

9. Bölüm

İTERSTİSYEL AKCİĞER HASTALIKLARI VE PULMONER HİPERTANSİYON

Selvi AŞKAR¹
Müntecep AŞKAR²

GİRİŞ

Pulmoner hipertansiyon (PH), pulmoner arteriyel basınçta yükselme ve bunun neticesinde sağ kalp yetmezliğiyle sonuçlanan, pulmoner arterlerde remodeling ve vazokonstriksiyonla karakterize ilerleyici pulmoner vasküler bir hastalıktır. Gecikmiş tanı ve yetersiz tedavi durumunda PH, pulmoner vasküler direnç artışı, sağ ventrikül yetmezliği ve erken ölüme neden olabilir. Pulmoner hipertansiyona neden olan hastalık grupları içerisinde akciğer hastalıkları önemli bir yere sahiptir.

2018 yılında yapılan PH toplantısında PH; ortalama PAB>20 mmHg, pulmoner arter kama basıncı (PAWP)<15mmHg ve pulmoner vasküler rezistans (PVR)>3 WU olarak tanımlanmıştır¹. Aynı sempozyumda PH'a neden olan hastalık grupları Tablo 1' de gösterildiği gibi düzenlenmiştir. Grup 1, Pulmoner arteriyel hipertansiyon (PAH) grubu olup, vasküler yapıda oluşan kalıcı yapısal değişikliklere bağlı olarak, sağ kalım ciddi olarak etkilenmektedir. PAH olmayan

¹ Doç. Dr., Van Yüzüncü Yıl Üniversitesi Tıp Fakültesi Göğüs Hastalıkları AD. selviasker@gmail.com

² Doç. Dr., Van Yüzüncü Yıl Üniversitesi Tıp Fakültesi Kardiyoloji AD. muntecepasker@gmail.com

Sjögren Hastalığı

Sjögren hastalığı daha çok küçük havayolu hasatlığı ve interstisyel akciğer hastalığı yapmaktadır. Bu hastalarda PH reyno fenomeni olanlarda interstisyel akciğer hastalığı olanlarda, deri vaskuliti olanlarda RF pozitif olanlarda antinükleer antikor,anti-Ro/SSA ve anti- Ro otoantikoru taşıyanlarda daha sık bildirilmiştir⁶⁵.

Miks Bağ Doku Hastalığı

Miks bağ dokusu hastalığı (MBDH), polimiyozit/dermatomiyozit, sistemik lupus eritematozus (SLE), ve romatoid artrit(RA,) sistemik skleroderma (SSk)'nın yer aldığı en az iki sistemik otoimmün hastalığa ait bulguların birlikte görüldüğü inflamatuvar romatizmal bir hastalıktır. Bu hastalarda PAH gelişme riski %25-29 olarak bildirilmiştir⁶⁶.

SONUÇ

Sonuç olarak, İnterstisyel akciğer hastalıklarında PH saptandığında PH ile İAH arasında net bir ilişki kurmadan önce diğer PH yapan tüm etkenler (obstruktif uyku apne snedromu, pulmoner emboli, troit hastalıkları, sol ventrikül yetmezliği ve kapak hastalıkları, hepatik hastalıklar , böbrek hastalıkları, HIV, ilaçlar (iştah kesiciler,toksik kolza yağı,kemoteropatik ilaçlar) vb) gözden geçirilmelidir. Hasta hangi İAH grubunda ise bu grubun tedavisini eksiksiz almış olmalıdır. Sonrasında etkenin kendisi ile açıklanamayan PH varlığında tedavi planı uzmanlaşmış merkezlerde oluşturulmalıdır.

Anahtar Kelimeler: İnterstisyel Akciğer Hastalıkları, Yoğun bakım, Pulmoner hipertansiyon,ekokardiyografi, idiyopatik pulmoner fibrozis, sarkoidozis, Sistemik Lupus Eriştamotozus, Romatoid artrit, Sjögren Hastalığı, Miks Bağ Doku Hastalığı, Kombine Pulmoner Fibrozis ve afizem hastalığı, Sistemik skleroz, skleroderma , Pulmoner kistik hastalıklar ,İdiyopatik interstisyel pnömoniler

KAYNAKLAR

- Galie N, McLaughlin VV, Rubin LJ, et al. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019 Jan; 53(1): 1802148. Published online 2019 Jan 24. doi: 10.1183/13993003.02148-2018
- Ramjug S, Weatherald J, Sahay S, et al. ERS International Congress 2019 research highlights from Assembly 13 - A focus upon ESC/ERS guidance of acute PE, PH in relation to lung disease and PAH. ERJ Open Res 2020; in press (<https://doi.org/10.1183/23120541.00304-2020>).
- Ryu JH, Krowka MJ, Pellikka PA, et al. Pulmonary hypertension in patients with interstitial lung diseases. Mayo Clin Proc 2007;82:342-350.

