systolic and diastolic blood pressure was also seen. After one month of operation, 25% patients showed complete remission of hypertension while 36% patients had an improvement in hypertension. After one year of operation, 46% patients showed complete remission of hypertension with 19% patients having an improvement in hypertension. Thus, a significant decrease in blood pressure was seen with a 14 % reduction (by 20mm Hg) in the systolic and 11% reduction (by 9mm Hg) in the diastolic pressure at 12 months postoperatively. Similarly, Fernstorm et al. [23] also did a study on 347 morbidly obese patients to observe the effect of Bariatric surgery on hypertension. These patients went through either RYGBP (n=285) or gastric banding Gastroplasty (n=62). Among those, 192 patients were hypertensive (103 with anti-hypertensive medicine and 89 with no medicine). After 18 months of operation, the results showed that 92 patients still have hypertension after the operation (68 patients with anti-hypertensive medicine and 24 with no medicine) while others had complete remission of their hypertension**.** From this study, it was concluded that the patients have changes in their blood pressure after the Bariatric surgery showing the relation between the Bariatric surgery and blood pressure. Adami et al. [24] performed a study on 458 severely obese patients (mean BMI = 49kg/m^2) with hypertension and had Biliopancreatic diversion (BPD). They found that in the first postoperative year, 50% of those patients (mean BMI = 30kg/m^2) had their blood pressure dropped to the normal range and further about 10% of the

remaining patients showed normal blood pressure in the second or third year of the operation (mean BMI = 29kg/m^2) with no relapse in the patients once having blood pressure dropped to the normal range after the operation.

Buchwald et al. [3] did a meta-analysis of 22,094 morbidly obese patients who underwent various Bariatric procedures: gastric binding, gastric bypass, gastroplasty and biliopancreatic diversion with duodenal switch and the result showed that 38.4%, 75.4%, 72.5% and 81.3% of patients, respectively, had their blood pressure dropped to the normal range. However, in 71.5%, 87.1%, 80.6% and 91.8% patients, respectively, showed resolution or improvement in hypertension. Maggard et al. [25] in his 19 studies described the changes in hypertension after the Bariatric surgery and found that in 25% to 75% of hypertensive patients were with complete resolution or improvement in hypertension and there was improvement in 95% to 100% of hypertensive patients.

In 2003, Sugerman et al. [26] performed a study on 1025 patients who underwent RYGBP. Among those patients, 521 were hypertensive. After 1-2 years of the operation, hypertension resolved in 69% of the patients. However, it maintained for 5-7 years and later drop-off in the control of hypertension from 69% to 37% in follow-up of 10-12 years. Similarly, in a survey of 37 hypertensive obese patients undergoing Bariatric surgery had marked decrease in blood pressure in the early stage after surgery (after 4 months). However, the weight reduction continued up to 12 months, but there was no any notable decline in blood pressure showing some hormonal mechanism in earlier reduction in blood pressure [27]. Thus, a large number of studies have confirmed that the Bariatric surgery has a significant role in the treatment of essential hypertension and other MS.

