

14

Pulmoner Hipertansiyon

Uzm. Dr. Abdulkadir Çakmak
Amasya Sabuncuoğlu Şerefeddin
Devlet Hastanesi Kardiyoloji Kliniği

Pulmoner hipertansiyon (PH), dinlenme halinde sağ kalp kateterizasyonu (SKK) ile değerlendirilen ortalama pulmoner arter basıncının (PAB) ≥ 25 mmb. Doğumsal Kalp Hastalıklarıyla Birlikte Seyreden Pulmoner Hipertansiyon

Pulmoner hipertansiyon konjenital kalp anomali-si bulunanlarda % 5-10 oranında görülmektedir¹³⁻¹⁷. Atrial septal defekt (ASD) erişkinde an sık görülen doğuştan kalp hastalığıdır ve tüm doğuştan kalp hastalıklarının % 5-10'unu oluşturur¹⁵. Tedavi edilmeyen ASD'li hastalarda 40 yaş civarında %35-40 oranında pulmoner hipertansiyon gelişir. Ventrikül septal defekti veya patent duktus arteriozusu bulunan hastalarda pulmoner hipertansiyon ASD 'si bulunanlardan daha hızlı gelişir. Atrial septal defekt başarılı bir şekilde kapatıldığında pulmoner arter basıncında düşmeyle birlikte sağ kalp volüm yükünden kurtulmakta ve sağ kalp boşluk boyutları azalmaktadır¹⁶.

Şant varlığında cerrahi düzeltmeden sonra dahi pulmoner hipertansiyon gelişebilmektedir. Eisenmenger sendromu, intrakardiyak sistemik-pulmoner bağlantıların yol açtığı ciddi pulmoner hipertansiyon sonucunda sol-sağ şantın ters dönmesini tanımlamaktadır¹⁵. Sağ ventrikül yetersizliği geliştikten sonra sağ-sol şant ortaya çıkar ve hastada siyanoz gelişir. Bu safhada tedavi fayda sağlamaz. Eisenmenger sendromu gelişmiş hastalarda 10 yıllık sağkalım % 80'dir¹⁸.

c. Portal Hipertansiyonla İlişkili Pulmoner Hipertansiyon

Portal hipertansiyonu olanlarda pulmoner hipertansiyon %2-6 oranında görülmektedir¹⁹. Pulmoner vasküler dirençte belirgin artış yoktur. Ağır pulmoner hipertansiyon geri dönüşümsüz sağ kalp yetersizliği yapabileceğinden bu grupta karaciğer nakli kontrendikedir.

d. HIV İlişkili Pulmoner Hipertansiyon

Hastaların % 0.6'sında pulmoner hipertansiyon görülür²⁰. Üç yıllık sağkalım %21'dir.

e. İlaçlara Bağlı Pulmoner Hipertansiyon

Aminoreks ve fenfluramin gibi anoreksijanların pulmoner hipertansiyona yol açtığı bilinmektedir²¹. Bu ajanlar pulmoner vazokonstriksiyon yaparlar.

f. Yenidoğanın Persistan Pulmoner Hipertansiyonu

Her 1000 canlı doğumun 2'sinde görülür. Çoğu zaman mekanik ventilasyon gereklidir.

g. Pulmoner Veno-Oklüzif Hastalık

Oldukça nadir görülür. Pulmoner ven ve venüllerin içinde fibröz intimal yastıkçıklar görülür²².

