

# BÖLÜM 28

## OBEZİTE VE HİPERTANSİYON

Türkan PAŞALI KİLİT<sup>1</sup>  
Celal KİLİT<sup>2</sup>

### Giriş

Obezite, dünya çapında sıklığı giderek artan ciddi bir halk sağlığı sorunudur. Obezite ile ilişkili hastalıklar da yıllar içerisinde artış göstermiştir. Kan basıncı artışı ile kilo alımı arasında açık bir ilişki vardır.<sup>(1)</sup> Obez bireylerde hipertansiyon görülme riski normal bireylere göre 3,5 kat daha yüksek bulunmuştur. National Health and Nutrition Examination Survey (NHANES) çalışmasından elde edilen verilerde vücut kitle indeksi (VKİ) 30 kg/m<sup>2</sup>den düşük olan bireylerde hipertansiyon sıklığı %15,3 iken, VKİ 30 kg/m<sup>2</sup>den yüksek olan obez bireylerde hipertansiyon sıklığı %42,5 olarak bulunmuştur.<sup>(2)</sup> Framingham Kalp Çalışmasından elde edilen veriler, erkeklerde esansiyel hipertansiyonun %78'inin, kadınlarda ise %65'inin kilo alımıyla bağlantılı olabileceğini göstermiştir.<sup>(3)</sup> Hipertansif obez bireyler kilo verdiklerinde kan basınçları düşmektedir.<sup>(4)</sup>

### Obezite ile İlişkili Hipertansiyonun Patofizyolojisi

Obezite ile ilişkili hipertansiyonun mekanizmaları karmaşıktır ve Tablo 1'de gösterilmiştir. Genetik ve çevresel faktörler dışında sempatik sinir sistemi, renal ve adrenal disfonksiyon, bozulmuş sodyum homeostazı, endotel disfonksiyonu, adipokinler ve insülin direnci, obeziteye bağlı hipertansiyon gelişiminde rol oynamaktadır.<sup>(5)</sup>

Obezite-hipertansiyon ilişkisi, 20. yüzyılın başlarından beri bilinmektedir. Obez bireylerde hipertansiyon oluşum mekanizmaları kompleks ve multifaktöriyeldir. İnsan ve hayvan çalışmaları, obezitede hipertansiyonun sıvı retansiyonu ile ilişkili olduğunu göstermektedir.<sup>(6)</sup>

<sup>1</sup> Dr. Öğr. Üyesi, Kütahya Sağlık Bilimleri Üniversitesi Tıp Fakültesi, İç Hastalıkları Ana Bilim Dalı, turkandr@yahoo.com  
<sup>2</sup> Doç. Dr., Uşak Üniversitesi Tıp Fakültesi, Kardiyoloji Ana Bilim Dalı, ckilit@hotmail.com

lerin ve beta blokerlerin olumsuz metabolik etkileri ve beta blokerlerin obeziteyi artırıcı etkileri nedeniyle bu grup ilaçlar ilk seçenek olarak tercih edilmelidir. Beta bloker kullanımı gerekiyorsa karvedilol veya nebivolol gibi kardiyoselektif beta blokerler tercih edilmelidir.