Possible mechanisms

After Bariatric surgery, it is usually seen that there is a decrease in blood pressure at the early stage of the postoperative period. This effect might not be directly related to the weight, but other mechanisms like alteration in the RAAS, development of insulin resistance, increased sympathetic nervous system (SNS) activity, leptin resistance and hyperleptinemia might also come into play. The main mechanism involved may be the reversal of the SNS disorders. Systemic SNS in patients with essential hypertension does not show high sensitivity, but is selectively activated by the SNS, such as by the activation of the skeletal muscle and the sympathetic nervous system of the kidney [28]. Activated SNS may cause an increase in blood pressure by activating peripheral vasoconstriction, causing sodium excretion and water absorption by stimulating the RAAS [29]. Weyer et al. [30] found that in the white population, the muscle SNS activation is associated with the body fat ratio. Therefore, the Bariatric surgery can lower the percentage of fat in obese patients to achieve the purpose of treatment of essential hypertension. Jacques et al. [31] studies have shown that the decrease in weight can improve the insulin sensitivity of the body and can improve the sympathetic nervous system disorders. Ten cases of severe obesity with hypertension underwent sleeve gastrectomy. The blood pressure, heart rate, plasma leptin and muscle sympathetic nerve activity were measured 2-3days before the surgery. After six months of the surgery, those measurements showed decreased BMI (9.1±1.4), systolic pressure (10.2±4.5 mmHg), heart rate (11.0 ± 2.4 times/min), plasma leptin (53.6±8.8 μg/L) and muscle sympathetic nerve impulses (15.0±3.4 times/min). These data demonstrated that sleeve gastrectomy causes sympathetic suppression that may have some relevance with the decreased blood pressure and decreased plasma leptin. In the pathogenesis of hypertension, the SNS plays a vital role in experimental animals and humans. The former stimulates the secretion of leptin and insulin, which can cause or aggravate insulin resistance [32]. There is evidence that leptin can cause excitement of SNS. The decrease in leptin levels after Bariatric surgery can inhibit the sympathetic nervous system. However, the study showed that the duration of insulin resistance was not long, and the sympathetic nerve activity remained low for 1 year after operation, and the plasma insulin level was increased gradually. Therefore, it is believed that the improvement of insulin resistance in patients with essential hypertension might be a transient, and not the mechanism of Bariatric surgery in the treatment of essential hypertension [33].

Another mechanism proposed in the improvement of hypertension might be a decrease in plasma leptin levels after Bariatric surgery. Leptin has many physiological functions, including promoting the function and regulation of glucose and insulin metabolism, the hypothalamic-pituitary-adrenal axis and vascular regeneration and contraction through a direct effect on the blood

vessel wall causing vascular contraction or relaxation, and thereby affecting the blood pressure [19, 34]. However, leptin might lack a direct effect on arterial blood pressure, but through vasoconstriction and vasodilatation effect of nitric oxide (NO) on sympathetic nervous system, it can cause the systematic hemodynamic balance [35]. Bravo et al. [36] believed that high leptin levels in the blood are the risk factors for hypertension. Leptin has a role not only through the peripheral nerve endings, but also through the central nervous system in the hypothalamus to activate the SNS causing an increase in the blood pressure [37]. Vila et al. [38] performed a study on 28 obese patients with primary hypertension who were to undergo RYGBP. Their preoperative weight was 129±2.9 kg, BMI 48.2±1.1 and plasma leptin level was 110.2±7.3 ng/ml. After one year (10.3~14.6 months) of surgery, weight was reduced to 95.2±3.1 kg, BMI 35.5±1.2 and plasma leptin level to 36.4±4.9 ng/ml. These results showed RYGBP has significant effect in reducing body mass and can effectively reduce the level of plasma leptin. The decrease of plasma leptin can make the systemic hemodynamics stable, and reduce the release of endothelin 1 and other strong vascular substances to treat the patients with essential hypertension [39].

Conclusions

The Bariatric surgery has a definite therapeutic effect on the resolution of essential hypertension. A large amount of fat factors is associated with the pathophysiology of primary hypertension, and has become one of the independent possible factors of hypertension. Bariatric surgery can be associated with improvement of hypertension in obese patients in long-term duration, along with the weight reduction, which might be due to the improvement of the SNS disorders and a variety of adipokines reduction along with the combined results of different combined factors. The outcome of different Bariatric procedures on primary hypertension is not the same. At present, there is only a preliminary understanding of the mechanisms of Bariatric surgery in the treatment of primary hypertension. It is necessary to study the mechanism of the multi center randomized controlled study in order to clarify its mechanisms. In addition, a discrete study should be performed on different types of Bariatric surgeries showing their efficacy in the resolution of hypertension and the reasons for their dissimilar results for the better understanding of its involved mechanisms.