4. Caminati A, Cassandro R, Harari S. Pulmonary hypertension in chronic interstitial lung diseases. *Eur Respir Rev* 2013; 22: 292–301.
5. ZP Onen. What Is the Incidence of Pulmonary Hypertension in Interstitial Lung Disease? How to Manage the Treatment? Is There Any Effect of Pulmonary Hypertension on Prognosis. *Güncel Göğüs Hastalıkları Serisi* 2014; 2 (3): 374-378
6. Chang B, Wigley FM, White B, et al. Scleroderma patients with combined pulmonary hypertension and interstitial lung disease. *J Rheumatol* 2003;30:2398–2405.
7. Nunes H, Humbert M, Capron F, et al. Pulmonary hypertension associated with sarcoidosis: mechanisms, haemodynamics and prognosis. *Thorax* 2006;61:68–74.
8. Bargout R, Kelly RF. Sarcoid heart disease: clinical course and treatment. *Int J Cardiol* 2004;97:173-82.
9. Roy AK, McCullagh BN, Segurado R, et al. Detection of high-sensitivity troponin in outpatients with stable pulmonary hypertension identifies a subgroup at higher risk of adverse outcomes. *J Cardiac Fail*.2016; 20(1):31–37. doi:10.1016/j.cardfail.2013.12.001
10. Leuchte HH, Neurohr C, Baumgartner R, et al. Brain natriuretic peptide and exercise capacity in lung fibrosis and pulmonary hypertension. *Am J Respir Crit Care Med* 2004;170:360–365.
11. Bourji KI, Hassoun PM. Right ventricle dysfunction in pulmonary hypertension: mechanisms and modes of detection. *Curr Opin Pulm Med*.2015. doi:10.1097/MCP.0000000000000192
12. Konstantinides SV, Meyer G, Becattini C, et al. ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J* 2020;41:543-603
13. Edwards PD, Bull RK, Coultan R. CT measurement of main pulmonary artery diameter. *Br J Radiol* 1998; 71:1018–1020.
14. Blyth KG, Groenning BA, Mark PB, et al. NT-proBNP can be used to detect right ventricular systolic dysfunction in pulmonary hypertension. *Eur Respir J* 2007; 29: 737–744.
15. Zamanian RT, Haddad F, Doyle RL, et al. Management strategies for patients with pulmonary hypertension in the intensive care unit. *Crit Care Med*.2007; 35(9):2037–2050
16. Bossone E, Paciocco G, Iarussi D, et al. The prognostic role of the ECG in primary pulmonary hypertension. *Chest*. 2002; 121(2):513–518
17. Bossone E, Bordini BD, Mazza A, et al. Pulmonary arterial hypertension—the key role of echocardiography. *Chest* 2005;127: 1836–43.
18. Barst RJ, McGoon M, Torbicki A, et al. Diagnosis and differential assessment of pulmonary arterial hypertension. *J Am Coll Cardiol* 2004;43:S40 –S47.
19. Lettieri CJ, Nathan SD, Barnett SD, et al. Prevalence and outcomes of pulmonary arterial hypertension in advanced idiopathic pulmonary fibrosis. *Chest* 2006;129:746–752.
20. Olschewski H, Ghofrani HA, Walrath D et al. Inhaled prostacyclin and iloprost in severe pulmonary hypertension secondary to lung fibrosis. *Am J Respir Crit Care Med* 1999; 160: 600-7.
21. Hallstrand TS, Boitano LJ, Johnson WC, et al. The timed walk test as a measure of severity and survival in idiopathic pulmonary fibrosis. *Eur Respir J* 2005;25:96–103.
22. Okumus NG, Önen ZP. Pulmoner Hipertansiyon Tanı ve Tedavi Uzlaşı Raporu. *Turkish Thoracic Society* 2020;(7):1-60 ISBN 978-975-349-100-6.
23. Seeger W, Adir Y, Barbera JA, et al. Pulmonary hypertension in chronic lung diseases. *JACC* 2013; 62: 109-116.
24. Olschewski H, Ghofrani HA, Walrath D, et al. Inhaled prostacyclin and iloprost in severe pulmonary hypertension secondary to lung fibrosis. *Am J Respir Crit Care Med* 1999;160:600–607.
25. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement — idiopathic pulmonary fibrosis: evidencebased guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011; 183:788-824.

