

POSTTROMBOTİK SENDROM VE TEDAVİ STRATEJİLERİ

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Giriş

Derin ven trombozu yaklaşık olarak toplumda 3/1000 oranında görülmektedir. Derin ven trombozu, ikincil derin venöz yetersizliğinin en sık sebebidir ve post-trombotik sendrom (PTS) ile yakın ilişkilidir. ⁽¹⁾ PTS, derin ven trombozu sonrasında gelişen kronik venöz yetmezlik bulgularını ifade eden yaygın bir komplikasyondur. PTS'de semptomlar fiziksel aktivite ve ayakta durmakla artar.

PTS, hastaların yaşam kalitesini düşüren bir klinik durumdur. Ve PTS'nin şiddeti ile yaşam kalitesi arasında ters orantı mevcuttur ⁽²⁾. PTS tanılı hastalarda yaşam kalitesini gösteren skorlar, PTS olmayan derin ven trombozu hastalarına veya venöz yetmezliği olan hastalara göre daha düşüktür ⁽³⁾.

Derin ven trombozu nedeniyle venöz kapakçıklarda oluşan hasar ve obstrüksiyona bağlı venöz hipertansiyon, klinik durumun ortaya çıkmasından sorumlu iki faktördür. ⁽⁴⁾ Bacaklarda ağrı, ağırlık hissi ve ödem, sık-

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örtüleri olarak iki gruba ayrılmaktadır. Son zamanlarda biyolojik yara örtüleri kullanılmaya başlamıştır. Bu örtülerin özellikleri; önemli büyüme faktörlerini içermeleri ve yara iyileşmesini hızlandırmalarıdır. Venöz ülser tedavisinde bugüne kadar en fazla kullanılan yara örtüsü çeşidi hidrokolloid içeren, geçirgen olmayan yara örtüleridir. Biyolojik yara örtüleri daha etkili olmalarına rağmen yüksek fiyatları nedeniyle sıklıkla kullanılmamaktadır. Yara örtüleri haftada iki kez ya da üç kez değiştirilmelidir.

Antibiyotik Tedavisi

Yaradan alınan kültürlerde üreme saptanması durumunda uygun antibiyotik başlanmalıdır. Ancak üreme tespit edilmeden antibiyotik başlanması dirençli mikroorganizmaların oluşmasına neden olacağı için önerilmemektedir. Venöz ülser hastalarının ancak %15'inde antibiyotik kullanımı gerekli olmaktadır. Kolonize olmuş mikroorganizmalar için topikal antibiyotikler yeterli olurken enfeksiyona neden olan mikroorganizmalar için sistemik antibiyotik tedavisi başlanması gerekir. Venöz ülser alanında en fazla enfeksiyona neden olan mikroorganizmalar *Staphylococcus aureus* ve *Pseudomonas aeruginosa*'dır.⁽⁶⁷⁾

KAYNAKÇA

1. Labropoulos N, Gasparis AP, Tassiopoulos AK. Prospective evaluation of the clinical deterioration in post-thrombotic limbs. *J Vasc Surg.* 2009; 50:826–830
2. Kahn SR, Shbaklo H, Lamping DL, et al. Determinants of health-related quality of life during the 2 years following deep vein thrombosis. *J Thromb Haemost.* 2008; 6:1105–12.10.1111/j.1538-7836.2008.03002.x
3. Kahn SR, M'LAN CE, Lamping DL, Kurz X, Berard A, Abenhaim L. The influence of venous thromboembolism on quality of life and severity of chronic venous disease. *J Thromb Haemost.* 2004; 2:2146–51.10.1111/j.1538-7836.2004.00957.x
4. Bergan JJ, Schmid-Schönbein GW, Smith PD, et al. Chronic venous disease. *N Engl J Med*2006; 355:488.)
5. Rice JB, Desai U, Cummings AK, Birnbaum HG, Skornicki M, Parsons N. Burden of venous leg ulcers in the United States. *J Med Econ.* 2014; 17:347–356.)
6. Markel A, Manzo RA, Bergelin RO, Strandness DE Jr. Valvular reflux after deep vein thrombosis: incidence and time of occurrence. *J Vasc Surg* 1992; 15:377.
7. Higley HR, Kassander GA, Gerhardt CO, Falanga V. Extravasation of macromolecules and possible trapping of transforming growth factor- β 1 in venous ulceration. *Br J Surg* 1995; 132: 79–85.)