References

[1] World Health Organisation: Obesity and overweight. Fact sheet N8311.Fact sheet N. 8–11, 2013. http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Media+centre+Obesity+and+overweight#5.

[2] Haslam DW, James WP. Obesity. Lancet 2005; 366:1197-1209.

[3] Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, et al. Bariatric surgery: a systematic review and meta-analysis. Jama 2004; 292:1724-1737.

[4] Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2005; 366:1640-1649.

[5] Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. Jama 1999; 282:1523-1529.

[6] Wilson PW, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Arch Intern Med 2002; 162:1867-1872.

[7] Flores L, Vidal J, Canivell S, Delgado S, Lacy A, Esmatjes E. Hypertension remission 1 year after bariatric surgery: predictive factors. Surg Obes Relat Dis 2014; 10:661-665.

[8] Juhaeri, Stevens J, Chambless LE, Tyroler HA, Rosamond W, Nieto FJ, et al. Associations between weight gain and incident hypertension in a bi-ethnic cohort: the Atherosclerosis Risk in Communities Study. Int J Obes Relat Metab Disord 2002; 26:58-64.

[9] Iwashima Y, Katsuya T, Ishikawa K, Ouchi N, Ohishi M, Sugimoto K, et al. Hypoadiponectinemia is an independent risk factor for hypertension. Hypertension 2004; 43:1318-1323.

[10] Yatagai T, Nagasaka S, Taniguchi A, Fukushima M, Nakamura T, Kuroe A, et al. Hypoadiponectinemia is associated with visceral fat accumulation and insulin resistance in Japanese men with type 2 diabetes mellitus. Metabolism 2003; 52:1274-1278.

[11] Chow WS, Cheung BM, Tso AW, Xu A, Wat NM, Fong CH, et al. Hypoadiponectinemia as a predictor for the development of hypertension: a 5-year prospective study. Hypertension. 2007; 49:1455-1461.

[12] Kubota N, Terauchi Y, Yamauchi T, Kubota T, Moroi M, Matsui J, et al. Disruption of adiponectin causes insulin resistance and neointimal formation. J Biol Chem 2002; 277:25863-25866.

[13] Ong KL, Li M, Tso AW, Xu A, Cherny SS, Sham PC, et al. Association of genetic variants in the adiponectin gene with adiponectin level and hypertension in Hong Kong Chinese. Eur J Endocrinol 2010; 163:251-257.

[14] Luo JD, Zhang GS, Chen MS. Leptin and cardiovascular diseases. Timely Top Med Cardiovasc Dis 2005; 9:E34.

[15] Quehenberger P, Exner M, Sunder-Plassmann R, Ruzicka K, Bieglmayer C, Endler G, et al. Leptin induces endothelin-1 in endothelial cells in vitro. Circ Res 2002; 90:711-718.

[16] Rosmond R, Chagnon YC, Holm G, Chagnon M, Perusse L, Lindell K, et al. Hypertension in obesity and the leptin receptor gene locus. J Clin Endocrinol Metab 2000; 85:3126-3131.

[17] Kota SK, Kota SK, Jammula S, Meher LK, Panda S, Tripathy PR, et al. Renin-angiotensin system activity in vitamin D deficient, obese individuals with hypertension: An urban Indian study. Indian J Endocrinol Metab 2011; 15 Suppl 4:S395-401.

[18] Levy BI, Schiffrin EL, Mourad JJ, Agostini D, Vicaut E, Safar ME, et al. Impaired tissue perfusion: a pathology common to hypertension, obesity, and diabetes mellitus. Circulation 2008; 118:968-976.