h. Pulmoner Kapiller Hemanjiyomatöz

Kaynaklar

1. Rubin LJ. Pathology and pathophysiology of primary pulmonary hypertension. *Am J Cardiol*. 1995;75:51A-54A.
2. Rubin LJ, Badesch DB. Evaluation and management of the patient with pulmonary arterial hypertension. *Ann Intern Med*. 2005;143:282-92.
3. Galiè N, Hoeper MM, Humbert M, Torbicki A, Vachiery JL, Barbera JA, Beghetti M, Corris P, Gaine S, Gibbs JS, Gomez-Sanchez MA, Jondeau G, Klepetko W, Opitz C, Peacock A, Rubin L, Zellweger M, Simonneau G; ESC Committee for Practice Guidelines (CPG). Guidelines for the diagnosis and treatment of pulmonary hypertension: the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). *Eur Heart J*. 2009;30:2493-537.
4. Kovacs G, Berghold A, Scheidl S, Olschewski H. Pulmonary arterial pressure during rest and exercise in healthy subjects. A systematic review. *Eur Respir J* 2009;doi: 10.1183/09031936.00145608.
5. Badesch BD, Champion HC, Gomez-Sanchez MA, Hoeper M, Loyd J, Manes A, McGoon M, Naeije R, Olschewski H, Oudiz R, Torbicki A. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol* 2009;54:S55-S56.
6. Naeije R, Melot C, Niset G, Delcroix M, Wagner PD. Mechanisms of improved arterial oxygenation after peripheral chemoreceptor stimulation during hypoxic exercise. *J Appl Physiol* 1993;74:1666-1671.
7. Recommendations on the management of pulmonary hypertension in clinical practice. *Heart* 2001;86:11-13.
8. Simonneau G, Robbins I, Beghetti M, Channick RN, Delcroix M, Denton CP, Elliott CG, Gaine S, Gladwin MT, Jing ZC, Krowka MJ, Langleben D, Nakanishi N, Souza R. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol* 2009;54:S43-S54.
9. Gabbay E, Yeow W, Playford D. Pulmonary arterial hypertension (PAH) is an uncommon cause of pulmonary hypertension (PH) in an unselected population: the Armadale echocardiography study. *Am J Resp Crit Care Med* 2007;175:A713.
10. Lilienfeld DE, Rubin LJ. Mortality from primary pulmonary hypertension in the United States, 1979-1996. *Chest*. 2000;117:796-800.
11. D'Alonzo GE, Barst RJ, Ayres SM, Bergofsky EH, Brundage BH, Detre KM, Fishman AP, Goldring RM, Groves BM, Kernis JT, et al. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. *Ann Intern Med*. 1991;115:343-9.
12. Sanchez O, Sitbon O, Jaïs X, Simonneau G, Humbert M. Immunosuppressive therapy in connective tissue diseases-associated pulmonary arterial hypertension. *Chest*. 2006;130:182-9.
13. Kidd L, Driscoll DJ, Gersony WM, Hayes CJ, Keane JF, O'Fallon WM, Pieroni DR, Wolfe RR, Weidman WH. Second natural history study of congenital heart defects. Results of treatment of patients with ventricular septal defects. *Circulation*. 1993;87:138-51.
14. Humbert M, Sanchez O, Fartoukh M, Jagot JL, Le Gall C, Sitbon O, Parent F, Simonneau G. Short-term and long-term epoprostenol (prostacyclin) therapy in pulmonary hypertension secondary to connective tissue diseases: results of a pilot study. *Eur Respir J*. 1999;13:1351-1356.
15. Diller GP, Gatzoulis MA. Pulmonary vascular disease in adults with congenital heart disease. *Circulation*. 2007;115:1039-50.
16. Kaya MG, Baykan A, Dogan A, Inanc T, Gunebakmaz O, Dogdu O, Uzum K, Eryol NK, Narin N. Intermediate-term effects of transcatheter secundum atrial septal defect closure on cardiac remodeling in children and adults. *Pediatr Cardiol*. 2010;31:474-82.
17. Steele PM, Fuster V, Cohen M, Ritter DG, McGoon DC. Isolated atrial septal defect with pulmonary vascular obstructive disease--long-term follow-up and prediction of outcome after surgical correction. *Circulation*. 1987;76:1037-42.
18. Hopkins WE, Ochoa LL, Richardson GW, Trulock EP. Comparison of the hemodynamics and survival of adults with severe primary pulmonary hypertension or Eisenmenger syndrome. *J Heart*

