



BÖLÜM 64

Pulmoner Hipertansiyon Sınıflandırması ve Genel Tedavi Yaklaşımı

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GİRİŞ

Pulmoner hipertansiyon (PH), birçok klinik durumu içinde barındıran, çeşitli kardiyovasküler ve solunum yolu hastalıkları ile ilişkili olan patofizyolojik bir hastalıktır. PH yönetiminin karmaşıklığı nedeniyle, klinisyenlerle ortaklaşa ve hastaların aktif katılımıyla bütüncül ve multidisipliner bir yaklaşım gerektirmektedir. Günlük klinik uygulamada PH'li hastaların bakımını düzene koymak, PH'yi etkili bir şekilde yönetmek zorlu süreç gerektirmektedir.

Son yıllarda, PH'nin saptanması ve yönetilmesinde önemli ilerlemeler kaydedilmiştir ve pulmoner hipertansiyonun tanı ve tedavisine yönelik yeni çalışmalarla yeni kanıtlar eklenmiştir.

TANIMLAR VE SINIFLANDIRMALAR

Tanımlar

PH tanımları, sağ kalp kateterizasyonu ile yapılan hemodinamik değerlendirmeye dayanmaktadır. (Tablo 1) Pulmoner hipertansiyon, istirahatte ortalama pulmoner arter basıncının (mPAP) >20 mmHg olması ile tanımlanır. Bu sağlıklı kişilerde normal pulmoner arter basıncının (PAB) üst sınırını değerlendiren çalışmalarla desteklenmek-

tedir ve artmış PAB'in prognostik önemi birçok çalışma ile ortaya konulmuştur (1-4).

Hemodinamik değerlendirme pulmoner vasküler direnç (PVR) ve pulmoner arteriyel kama basıncını (PAWP) göre sınıflandırılmaktadır. Pulmoner vasküler hastalık ve sol kalp hastalığına bağlı PAB yüksekliğinin ayırımında kullanılmaktadır.

Mevcut verilere göre, normal PVR'nin üst sınırı ve PVR'nin prognostik açıdan en düşük eşiği yaklaşık 2 Wood ünitesidir (WU) (3, 5). Pulmoner vasküler direnç, vücut yüzey alanına ve yaşa bağlıdır ve yaşlı sağlıklı kişilerde daha yüksek değerlerde bulunmaktadır.

Pre ve postkapiller PH'ı ayırt eden PAWP için eşik değeri hakkındaki mevcut veriler çelişkilidir. Normal PAWP'nin üst sınırı 12 mmHg olarak kabul edilse de, PH tanı ve tedavisi için önceki ESC/ERS Kılavuzları ve ESC Kalp Yetmezliği Derneği'nin yakın tarihli fikir birliğinde, 15 mmHg eşik olarak önerilmektedir. Ayrıca, PAH ile ilgili neredeyse tüm terapötik çalışmalarda PAWP ≤15 mmHg eşiği kullanılmıştır (6, 7).

Pulmoner arteriyel hipertansiyon (PAH), kronik tromboembolik pulmoner hipertansiyon (KTEPH) ve akciğer hastalıklarıyla ilişkili PH ne-

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KAYNAKLAR:

1. Douschan P, Kovacs G, Avian A, et al. Mild Elevation of Pulmonary Arterial Pressure as a Predictor of Mortality. *Am J Respir Crit Care Med.* 2018;197(4):509-16.
2. Kolte D, Lakshmanan S, Jankowich MD, Brittain EL, Maron BA, Choudhary G. Mild Pulmonary Hypertension Is Associated With Increased Mortality: A Systematic Review and Meta-Analysis. *J Am Heart Assoc.* 2018;7(18):e009729.
3. Kovacs G, Olschewski A, Berghold A, Olschewski H. Pulmonary vascular resistances during exercise in normal subjects: a systematic review. *Eur Respir J.* 2012;39(2):319-28.
4. Wolsk E, Bakkestrom R, Thomsen JH, et al. The Influence of Age on Hemodynamic Parameters During Rest and Exercise in Healthy Individuals. *JACC Heart Fail.* 2017;5(5):337-46.
5. 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;34(4):888-94.
6. Paulus WJ, Tschope C, Sanderson JE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *Eur Heart J.* 2007;28(20):2539-50.
7. Pieske B, Tschope C, de Boer RA, et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). *Eur Heart J.* 2019;40(40):3297-317.
8. Zeder K, Banfi C, Steinrisser-Allex G, et al. Diagnostic, prognostic and differential-diagnostic relevance of pulmonary haemodynamic parameters during exercise: a systematic review. *Eur Respir J.* 2022;60(4).
9. Ho JE, Zern EK, Lau ES, et al. Exercise Pulmonary Hypertension Predicts Clinical Outcomes in Patients With Dyspnea on Effort. *J Am Coll Cardiol.* 2020;75(1):17-26.
10. Stamm A, Saxer S, Lichtblau M, et al. Exercise pulmonary haemodynamics predict outcome in patients with systemic sclerosis. *Eur Respir J.* 2016;48(6):1658-67.
11. Lewis GD, Murphy RM, Shah RV, et al. Pulmonary vascular response patterns during exercise in left ventricular systolic dysfunction predict exercise capacity and outcomes. *Circ Heart Fail.* 2011;4(3):276-85.
12. Zeder K, Avian A, Bachmaier G, et al. Exercise Pulmonary Resistances Predict Long-Term Survival in Systemic Sclerosis. *Chest.* 2021;159(2):781-90.
13. Eisman AS, Shah RV, Dhakal BP, et al. Pulmonary Capillary Wedge Pressure Patterns During Exercise Predict Exercise Capacity and Incident Heart Failure. *Circ Heart Fail.* 2018;11(5):e004750.
14. Bentley RF, Barker M, Esfandiari S, et al. Normal and Abnormal Relationships of Pulmonary Artery to Wedge Pressure During Exercise. *J Am Heart Assoc.* 2020;9(22):e016339.
15. Hoepfer MM, Humbert M, Souza R, et al. A global view of pulmonary hypertension. *Lancet Respir Med.* 2016;4(4):306-22.
16. Leber L, Beaudet A, Muller A. Epidemiology of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: identification of the most accurate estimates from a systematic literature review. *Pulm Circ.* 2021;11(1):2045894020977300.
17. Lau EMT, Giannoulatou E, Celermajer DS, Humbert M. Epidemiology and treatment of pulmonary arterial hypertension. *Nat Rev Cardiol.* 2017;14(10):603-14.
18. Montani D, Girerd B, Jais X, et al. Screening for pulmonary arterial hypertension in adults carrying a BMPR2 mutation. *Eur Respir J.* 2021;58(1).
19. Certain MC, Chaumais MC, Jais X, et al. Characteristics and Long-term Outcomes of Pulmonary Venocclusive Disease Induced by Mitomycin C. *Chest.* 2021;159(3):1197-207.
20. Timlin MR, Black AB, Delaney HM, Matos RI, Percival CS. Development of Pulmonary Hypertension During Treatment with Diazoxide: A Case Series and Literature Review. *Pediatr Cardiol.* 2017;38(6):1247-50.
21. Global Burden of Disease Study C. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet.* 2015;386(9995):743-800.
22. Rosenkranz S, Gibbs JS, Wachter R, De Marco T, Vonk-Noordegraaf A, Vachiery JL. Left ventricular heart failure and pulmonary hypertension. *Eur Heart J.* 2016;37(12):942-54.
23. Lam CS, Roger VL, Rodeheffer RJ, Borlaug BA, Enders FT, Redfield MM. Pulmonary hypertension in heart failure with preserved ejection fraction: a community-based study. *J Am Coll Cardiol.* 2009;53(13):1119-26.
24. Tichelbacker T, Dumitrescu D, Gerhardt F, et al. Pulmonary hypertension and valvular heart disease. *Herz.* 2019;44(6):491-501.
25. Weber L, Rickli H, Haager PK, et al. Haemodynamic mechanisms and long-term prognostic impact of pulmonary hypertension in patients with severe aortic stenosis undergoing valve replacement. *Eur J Heart Fail.* 2019;21(2):172-81.
26. Hurdman J, Condliffe R, Elliot CA, et al. Pulmonary hypertension in COPD: results from the ASPIRE registry. *Eur Respir J.* 2013;41(6):1292-301.
27. Nathan SD, Barbera JA, Gaine SP, et al. Pulmonary hypertension in chronic lung disease and hypoxia. *Eur Respir J.* 2019;53(1).
28. Naeije R. Pulmonary hypertension at high altitude. *Eur Respir J.* 2019;53(6).
29. Delcroix M, Torbicki A, Gopalan D, et al. ERS statement on chronic thromboembolic pulmonary hypertension. *Eur Respir J.* 2021;57(6).
30. Kramm T, Wilkens H, Fuge J, et al. Incidence and characteristics of chronic thromboembolic pulmonary hypertension in Germany. *Clin Res Cardiol.* 2018;107(7):548-53.