## KAYNAKÇA

- Wang Y, Wang QJ. The prevalence of prehypertension and hypertension among US adults according to the new joint national committee guidelines: new challenges of the old problem. *Arch Intern Med.* 2004; 164(19): 2126-2134. Doi: 10.1001/archinte.164.19.2126
- Landsberg L, Aronne LJ, Beilin LJ, et al. Obesity-related hypertension: pathogenesis, cardiovascular risk, and treatment--a position paper of the The Obesity Society and The American Society of Hypertension. *Obesity (Silver Spring).* 2013; 21(1): 8-24. Doi: 10.1002/oby.20181
- Garrison RJ, Kannel WB, Stokes J 3rd, et al. Incidence and precursors of hypertension in young adults: the Framingham Offspring Study. *Prev Med.* 1987; 16(2): 235-251. Doi: 10.1016/0091-7435(87)90087-9
- Stevens VJ, Obarzanek E, Cook NR, et al. Trials for the Hypertension Prevention Research Group. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. *Ann Intern Med.* 2001; 134(1): 1-11. Doi: 10.7326/0003-4819-134-1-200101020-00007
- Brown CD, Higgins M, Donato KA, et al. Body mass index and the prevalence of hypertension and dyslipidemia. *Obes Res.* 2000; 8(9): 605-619. Doi: 10.1038/oby.2000.79
- Rocchini AP. Obesity hypertension. *Am J Hypertens.* 2002; 15(2 Pt 2): 50S-52S. Doi: 10.1016/s0895-7061(01)02299-3
- Messerli FH, Sundgaard-Riise K, Reisin E, et al. Disparate cardiovascular effects of obesity and arterial hypertension. *Am J Med.* 1983; 74(5): 808-812. Doi: 10.1016/0002-9343(83)91071-9
- Corry DB, Tuck ML. (2001). Endocrine aspects of hypertension. In Kenneth L Becker, John P. Bilezikian, William J. Bremner, & Wellington Hung (Eds.), *Principles and Practice of Endocrinology and Metabolism* (3<sup>rd</sup> ed., pp. 791-805). Philadelphia: Lippincott Williams & Wilkins.
- Hall JE, Hildebrandt DA, Kuo J. Obesity hypertension: role of leptin and sympathetic nervous system. *Am J Hypertens.* 2001; 14(6 Pt 2): 103S-115S. Doi: 10.1016/s0895-7061(01)02077-5
- Levy Y, Elias N, Cogan U, et al. Abnormal erythrocyte rheology in patients with morbid obesity. *Angiology.* 1993; 44(9): 713-717. Doi: 10.1177/000331979304400907
- Messerli FH, Sundgaard-Riise K, Reisin ED, et al. Dimorphic cardiac adaptation to obesity and arterial hypertension. *Ann Intern Med.* 1983; 99(6): 757-761. Doi: 10.7326/0003-4819-99-6-757
- Hubert HB, Feinleib M, McNamara PM, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation.* 1983; 67(5): 968-977. Doi: 10.1161/01.cir.67.5.968
- Stamler J. The INTERSALT Study: background, methods, findings, and implications. *Am J Clin Nutr.* 1997; 65(2 Suppl): 626S-642S. Doi: 10.1093/ajcn/65.2.626S
- Yang Q, Zhang Z, Kuklina EV, et al. Sodium intake and blood pressure among US children and adolescents. *Pediatrics.* 2012; 130(4): 611-619. Doi: 10.1542/peds.2011-3870
- Frohlich ED. Obesity and hypertension. Hemodynamic aspects. *Ann Epidemiol.* 1991; 1(4): 287-293. Doi: 10.1016/1047-2797(91)90039-f
- Oberleithner H, Riethmüller C, Schillers H, et al. Plasma sodium stiffens vascular endothelium and reduces nitric oxide release. *Proc Natl Acad Sci U S A.* 2007; 104(41): 16281-16286. Doi: 10.1073/pnas.0707791104
- Chughtai HL, Morgan TM, Rocco M, et al. Renal sinus fat and poor blood pressure control in middle-aged and elderly individuals at risk for cardiovascular events. *Hypertension.* 2010; 56(5): 901-906. Doi: 10.1161/HYPERTENSIONAHA.110.157370
- Chandra A, Neeland JJ, Berry JD, et al. The relationship of body mass and fat distribution with incident hypertension: observations from the Dallas Heart Study. *J Am Coll Cardiol.* 2014; 64(10): 997-1002. Doi: 10.1016/j.jacc.2014.05.057
- Engeli S, Sharma AM. The renin-angiotensin system and natriuretic peptides in obesity-associated hypertension. *J Mol Med (Berl).* 2001; 79(1): 21-29. Doi: 10.1007/s001090000144
- Calhoun DA. Hyperaldosteronism as a common cause of resistant hypertension. *Annu Rev Med.* 2013; 64: 233-247. Doi: 10.1146/annurev-med-042711-135929
- Alonso-Galicia M, Brands MW, Zappe DH, et al. Hypertension in obese Zucker rats. Role of angiotensin II and adrenergic activity. *Hypertension.* 1996; 28(6): 1047-1054. Doi: 10.1161/01.hyp.28.6.1047
- Robles RG, Villa E, Santirso R, et al. Effects of captopril on sympathetic activity, lipid and carbohydrate metabolism in a model of obesity-induced hypertension in dogs. *Am J Hypertens.* 1993; 6(12): 1009-1015. Doi: 10.1093/ajh/6.12.1009