- Lung Transplant. 1996; 15:100-5.
19. Hadengue A, Benhayoun MK, Lebrec D, Benhamou JP. Pulmonary hypertension complicating portal hypertension: prevalence and relation to splanchnic hemodynamics. *Gastroenterology*. 1991;100:520-8.
 20. Opravil M, Pechère M, Speich R, Joller-Jemelka HI, Jenni R, Russi EW, Hirschel B, Lüthy R. HIV-associated primary pulmonary hypertension. A case control study. Swiss HIV Cohort Study. *Am J Respir Crit Care Med*. 1997;155:990-5.
 21. Abenhaim L, Moride Y, Brenot F, Rich S, Benichou J, Kurz X, Higenbottam T, Oakley C, Wouters E, Aubier M, Simonneau G, Bégaud B. Appetite-suppressant drugs and the risk of primary pulmonary hypertension. International Primary Pulmonary Hypertension Study Group. *N Engl J Med*. 1996;335:609-16.
 22. Montani D, Kemp K, Dorfmüller P, Sitbon O, Simonneau G, Humbert M. Idiopathic pulmonary arterial hypertension and pulmonary veno-occlusive disease: similarities and differences. *Semin Respir Crit Care Med*. 2009; 30:411-20.
 23. El-Gabaly M, Farver CF, Budev MA, Mohammed TL. Pulmonary capillary hemangiomatosis imaging findings and literature update. *J Comput Assist Tomogr*. 2007;31:608-10.
 24. Türkiye Klinikleri Journal of Cardiology, 2010;3-1;60.
 25. Wood P. Pulmonary hypertension with special reference to the vasoconstrictive factor. *Br Heart J*. 1958;20:557-70.
 26. Zener JC, Hancock EW, Shumway NE, Harrison DC. Regression of extreme pulmonary hypertension after mitral valve surgery. *Am J Cardiol*. 1972;30:820-6.
 27. Scharf SM, Iqbal M, Keller C, Criner G, Lee S, Fessler HE; National Emphysema Treatment Trial (NETT) Group. Hemodynamic characterization of patients with severe emphysema. *Am J Respir Crit Care Med*. 2002;166:314-22.
 28. Chaouat A, Bugnet AS, Kadaoui N, Schott R, Enache I, Ducoloné A, Ehrhart M, Kessler R, Weitzenblum E. Severe pulmonary hypertension and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2005; 172:189-94.
 29. Thabut G, Dauriat G, Stern JB, Logeart D, Lévy A, Marrash-Chahla R, Mal H. Pulmonary hemodynamics in advanced COPD candidates for lung volume reduction surgery or lung transplantation. *Chest*. 2005;127:1531-6.
 30. Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen therapy in hypoxemic chronic obstructive lung disease: a clinical trial. *Ann Intern Med*. 1980;93:391-8.
 31. Weitzenblum E, Sautegeau A, Ehrhart M, Mammosser M, Pelletier A. Long-term oxygen therapy can reverse the progression of pulmonary hypertension in patients with chronic obstructive pulmonary disease. *Am Rev Respir Dis*. 1985;131:493-8.
 32. Harari S, Simonneau G, De Juli E, Brenot F, Cerrina J, Colombo P, Gronda E, Micallef E, Parent F, Darteville P. Prognostic value of pulmonary hypertension in patients with chronic interstitial lung disease referred for lung or heart-lung transplantation. *J Heart Lung Transplant*. 1997;16:460-3.
 33. Noth I, Martinez FJ. Recent advances in idiopathic pulmonary fibrosis. *Chest*. 2007;132:637-50.
 34. Coffey MJ, FitzGerald MX, McNicholas WT. Comparison of oxygen desaturation during sleep and exercise in patients with cystic fibrosis. *Chest*. 1991;100:659-62.
 35. Marrone O, Bonsignore MR. Pulmonary haemodynamics in obstructive sleep apnoea. *Sleep Med Rev*. 2002;6:175-93.
 36. Bourbonnais JM, Samavati L. Clinical predictors of pulmonary hypertension in sarcoidosis. *Eur Respir J*. 2008;32:296-302.
 37. Galiè N, Hoeper MM, Humbert M, Torbicki A, Vachiery JL, Barbera JA, Beghetti M, Corris P, Gaine S, Gibbs JS, Gomez-Sanchez MA, Jondeau G, Klepetko W, Opitz C, Peacock A, Rubin L, Zellweger M, Simonneau G; ESC Committee for Practice Guidelines (CPG). Guidelines for the diagnosis and treatment of pulmonary hypertension: the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). *Eur Heart J*. 2009;30:2493-537.
 38. Rich S, Dantzker DR, Ayres SM, Bergofsky EH,