31. Swietlik EM, Ruggiero A, Fletcher AJ, et al. Limitations of resting haemodynamics in chronic thromboembolic disease without pulmonary hypertension. *Eur Respir J.* 2019;53(1).
32. Kalantari S, Gomberg-Maitland M. Group 5 Pulmonary Hypertension: The Orphan's Orphan Disease. *Cardiol Clin.* 2016;34(3):443-9.
33. Shlobin OA, Kouranos V, Barnett SD, et al. Physiological predictors of survival in patients with sarcoidosis-associated pulmonary hypertension: results from an international registry. *Eur Respir J.* 2020;55(5).
34. Boucly A, Cottin V, Nunes H, et al. Management and long-term outcomes of sarcoidosis-associated pulmonary hypertension. *Eur Respir J.* 2017;50(4).
35. Hoeper MM, Lee SH, Voswinckel R, et al. Complications of right heart catheterization procedures in patients with pulmonary hypertension in experienced centers. *J Am Coll Cardiol.* 2006;48(12):2546-52.
36. Kovacs G, Avian A, Olschewski A, Olschewski H. Zero reference level for right heart catheterisation. *Eur Respir J.* 2013;42(6):1586-94.
37. Sitbon O, Humbert M, Jais X, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation.* 2005;111(23):3105-11.
38. Opitz CF, Wensel R, Bettmann M, et al. Assessment of the vasodilator response in primary pulmonary hypertension. Comparing prostacyclin and iloprost administered by either infusion or inhalation. *Eur Heart J.* 2003;24(4):356-65.
39. Jing ZC, Jiang X, Han ZY, et al. Iloprost for pulmonary vasodilator testing in idiopathic pulmonary arterial hypertension. *Eur Respir J.* 2009;33(6):1354-60.
40. Rosenkranz S, Howard LS, Gomberg-Maitland M, Hoeper MM. Systemic Consequences of Pulmonary Hypertension and Right-Sided Heart Failure. *Circulation.* 2020;141(8):678-93.
41. Grunig E, MacKenzie A, Peacock AJ, et al. Standardized exercise training is feasible, safe, and effective in pulmonary arterial and chronic thromboembolic pulmonary hypertension: results from a large European multicentre randomized controlled trial. *Eur Heart J.* 2021;42(23):2284-95.
42. Olsson KM, Delcroix M, Ghofrani HA, et al. Anticoagulation and survival in pulmonary arterial hypertension: results from the Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension (COMPERA). *Circulation.* 2014;129(1):57-65.
43. Preston IR, Roberts KE, Miller DP, et al. Effect of Warfarin Treatment on Survival of Patients With Pulmonary Arterial Hypertension (PAH) in the Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL). *Circulation.* 2015;132(25):2403-11.
44. Khan MS, Usman MS, Siddiqi TJ, et al. Is Anticoagulation Beneficial in Pulmonary Arterial Hypertension? *Circ Cardiovasc Qual Outcomes.* 2018;11(9):e004757.
45. Stickel S, Gin-Sing W, Wagenaar M, Gibbs JSR. The practical management of fluid retention in adults with right heart failure due to pulmonary arterial hypertension. *Eur Heart J Suppl.* 2019;21(Suppl K):K46-K53.