23. Asferg CL, Nielsen SJ, Andersen UB, et al. Relative atrial natriuretic peptide deficiency and inadequate renin and angiotensin II suppression in obese hypertensive men. *Hypertension*. 2013; 62(1): 147-153. Doi: 10.1161/HYPERTENSIONAHA.111.00791
24. Messerli FH, Christie B, DeCarvalho JG, et al. Obesity and essential hypertension. Hemodynamics, intravascular volume, sodium excretion, and plasma renin activity. *Arch Intern Med*. 1981; 141(1): 81-85. Doi: 10.1001/archinte
25. Hall ME, do Carmo JM, da Silva AA, et al. Obesity, hypertension, and chronic kidney disease. *Int J Nephrol Renovasc Dis*. 2014; 7: 75-88. Doi: 10.2147/IJNRD.S39739
26. Amann K, Benz K. Structural renal changes in obesity and diabetes. *Semin Nephrol*. 2013; 33(1): 23-33. Doi: 10.1016/j.semephrol.2012.12.003
27. Burton JO, Gray LJ, Webb DR, et al. Association of anthropometric obesity measures with chronic kidney disease risk in a non-diabetic patient population. *Nephrol Dial Transplant*. 2012; 27(5): 1860-1866. Doi: 10.1093/ndt/gfr574
28. Hausberg M, Mark AL, Hoffman RP, et al. Dissociation of sympathoexcitatory and vasodilator actions of modestly elevated plasma insulin levels. *J Hypertens*. 1995; 13(9): 1015-1021. Doi: 10.1097/00004872-199509000-00012
29. Montagnani M, Quon MJ. Insulin action in vascular endothelium: potential mechanisms linking insulin resistance with hypertension. *Diabetes Obes Metab*. 2000; 2(5): 285-292. Doi: 10.1046/j.1463-1326.2000.00092.x
30. Anderson EA, Balon TW, Hoffman RP, et al. Insulin increases sympathetic activity but not blood pressure in borderline hypertensive humans. *Hypertension*. 1992; 19(6 Pt 2): 621-627. Doi: 10.1161/01.hyp.19.6.621
31. Wang ZV, Scherer PE. Adiponectin, cardiovascular function, and hypertension. *Hypertension*. 2008; 51(1): 8-14. Doi: 10.1161/HYPERTENSIONAHA.107.099424
32. Weyer C, Funahashi T, Tanaka S, et al. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. *J Clin Endocrinol Metab*. 2001; 86(5): 1930-1935. Doi: 10.1210/jcem.86.5.7463
33. Tanida M, Shen J, Horii Y, et al. Effects of adiponectin on the renal sympathetic nerve activity and blood pressure in rats. *Exp Biol Med (Maywood)*. 2007; 232(3): 390-397.
34. Korda M, Kubant R, Patton S, et al. Leptin-induced endothelial dysfunction in obesity. *Am J Physiol Heart Circ Physiol*. 2008; 295(4): H1514-1521. Doi: 10.1152/ajpheart.00479.2008
35. Whitworth JA, Schyvens CG, Zhang Y, et al. Glucocorticoid-induced hypertension: from mouse to man. *Clin Exp Pharmacol Physiol*. 2001; 28(12): 993-996. Doi: 10.1046/j.1440-1681.2001.03584.x