26. Network TIPFCR. A controlled trial of sildenafil in advanced idiopathic pulmonary fibrosis. *N Eng J Med* 2010; 363: 620-8.
27. Dimadi M, Kokkinis F, Trigidou R, et al. Long term treatment with endothelin receptor blockade in pulmonary arterial hypertension associated with interstitial lung disease. *Am J Respir Crit Care Med* 2007; 175: A497.
28. Raghu B, Behr J, Brown KK, et al. Treatment of idiopathic pulmonary fibrosis with ambrisentan: a parallel, randomized trial. *Ann Intern Med* 2013; 158: 641-9.
29. Chandran N, Sharma N, Wollin L, et al. Nintedanib has acute pulmonary vasodilatory effects in transgenic Fra2 mice with spontaneous progressive pulmonary hypertension and lung fibrosis. *Eur Respir J* 2019; 54: Suppl. 63, PA5382.
30. Nathan SD, Barbera JA, Gaine SP, et al. Pulmonary hypertension in chronic lung disease and hypoxia. *Eur Respir J* 2019; 53: 1801914.
31. Kaymaz C, Kucukoglu MS. Pulmoner hipertansiyon. 2012;(1). İstanbul: Aves yayınevi.
32. Zisman DA, Karlamangla AS, Ross DJ, et al. High-resolution chest CT findings do not predict the presence of pulmonary hypertension in advanced idiopathic pulmonary fibrosis. *Chest* 2007;132:773-779
33. Nadrous HF, Pellikka PA, Krowka MJ, et al. Pulmonary hypertension in patients with idiopathic pulmonary fibrosis. *Chest* 2005;128:2393-2399.
34. Kapasi A, Halloran K, Hirji A, et al. Elevated pulmonary vascular resistance is associated with increased risk of death in IPF. *Eur Respir J* 2019; 54: Suppl. 63, PA1428.
35. Charbeneau RP, Peters-Golden M. Eicosanoids: mediators and therapeutic targets in fibrotic lung disease. *Clin Sci (Lond)* 108: 479 - 491, 2005
36. Mutsaers SE, Foster ML, Chambers RC, et al. Increased endothelin-1 and its localization during the development of bleomycin-induced pulmonary fibrosis in rats. *Am J Respir Cell Mol Biol* 1998, 18:611-619
37. Corte TJ, Wort SJ, Gatzoulis MA, Macdonald P, Hansell DM, Wells AU. Pulmonary vascular resistance predicts early mortality in patients with diffuse fibrotic lung disease and suspected pulmonary hypertension. *Thorax* 2009;64:883-888
38. Ghofrani HA, Wiedemann R, Rose F, Schermuly RT, Olschewski H, Weissmann N, Gunther A, Walmrath D, Seeger W, Grimminger F. Sildenafil for treatment of lung fibrosis and pulmonary hypertension: a randomised controlled trial. *Lancet* 2002;360:895-900.
39. King TE Jr, Behr J, Brown KK, du Bois RM, et al. BUILD-1: a randomized American Thoracic Society Documents 819 placebo-controlled trial of bosentan in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2008;177:75-81.
40. Handa T, Nagai S, Miki S, et al. Incidence of pulmonary hypertension and its clinical relevance in patients with sarcoidosis. *Chest* 2006; 129: 1246-52.
41. Shorr AF, Helman DL, Davies DB, et al. Pulmonary hypertension in advanced sarcoidosis: epidemiology and clinical characteristics. *Eur Respir J* 2005; 25: 783- 8.
42. Foley RJ, Metersky ML. Successful treatment of sarcoidosis-associated pulmonary hypertension with bosentan. *Respiration* 2008; 75: 211-4.
43. Cottin V, Harari S, Humbert M, et al. Pulmonary hypertension in lymphangioleiomyomatosis: characteristics in 20 patients. *Eur Respir J* 2012; 40: 630-640.
44. Dauriat G, Mal H, Thabut G, et al. Lung transplantation for pulmonary Langerhans' cell histiocytosis: a multicenter analysis. *Transplantation* 2006; 81: 746-750.
45. Chaowalit N, Pellikka PA, Decker PA, et al. Echocardiographic and clinical characteristics of pulmonary hypertension complicating pulmonary Langerhans cell histiocytosis. *Mayo Clin Proc* 2004; 79: 1269-1275.
46. Hallowell RW, Reed RM, Fraig M, et al. Severe pulmonary hypertension in idiopathic non-specific interstitial pneumonia. *Pulm Circ* 2012; 2: 101-106.