8. Peschen M, Lahaye T, Gennig B, et al. Expression of the adhesion molecules ICAM-1, VCAM-1, LFA-1 and VLA-4 in the skin is modulated in progressing stages of chronic venous insufficiency. *Acta Derm Venereol* 1999; 79: 27–32.
9. Shbaklo H, Kahn SR. Long-term prognosis after deep venous thrombosis. *Curr Opin Hematol*. 2008; 15:494–8.10.1097/MOH.0b013e32830abde2
10. Meissner MH, Zierler BK, Bergelin RO, et al. Coagulation, fibrinolysis, and recanalization after acute deep venous thrombosis. *J Vasc Surg* 2002; 35:278.)
11. Singh H, Masuda EM. Comparing short-term outcomes of femoral-popliteal and iliofemoral deep venous thrombosis: early lysis and development of reflux. *Ann VascSurg* 2005; 19:74
12. Tick LW, Doggen CJ, Rosendaal FR, et al. Predictors of the post-thrombotic syndrome with non-invasive venous examinations in patients 6 weeks after a first episode of deep vein thrombosis. *J Thromb Haemost* 2010; 8:2685.)
13. Tick LW, Kramer MH, Rosendaal FR, Faber WR, Doggen CJ. Risk factors for post-thrombotic syndrome in patients with a first deep venous thrombosis. *J Thromb Haemost*. 2008; 6:2075–81.10.1111/j.1538-7836.2008.03180.x
14. Kahn SR, Shrier I, Julian JA, et al. Determinants and time course of the postthrombotic syndrome after acute deep venous thrombosis. *Ann Intern Med* 2008; 149:698.)
15. Labropoulos N, Gasparis AP, Pefanis D, et al. Secondary chronic venous disease progresses faster than primary. *J Vasc Surg* 2009; 49:704.
16. Kahn SR, Ginsberg JS. Relationship between deep venous thrombosis and the postthrombotic syndrome. *Arch Intern Med*. 2004; 164:17–26
17. Prandoni P, Frulla M, Sartor D, Concolato A, Girolami A. Vein abnormalities and the postthrombotic syndrome. *J Thromb Haemost*. 2005; 3:401–2.10.1111/j.1538-7836.2004.01106.x
18. Prandoni P, Lensing AW, Prins MH, et al. Below-knee elastic compression stockings to prevent the post-thrombotic syndrome: a randomized, controlled trial. *Ann Intern Med*. 2004; 141:249–56
19. Ageno W, Piantanida E, Dentali F, et al. Body mass index is associated with the development of the post-thrombotic syndrome. *Thromb Haemost*. 2003; 89:305–9.10.1267/THRO03020305
20. Kahn SR, Kearon C, Julian JA, et al. Predictors of the post-thrombotic syndrome during long-term treatment of proximal deep vein thrombosis. *J Thromb Haemost* 2005; 3:718.)
21. Brandjes DP, Büller HR, Heijboer H, et al. Randomised trial of effect of compression stockings in patients with symptomatic proximal-vein thrombosis. *Lancet* 1997; 349:759.
22. Kahn SR, Shapiro S, Wells PS, et al. Compression stockings to prevent post-thrombotic syndrome: a randomised placebo-controlled trial. *Lancet* 2014; 383:880.
23. Baglin T. Prevention of post-thrombotic syndrome: a case for new oral anticoagulant drugs or for heparins? *J Thromb Haemost* 2012; 10:1702.)
24. Chitsike RS, Rodger MA, Kovacs MJ, et al. Risk of post-thrombotic syndrome after subtherapeutic warfarin anticoagulation for a first unprovoked deep vein thrombosis: results from the REVERSE study. *J Thromb Haemost* 2012; 10:2039.
25. Prandoni P, Ageno W, Ciammaichella M, et al. The risk of post-thrombotic syndrome in patients with proximal deep vein thrombosis treated with the direct oral anticoagulants. *Intern Emerg Med* 2020; 15:447.)
26. Cheung YW, Middeldorp S, Prins MH, et al. Post-thrombotic syndrome in patients treated with rivaroxaban or enoxaparin/vitamin K antagonists for acute deep-vein thrombosis. A post-hoc analysis. *Thromb Haemost* 2016; 116:733.)
27. Notten P, Ten Cate-Hoek AJ, Arnoldussen CWKP, et al. Ultrasound-accelerated catheter-directed thrombolysis versus anticoagulation for the prevention of post-thrombotic syndrome.