46. Sandoval J, Aguirre JS, Pulido T, et al. Nocturnal oxygen therapy in patients with the Eisenmenger syndrome. *Am J Respir Crit Care Med.* 2001;164(9):1682-7.
47. Clozel M, Maresta A, Humbert M. Endothelin receptor antagonists. *Handb Exp Pharmacol.* 2013;218:199-227.
48. Humbert M, Segal ES, Kiely DG, Carlsen J, Schwierin B, Hoeper MM. Results of European post-marketing surveillance of bosentan in pulmonary hypertension. *Eur Respir J.* 2007;30(2):338-44.
49. Galie N, Olschewski H, Oudiz RJ, et al. Ambrisentan for the treatment of pulmonary arterial hypertension: results of the ambrisentan in pulmonary arterial hypertension, randomized, double-blind, placebo-controlled, multicenter, efficacy (ARIES) study 1 and 2. *Circulation.* 2008;117(23):3010-9.
50. Pulido T, Adzerikho I, Channick RN, et al. Macitentan and morbidity and mortality in pulmonary arterial hypertension. *N Engl J Med.* 2013;369(9):809-18.
51. Galie N, Ghofrani HA, Torbicki A, et al. Sildenafil citrate therapy for pulmonary arterial hypertension. *N Engl J Med.* 2005;353(20):2148-57.
52. Galie N, Brundage BH, Ghofrani HA, et al. Tadalafil therapy for pulmonary arterial hypertension. *Circulation.* 2009;119(22):2894-903.
53. Ghofrani HA, Galie N, Grimminger F, et al. Riociguat for the treatment of pulmonary arterial hypertension. *N Engl J Med.* 2013;369(4):330-40.
54. Barst RJ, Rubin LJ, Long WA, et al. A comparison of continuous intravenous epoprostenol (prostacyclin) with conventional therapy for primary pulmonary hypertension. *N Engl J Med.* 1996;334(5):296-301.
55. Olschewski H, Simonneau G, Galie N, et al. Inhaled iloprost for severe pulmonary hypertension. *N Engl J Med.* 2002;347(5):322-9.
56. Simonneau G, Barst RJ, Galie N, et al. Continuous subcutaneous infusion of treprostinil, a prostacyclin analogue, in patients with pulmonary arterial hypertension: a double-blind, randomized, placebo-controlled trial. *Am J Respir Crit Care Med.* 2002;165(6):800-4.
57. Bourge RC, Waxman AB, Gomberg-Maitland M, et al. Treprostinil Administered to Treat Pulmonary Arterial Hypertension Using a Fully Implantable Programmable Intravascular Delivery System: Results of the DelIVery for PAH Trial. *Chest.* 2016;150(1):27-34.
58. Tapson VF, Torres F, Kermeen F, et al. Oral treprostinil for the treatment of pulmonary arterial hypertension in patients on background endothelin receptor antagonist and/or phosphodiesterase type 5 inhibitor therapy (the FREDOM-C study): a randomized controlled trial. *Chest.* 2012;142(6):1383-90.
59. Barst RJ, McGoan M, McLaughlin V, et al. Beraprost therapy for pulmonary arterial hypertension. *J Am Coll Cardiol.* 2003;41(12):2119-25.
60. Sitbon O, Channick R, Chin KM, et al. Selexipag for the Treatment of Pulmonary Arterial Hypertension. *N Engl J Med.* 2015;373(26):2522-33.
61. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J.* 2022;43(38):3618-731.