- Brundage BH, Detre KM, Fishman AP, Goldring RM, Groves BM, Koerner SK, et al. Primary pulmonary hypertension. A national prospective study. *Ann Intern Med.* 1987;107:216-23.
39. Bossone E, Paciocco G, Iarussi D, Agretto A, Iacono A, Gillespie BW, Rubenfire M. The prognostic role of the ECG in primary pulmonary hypertension. *Chest.* 2002;121:513-8.
40. Galiè N, Manes A, Branzi A. Evaluation of pulmonary arterial hypertension. *Curr Opin Cardiol.* 2004;19:575-81.
41. Paciocco G, Martinez FJ, Bossone E, Pielsticker E, Gillespie B, Rubenfire M. Oxygen desaturation on the six-minute walk test and mortality in untreated primary pulmonary hypertension. *Eur Respir J.* 2001;17:647-52.
42. Fisher MR, Forfia PR, Chamera E, Houston-Harris T, Champion HC, Girgis RE, Corretti MC, Hassoun PM. Accuracy of Doppler echocardiography in the hemodynamic assessment of pulmonary hypertension. *Am J Resp Crit Care Med* 2009;179:615-621.
43. Denton CP, Cailes JB, Phillips GD, Wells AU, Black CM, Bois RM. Comparison of Doppler echocardiography and right heart catheterization to assess pulmonary hypertension in systemic sclerosis. *Br J Rheumatol.* 1997;36:239-43.
44. Tunariu N, Gibbs SJR, Win Z, Gin-Sing W, Graham A, Gishen P, Al-Nahhas A. Ventilation-perfusion scintigraphy is more sensitive than multidetector CTPA in detecting chronic thromboembolic pulmonary disease as a treatable cause of pulmonary hypertension. *J Nucl Med* 2007;48:680-684.
45. Resten A, Maitre S, Humbert M, Rabiller A, Sitbon O, Capron F, Simonneau G, Musset D. Pulmonary hypertension: CT of the chest in pulmonary venoocclusive disease. *Am J Roentgenol* 2004; 183:65-70.
46. Dartevelle P, Fadel E, Mussot S, Chapelier A, Herve P, de Perrot M, Cerrina J, Ladurie FL, Lehouerou D, Humbert M, Sitbon O, Simonneau G. Chronic thromboembolic pulmonary hypertension. *Eur Respir J* 2004;23:637-648.
47. Marcus JT, Gan CT, Zwanenburg JJ, Boonstra A, Allaart CP, Go"tte MJW, Vonk-Noordegraaf A. Interventricular mechanical asynchrony in pulmonary arterial hypertension: left-to-right delay in peak shortening is related to right ventricular overload and left ventricular underfilling. *J Am Coll Cardiol* 2008;51:750-757.
48. Galiè N, Branzi A. Pulmonary arterial hypertension: therapeutic algorithm. *Ital Heart J.* 2005;6:856-60.
49. Barst RJ, Gibbs JS, Ghofrani HA, Hoeper MM, McLaughlin VV, Rubin LJ, Sitbon O, Tapson VF, Galiè N. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54: S78-84.
50. Trow TK, McArdle JR. Diagnosis of pulmonary arterial hypertension. *Clin Chest Med.* 2007;28:59-73.
51. McArdle JR, Trow TK, Lerz K. Pulmonary hypertension in older adults. *Clin Chest Med.* 2007;28:717-33.
52. Eysmann SB, Palevsky HI, Reichel N, Hackney K, Douglas PS. Two-dimensional and Doppler echocardiographic and cardiac catheterization correlates of survival in primary pulmonary hypertension. *Circulation* 1989;80:353-360.
53. Raymond RJ, Hinderliter AL, Willis PW, Ralph D, Caldwell EJ, Williams W, Ettinger NA, Hill NS, Summer WR, de Boisblanc B, Schwartz T, Koch G, Clayton LM, Jobsis MM, Crow JW, Long W. Echocardiographic predictors of adverse outcomes in primary pulmonary hypertension. *J Am Coll Cardiol* 2002; 39:1214-1219.
54. Tei C, Dujardin KS, Hodge DO, Bailey KR, McGoon MD, Tajik AJ, Seward SB. Doppler echocardiographic index for assessment of global right ventricular function. *J Am Soc Echocardiogr* 1996;9:838-847.
55. Yeo TC, Dujardin KS, Tei C, Mahoney DW, McGoon MD, Seward JB. Value of aDoppler-derived index combining systolic and diastolic time intervals in predicting outcome in primary pulmonary hypertension. *Am J Cardiol* 1998;81:1157-1161.
56. Forfia PR, Fisher MR, Mathai SC, Houston-Harris T, Hemnes AR, Borlaug BA, Chamera E, Corretti MC, Champion HC, Abraham TP, Girgis RE, Hassoun PM. Tricuspid annular displacement predicts survival in pulmonary hypertension. *Am J Respir Crit Care Med* 2006;174:1034-1041.
57. D'Alonzo GE, Barst RJ, Ayres SM, Bergofsky