[19] Kalil GZ, Haynes WG. Sympathetic nervous system in obesity-related hypertension: mechanisms and clinical implications. Hypertens Res 2012; 35:4-16.
[20] Cerci M, Bellini MI, Russo F, Benavoli D, Capperucci M, Gaspari AL, et al. Bariatric surgery in moderately obese patients: a prospective study. Gastroenterol Res Pract 2013; 2013:276183.
[21] Sarkhosh K, Birch DW, Shi X, Gill RS, Karmali S. The impact of sleeve gastrectomy on hypertension: a systematic review. Obes Surg 2012; 22:832-837.
[22] Hinojosa MW, Varela JE, Smith BR, Che F, Nguyen NT. Resolution of systemic hypertension after laparoscopic gastric bypass. J Gastrointest Surg 2009; 13:793-797.
[23] Fernstrom JD, Courcoulas AP, Houck PR, Fernstrom MH. Long-term changes in blood pressure in extremely obese patients who have undergone bariatric surgery. Arch Surg 2006; 141:276-283.
[24] Adami GF, Papadia F, Carlini F, Murelli F, Scopinaro N. Effect of biliopancreatic diversion on hypertension in severely obese patients. Hypertens Res 2005; 28:119-123.
[25] Maggard MA, Shugarman LR, Suttorp M, Maglione M, Sugerman HJ, Livingston EH, et al. Meta-analysis: surgical treatment of obesity. Ann Intern Med 2005; 142:547-559.
[26] Sugerman HJ, Wolfe LG, Sica DA, Clore JN. Diabetes and hypertension in severe obesity and effects of gastric bypass-induced weight loss. Ann Surg 2003; 237:751-756; discussion 757-758.
[27] Flores L, Vidal J, Nunez I, Rueda S, Viaplana J, Esmatjes E. Longitudinal changes of blood pressure after weight loss: factors involved. Surg Obes Relat Dis 2015; 11:215-221.
[28] da Silva AA, do Carmo J, Dubinion J, Hall JE. The role of the sympathetic nervous system in obesity-related hypertension. Curr Hypertens Rep 2009; 11:206-211.
[29] Dorresteijn JA, Visseren FL, Spiering W. Mechanisms linking obesity to hypertension. Obes Rev 2012; 13:17-26.
[30] Weyer C, Pratley RE, Snitker S, Spraul M, Ravussin E, Tataranni PA. Ethnic differences in insulinemia and sympathetic tone as links between obesity and blood pressure. Hypertension 2000; 36:531-537.
[31] Himpens J, Cadiere GB, Bazi M, Vouche M, Cadiere B, Dapri G. Long-term outcomes of laparoscopic adjustable gastric banding. Arch Surg 2011; 146:802-807.
[32] De Angelis K, Senador DD, Mostarda C, Irigoyen MC, Morris M. Sympathetic overactivity precedes metabolic dysfunction in a fructose model of glucose intolerance in mice. Am J Physiol Regul Integr Comp Physiol 2012; 302:950-957.
[33] Mark AL. Selective leptin resistance revisited. Am J Physiol Regul Integr Comp Physiol 2013; 305:566-581.
[34] Rahmouni K, Fath MA, Seo S, Thedens DR, Berry CJ, Weiss R, et al. Leptin resistance contributes to obesity and hypertension in mouse models of Bardet-Biedl syndrome. J Clin Invest 2008; 118:1458-1467.
[35] Fruhbeck G. Pivotal role of nitric oxide in the control of blood pressure after leptin administration. Diabetes 1999; 48:903-908.
[36] Bravo PE, Morse S, Borne DM, Aguilar EA, Reisin E. Leptin and hypertension in obesity. Vasc Health Risk Manag 2006; 2:163-169.
[37] Razny U, Kiec-Wilk B, Polus A, Wator L, Dyduch G, Partyka L, et al. The adipose tissue gene expression in mice with different nitric oxide availability. J Physiol Pharmacol 2010; 61:607-618.
[38] Vila G, Riedl M, Maier C, Struck J, Morgenthaler NG, Handisurya A, et al. Plasma MR-proADM correlates to BMI and decreases in relation to leptin after gastric bypass surgery. Obesity (Silver Spring) 2009; 17:1184-1188.
[39] Mendizábal Y, Llorens S, Nava E. Hypertension in Metabolic Syndrome: Vascular Pathophysiology. Int J Hypertens 2013; 2013:230868.