- me (CAVA): a single-blind, multicentre, randomised trial. *Lancet Haematol* 2020;7:e40.)
28. Franzeck UK, Schalch I, Jäger KA, et al. Prospective 12-year follow-up study of clinical and hemodynamic sequelae after deep vein thrombosis in low-risk patients (Zürich study). *Circulation* 1996; 93:74.)
 29. Kahn SR, Partsch H, Vedantham S, Prandoni P, Kearon C; Subcommittee on Control of Anticoagulation of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of post-thrombotic syndrome of the leg for use in clinical investigations: a recommendation for standardization. *J Thromb Haemost.* 2009 May;7(5):879-83. doi: 10.1111/j.1538-7836.2009.03294.x. Epub 2009 Jan 19. PMID: 19175497.)
 30. Kahn SR, Shrier I, Shapiro S, et al. Six-month exercise training program to treat post-thrombotic syndrome: a randomized controlled two-centre trial. *CMAJ* 2011; 183:37.)
 31. Partsch H, Kaulich M, Mayer W. Immediate mobilisation in acute vein thrombosis reduces postthrombotic syndrome. *Int Angiol.* 2004; 23:206–12.)
 32. Kolbach DN, Sandbrink MW, Hamulyak K, Neumann HA, Prins MH. Non-pharmaceutical measures for prevention of post-thrombotic syndrome. *Cochrane Database Syst Rev.* 2004: CD004174.10.1002/14651858.CD004174.pub2)
 33. Kearon, C.; Kahn, SR.; Agnelli, G.; Goldhaber, S.; Raskob, GE.; Comerota, AJ. Chest. 8. Vol. 133. 2008. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines; p. 454S-545S.)
 34. Aschwanden M, Jeanneret C, Koller MT, Thalhammer C, Bucher HC, Jaeger KA. Effect of prolonged treatment with compression stockings to prevent post-thrombotic sequelae: a randomized controlled trial. *J Vasc Surg.* 2008; 47:1015–21.10.1016/j.jvs.2008.01.008
 35. Snow V, Qaseem A, Barry P, et al. Management of venous thromboembolism: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med.* 2007; 146:204–10.)
 36. Prandoni P, Kahn SR. Post-thrombotic syndrome: prevalence, prognostication and need for progress. *Br J Haematol* 2009; 145:286
 37. Benko T, Cooke EA, McNally MA, Mollan RA. Graduated compression stockings: knee length or thigh length. *Clin Orthop Relat Res.* 2001; 383:197–203.
 38. Holmes CE, Bambace NM, Lewis P, et al. Efficacy of a short course of complex lymphedema therapy or graduated compression stocking therapy in the treatment of post-thrombotic syndrome. *Vasc Med* 2014; 19:42
 39. Kahn SR, Comerota AJ, Cushman M, Evans NS, Ginsberg JS, Goldenberg NA, et al. The postthrombotic syndrome: evidence-based prevention, diagnosis, and treatment strategies: a scientific statement from the American Heart Association. *Circulation* 2014;130:1636-61.
 40. Galanaud, J.P.; Righini, M.; Quéré, I. Compression stockings to prevent post-thrombotic syndrome. *Lancet* 2014, 384, 129.)
 41. Van Dongen, C.J.J.; Prandoni, P.; Frulla, M.; Marchiori, A.; Prins, M.H.; Hutten, B.A. Relation between quality of anticoagulant treatment and the development of the postthrombotic syndrome. *J. Thromb. Haemost.* 2005, 3, 939–942.
 42. Hull, R.D.; Liang, J.; Townshend, G. Long-term low-molecular-weight heparin and the post-thrombotic syndrome: A systematic review. *Am. J. Med.* 2011, 124, 756–765.
 43. Hull, R.D.; Pineo, G.F.; Brant, R.; Liang, J.; Cook, R.; Solymoss, S.; Poon, M.-C.; Raskob, G.; LITE Trial Investigators. Home therapy of venous thrombosis with long-term LMWH versus usual care: Patient satisfaction and post-thrombotic syndrome. *Am. J. Med.* 2009, 122, 762–769.e3
 44. Downing, L.J.; Strieter, R.M.; Kadell, A.M.; Wilke, C.A.; Greenfield, L.J.; Wakefield, T.W. Low-dose low-molecular-weight heparin is anti-inflammatory during venous thrombosis. *J. Vasc. Surg.* 1998, 28, 848–854