47. Ahmad S, Barnett, SD, Shlobin, OA, Nathan, SD. Comparison of the Prevalence of Pulmonary Arterial Hypertension (PAH) in Patients with Idiopathic Pulmonary Fibrosis (IPF) and Non-Specific Interstitial Pneumonia (NSIP). *Am J Respir Crit Care Med* 2006;3:S242.
48. Tuder RM, Marecki JC, Richter A, et al. Pulmoner hipertansiyon patolojisi. *Clin Chest Med*. 2007; 28 : 23–42.
49. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J* 2019; 53: 1801913.
50. Ergur GA, Bingöl Z, Kumbasar ÖÖ, Moğulkoç N, Müsellim B, Okumuş NF, Öngen HG, Tabak L, Türктаş H, Uzun O. Türk Toraks Derneği idiyopatik pulmoner fibrozis tanı ve tedavi uzlaşı raporu 2018. Bilimsel Tıp Yayınevi, Ankara 2018
51. McGoon MD, Benza RL, Escribano-Subias P, et al. Pulmonary arterial hypertension: Epidemiology and registries. *J Am Coll Cardiol* 2013; 62: 51-9.
52. Udayakumar N, Venkatesan S, Rajendiran C. Pulmonary hypertension in rheumatoid arthritis–relation with the duration of the disease. *Int J Cardiol* 2008;127:410–2
53. Wells AU, Steen V, Valentini G. Pulmonary complications: one of the most challenging complications of systemic sclerosis. *Rheumatology* 2009;48(Suppl. 3):iii404.
54. Young A, Vummidi D, Visovatti S et al.: Prevalence, Treatment, and Outcomes of Coexistent Pulmonary Hypertension and Interstitial Lung Disease in Systemic Sclerosis. *Arthritis Rheumatol* 2019; 71: 1339-49.
55. Hinchcliff M, Fischer A, Schioppa E, et al. Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma (PHAROS): baseline characteristics and description of study population. *J Rheumatol* 2011;38(10):2172–9. 10.3899/jrheum.101243. [PubMed: 21844142]
56. Coghlan JG, Denton CP, Grunig E, et al. Evidence-based detection of pulmonary arterial hypertension in systemic sclerosis: the DETECT study. *Ann Rheum Dis* 2014;73(7):1340–9. 10.1136/annrheumdis-2013-203301. [PubMed: 23687283]
57. Lambova S, Muller-Ladner U. Pulmonary arterial hypertension in systemic sclerosis. *Autoimmun Rev* 2010;9:761–70
58. Humbert M, Sitbon O, Chaouat A, et al. Pulmonary arterial hypertension in France: results from a national registry. *Am J Respir Crit Care Med* 2006;173:1023 –1030
59. Hassoun PM. Pulmonary arterial hypertension complicating connective tissue diseases. *Semin Respir Crit Care Med* 2009;30:429–439
60. Mathai SC, Hassoun PM. Therapy for pulmonary arterial hypertension associated with systemic sclerosis. *Curr Opin Rheumatol* 2009; 21: 642-648
61. Simonson JS, Schiller NB, Petri M, et al. Pulmonary hypertension in systemic lupus erythematosus. *J Rheumatol* 1989; 16:918–25
62. Torre O, Harari S. Pleural and pulmonary involvement in systemic lupus erythematosus. *Presse Med* 2011;40(2):19–29.
63. Asherson, R.A., Morgan, S.H., Hackett, D., et al. Rheumatoid arthritis and pulmonary hypertension : a report of three cases. *J Rheumatol* 1985, 12, 154-159
64. Dawson JK, Goodson NG, Graham DR, et al. Raised pulmonary artery pressures measured with Doppler echocardiography in rheumatoid arthritis patients. *Rheumatology (Oxford)* 2000;39: 1320–5.
65. Launay D, Hachulla E, Hatron PY, et al. Pulmonary arterial hypertension: a rare complication of primary Sjögren syndrome: report of 9 new cases and review of the literature. *Medicine (Baltimore)* 2007;86:299–315.
66. Haroon N, Nisha RS, Chandran V, et al. Pulmonary hypertension not a major feature of early mixed connective tissue disease: A prospective clinicoserological study. *J Postgrad Med* 2005;51:104-8.