36. Ruano M, Silvestre V, Castro R, et al. Morbid obesity, hypertensive disease and the renin-angiotensin-aldosterone axis. *Obes Surg*. 2005; 15(5): 670-676. Doi: 10.1381/0960892053923734
37. Engeli S, Negrel R, Sharma AM. Physiology and pathophysiology of the adipose tissue renin-angiotensin system. *Hypertension*. 2000; 35(6): 1270-1277. Doi: 10.1161/01.hyp.35.6.1270
38. Dorresteijn JA, Schrover IM, Visseren FL, et al. Differential effects of renin-angiotensin-aldosterone system inhibition, sympathoinhibition and diuretic therapy on endothelial function and blood pressure in obesity-related hypertension: a double-blind, placebo-controlled cross-over trial. *J Hypertens*. 2013; 31(2): 393-403. Doi: 10.1097/JHH.0b013e32835b6c02
39. Bentley-Lewis R, Adler GK, Perlstein T, et al. Body mass index predicts aldosterone production in normotensive adults on a high-salt diet. *J Clin Endocrinol Metab*. 2007; 92(11): 4472-4475. Doi: 10.1210/jc.2007-1088
40. Shaltout HA, Rose JC, Chappell MC, et al. Angiotensin-(1-7) deficiency and baroreflex impairment precede the antenatal Betamethasone exposure-induced elevation in blood pressure. *Hypertension*. 2012; 59(2): 453-458. Doi: 10.1161/HYPERTENSIONAHA.111.185876
41. Hirsch J, Leibel RL, Mackintosh R, et al. Heart rate variability as a measure of autonomic function during weight change in humans. *Am J Physiol*. 1991; 261(6 Pt 2): R1418-1423. Doi: 10.1152/ajpregu.1991.261.6.R1418
42. Arone LJ, Mackintosh R, Rosenbaum M, et al. Autonomic nervous system activity in weight gain and weight loss. *Am J Physiol*. 1995; 269(1 Pt 2): R222-225. Doi: 10.1152/ajpregu.1995.269.1.R222
43. Lambert E, Sari CI, Dawood T, et al. Sympathetic nervous system activity is associated with obesity-induced subclinical organ damage in young adults. *Hypertension*. 2010; 56(3): 351-358. Doi: 10.1161/HYPERTENSIONAHA.110.155663
44. Hall JE, Hildebrandt DA, Kuo J. Obesity hypertension: role of leptin and sympathetic nervous system. *Am J Hypertens*. 2001; 14(6 Pt 2): 103S-115S. Doi: 10.1016/s0895-7061(01)02077-5
45. Aroor AR, Demarco VG, Jia G, et al. The role of tissue Renin-Angiotensin-aldosterone system in the development of endothelial dysfunction and arterial stiffness. *Front Endocrinol (Lausanne)*. 2013; 4: 161. Doi: 10.3389/fendo.2013.00161
46. Liao D, Arnett DK, Tyroler HA, et al. Arterial stiffness and the development of hypertension. The