- EH, Brundage BH, Detre KM, Fishman AP, Goldring RM, Groves BM, Kernis JT. Survival in patients with primary pulmonary hypertension. Results from a national prospective registry. *Ann Intern Med* 1991;115:343–349.
58. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;166:111–117.
59. Williams MH, Handler CE, Akram R, Smith CJ, Das C, Smee J, Nair D, Denton CP, Black CM, Coghlan JG. Role of N-terminal brain natriuretic peptide (N-TproBNP) in scleroderma-associated pulmonary arterial hypertension. *Eur Heart J* 2006;27:1485–1494.
60. Mereles D, Ehlken N, Kreuscher S, Ghofrani S, Hoepfer MM, Halank M, Meyer FJ, Karger G, Buss J, Juenger J, Holzappel N, Opitz C, Winkler J, Herth FFJ, Wilkens H, Katus HA, Olschewski H, Grunig E. Exercise and respiratory training improve exercise capacity and quality of life in patients with severe chronic pulmonary hypertension. *Circulation* 2006;114:1482–1489.
61. Herve P, Humbert M, Sitbon O, Parent F, Nunes H, Legal C, Garcia G, Simonneau G. Pathobiology of pulmonary hypertension: the role of platelets and thrombosis. *Clin Chest Med* 2001;22:451–458.
62. Hoepfer MM, Sosada M, Fabel H. Plasma coagulation profiles in patients with severe primary pulmonary hypertension. *Eur Respir J* 1998;12:1446–1449.
63. Huber K, Beckmann R, Frank H, Kneussl M, Mlczech J, Binder BR. Fibrinogen, t-PA, and PAI-1 plasma levels in patients with pulmonary hypertension. *Am J Respir Crit Care Med* 1994;150:929–933.
64. Rich S, Kaufmann E, Levy PS. The effect of high doses of calcium-channel blockers on survival in primary pulmonary hypertension. *N Engl J Med* 1992;327:76–81.
65. Sitbon O, Humbert M, Jais X, Ioos V, Hamid AM, Provencher S, Garcia G, Parent F, Herve P, Simonneau G. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation* 2005;111:3105–3111.
66. Farber HW, Loscalzo J. Pulmonary arterial hypertension. *N Engl J Med*. 2004;351:1655–65.
67. Cacoub P, Dorent R, Nataf P, Carayon A. Endothelin-1 in pulmonary hypertension. *N Engl J Med*. 1993;329:1967–8.
68. Sastry BK, Narasimhan C, Reddy NK, Raju BS. Clinical efficacy of sildenafil in primary pulmonary hypertension: a randomized, placebo-controlled, double-blind, crossover study. *J Am Coll Cardiol*. 2004;43: 1149–53.
69. Prasad S, Wilkinson J, Gatzoulis MA. Sildenafil in primary pulmonary hypertension. *N Engl J Med*. 2000;343:1342.
70. Bhatia S, Frantz RP, Severson CJ, Durst LA, McGoon MD. Immediate and longterm hemodynamic and clinical effects of sildenafil in patients with pulmonary arterial hypertension receiving vasodilator therapy. *Mayo Clin Proc* 2003;78:1207–1213.
71. Michelakis ED, Tymchak W, Noga M, Webster L, Wu XC, Lien D, Wang SH, Modry D, Archer SL. Long-term treatment with oral sildenafil is safe and improves functional capacity and hemodynamics in patients with pulmonary arterial hypertension. *Circulation* 2003;108:2066–2069.
72. Ghofrani HA, Schermuly RT, Rose F, Wiedemann R, Kohstall MG, Kreckel A, Olschewski H, Weissmann N, Enke B, Ghofrani S, Seeger W, Grimminger F. Sildenafil for long-term treatment of nonoperable chronic thromboembolic pulmonary hypertension. *Am J Respir Crit Care Med* 2003;167:1139–1141.
73. Galie` N, Brundage B, Ghofrani A, Oudiz R, Simonneau G, Safdar Z, Shapiro RS, White J, Chan M, Beardsworth A, Frumkin LR, Barst R. Tadalafil therapy for pulmonary arterial hypertension. *Circulation* 2009;119:2894–2903.
74. Manes A, Marinelli A, Palazzini M, Negro L, Leci E, Gambetti S, Bachetti C, Beciani E, Conficoni E, Branzi A, Galie` N. [Pulmonary arterial hypertension. Part II: Medical and surgical treatment]. *G Ital Cardiol (Rome)*. 2009; 10: 366–81.