- ARIC study. *Hypertension*. 1999; 34(2): 201-206. Doi: 10.1161/01.hyp.34.2.201
47. Kotsis VT, Stabouli SV, Papamichael CM, et al. Impact of obesity in intima media thickness of carotid arteries. *Obesity (Silver Spring)*. 2006; 14(10): 1708-1715. Doi: 10.1038/oby.2006.196
48. Furukawa S, Fujita T, Shimabukuro M, et al. Increased oxidative stress in obesity and its impact on metabolic syndrome. *J Clin Invest*. 2004; 114(12): 1752-1761. Doi: 10.1172/JCI21625
49. Chae CU, Lee RT, Rifai N, et al. Blood pressure and inflammation in apparently healthy men. *Hypertension*. 2001; 38(3): 399-403. Doi: 10.1161/01.hyp.38.3.399
50. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019; 140(11): e563-e595. Doi: 10.1161/CIR.0000000000000677
51. Jensen MD, Ryan DH, Apovian CM, et al. American College of Cardiology/American Heart Association Task Force on Practice Guidelines; Obesity Society. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *J Am Coll Cardiol*. 2014; 63(25 Pt B): 2985-3023. Doi: 10.1016/j.jacc.2013.11.004
52. Kaplan, NM. (2005). Kaplan's Clinical Hypertension. (9<sup>th</sup> ed.). Philadelphia: Lippincott Williams & Wilkins.
53. Masuo K, Mikami H, Ogihara T, et al. Weight reduction and pharmacologic treatment in obese hypertensives. *Am J Hypertens*. 2001; 14(6 Pt 1): 530-538. Doi: 10.1016/s0895-7061(00)01279-6
54. Narkiewicz K. Obesity-related hypertension: relevance of vascular responses to mental stress. *J Hypertens*. 2002; 20(7): 1277-1278. Doi: 10.1097/00004872-200207000-00009. PMID: 12131519
55. Wofford MR, Davis MM, Harkins KG, et al. Therapeutic considerations in the treatment of obesity hypertension. *J Clin Hypertens (Greenwich)*. 2002; 4(3): 189-196. Doi: 10.1111/j.1524-6175.2002.00502.x
56. Swales, JD. (1995). Manual of Hypertension. Oxford: Blackwell Science.
57. Appel LJ, Brands MW, Daniels SR, et al.; American Heart Association. Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. *Hypertension*. 2006; 47(2): 296-308. Doi: 10.1161/01.HYP.0000202568.01167.B6
58. Jee SH, Miller ER 3rd, Guallar E, et al. The effect of magnesium supplementation on blood pressure: a meta-analysis of randomized clinical trials. *Am J Hypertens*. 2002; 15(8): 691-696. Doi: 10.1016/s0895-7061(02)02964-3
59. Griffith LE, Guyatt GH, Cook RJ, et al. The influence of dietary and nondietary calcium supplementation on blood pressure: an updated metaanalysis of randomized controlled trials. *Am J Hypertens*. 1999; 12(1 Pt 1): 84-92. Doi: 10.1016/s0895-7061(98)00224-6
60. Neter JE, Stam BE, Kok FJ, et al. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*. 2003; 42(5): 878-884. Doi: 10.1161/01.HYP.0000094221.86888.AE
61. Van Gaal LF, Scheen AJ, Rissanen AM, et al.; RIO-Europe Study Group. Long-term effect of CB1 blockade with rimonabant on cardiometabolic risk factors: two year results from the RIO-Europe Study. *Eur Heart J*. 2008; 29(14): 1761-1771. Doi: 10.1093/eurheartj/ehn076
62. Scholze J, Grimm E, Herrmann D, et al. Optimal treatment of obesity-related hypertension: the Hypertension-Obesity-Sibutramine (HOS) study. *Circulation*. 2007; 115(15): 1991-1998. Doi: 10.1161/CIRCULATIONAHA.106.625400
63. Poirier P, Giles TD, Bray GA, et al. American Heart Association; Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation*. 2006; 113(6): 898-918. Doi: 10.1161/CIRCULATIONAHA.106.171016
64. Russell-Jones D, Vaag A, Schmitz O, et al. Liraglutide Effect and Action in Diabetes 5 (LEAD-5) met+SU Study Group. Liraglutide vs insulin glargine and placebo in combination with metformin and sulfonylurea therapy in type 2 diabetes mellitus (LEAD-5 met+SU): a randomised controlled trial. *Diabetologia*. 2009; 52(10): 2046-2055. Doi: 10.1007/s00125-009-1472-y
65. Sjöström L, Narbro K, Sjöström CD, et al. Swedish Obese Subjects Study. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med*. 2007; 357(8): 741-752. Doi: 10.1056/NEJMoa066254
66. Mancia G, Grassi G, Zanchetti A. New-onset diabetes and antihypertensive drugs. *J Hypertens*. 2006; 24(1): 3-10. Doi: 10.1097/01.hjh.0000194119.42722.21

67. Kaiser T, Heise T, Nosek L, et al. Influence of nebivolol and enalapril on metabolic parameters and arterial stiffness in hypertensive type 2 diabetic patients. *J Hypertens.* 2006; 24(7): 1397-1403. Doi: 10.1097/01.hjh.0000234121.48272.67
68. Pepine CJ, Handberg EM, Cooper-DeHoff RM, et al. INVEST Investigators. A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial. *JAMA.* 2003; 290(21): 2805-2816. Doi: 10.1001/jama.290.21.2805
69. Frohlich ED. Clinical management of the obese hypertensive patient. *Cardiol Rev.* 2002; 10(3): 127-138. Doi: 10.1097/00045415-200205000-00001
70. Symplicity HTN-2 Investigators, Esler MD, Krum H, Sobotka PA, et al. Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial. *Lancet.* 2010; 376(9756): 1903-1909. Doi: 10.1016/S0140-6736(10)62039-9
71. Phillips SA, Kung JT. Mechanisms of adiponectin regulation and use as a pharmacological target. *Curr Opin Pharmacol.* 2010; 10(6): 676-683. Doi: 10.1016/j.coph.2010.08.002