45. Moaveni, D.K.; Lynch, E.M.; Luke, C.; Sood, V.; Upchurch, G.R.; Wakefield, T.W.; Henke, P.K. Vein Wall re-endothelialization after deep vein thrombosis is improved with low-molecular-weight heparin. *J. Vasc. Surg.* 2008, 47, 616–624
46. (Jeraj, L.; Jezovnik, M.K.; Poredos, P. Rivaroxaban versus warfarin in the prevention of post-thrombotic syndrome. *Thromb. Res.* 2017, 157, 46–48
47. Makedonov I, Kahn SR, Galanaud JP. Prevention and Management of the Post-Thrombotic Syndrome. *J Clin Med.* 2020 Mar 27;9(4):923. doi: 10.3390/jcm9040923. PMID: 32230912; PMCID: PMC7230648
48. Strandness DE Jr, Langlois Y, Cramer M, Randlett A, Thiele BL. Long-term sequelae of acute venous thrombosis. *JAMA.* 1983; 250:1289–92
49. Eklof B, Kistner RL. Is there a role for thrombectomy in iliofemoral venous thrombosis? *Semin Vasc Surg.* 1996; 9:34–45
50. Colgan MP, Dormandy JA, Jones PW, Schraibman IG, Shanik DG, Young RA. Oxpentifylline treatment of venous ulcers of the leg. *BMJ.* 1990; 300:972–5
51. Lyseng-Williamson KA, Perry CM. Micronised purified flavonoid fraction. A review of its use in chronic venous insufficiency, venous ulcers and haemorrhoids. *Drugs* 2003; 63: 71–100
52. Pittler MH, Ernst E. Horse-chestnut seed extract for chronic venous insufficiency. A criteria-based systematic review. *Arch Dermatol.* 1998; 134:1356–60
53. European Medicines Agency. Assessment report on *Aesculus Hippocastanum L.*, semen; 2009. Available from: http://www.ema.europa.eu/documents/herbal-report/assessment-report-aesculus-hippocastanum-l-semen_en.pdf. Accessed October 30, 2018
54. Diehm C, Trampisch HJ, Lange S, Schmidt C. Comparison of leg compression stocking and oral horse-chestnut seed extract therapy in patients with chronic venous insufficiency. *Lancet.* 1996; 347:292–4
55. Belcaro G, Rosaria Cesarone M, Ledda A, et al. O-(beta-hydroxyethyl)-rutosides systemic and local treatment in chronic venous disease and microangiopathy: an independent prospective comparative study. *Angiology.* 2008; 59:7S–13S.10.1177/0003319707312021)
56. Akbulut B. Calcium dobesilate and oxerutin: effectiveness of combination therapy. *Phlebology.* 2010 Apr;25(2):66-71. doi: 10.1258/phleb.2009.008085. PMID: 20348452
57. AbuRahma AF, Perkins SE, Wulu JT, Ng HK. Iliofemoral deep vein thrombosis: conventional therapy versus lysis and percutaneous transluminal angioplasty and stenting. *Ann Surg.* 2001; 233:752–60
58. Neglen P, Hollis KC, Olivier J, Raju S. Stenting of the venous outflow in chronic venous disease: long-term stent-related outcome, clinical, and hemodynamic result. *J Vasc Surg.* 2007; 46:979–990
59. Khanna AK, Singh S. Postthrombotic syndrome: surgical possibilities. *Thrombosis* 2012; 2012:520604
60. Hutschenreiter S, Vollmar J, Loeprecht H, Abendschein A, Rodl W. Reconstructive operations on the venous system: late results with a critical assessment of the functional and vascular morphological criteria (in German). *Chirurg.* 1979; 50:555–563
61. AbuRahma AF, Robinson PA, Boland JP. Clinical, hemodynamic, and anatomic predictors of long-term outcome of lower extremity venovenous bypasses. *J Vasc Surg.* 1991; 14:635–644
62. O'Donnell TF Jr, Mackey WC, Shepard AD, Callow AD. Clinical, hemodynamic, and anatomic follow-up of direct venous reconstruction. *Arch Surg.* 1987; 122:474–482
63. Garg N, Gloviczki P, Karimi KM, Duncan AA, Bjarnason H, Kalra M, Oderich GS, Bower TC. Factors affecting outcome of open and hybrid reconstructions for nonmalignant obstruction of iliofemoral veins and inferior vena cava. *J Vasc Surg.* 2011; 53:383–393

64. Masuda EM, Kistner RL. Long-term results of venous valve reconstruction: a four- to twenty-one-year follow-up. *J Vasc Surg.* 1994; 19:391-403
65. Williams E, Enoch S, Miller D, et al. Effect of sharp debridement using curette or recalcitrant non-healing venous leg ulcers: a currently controlled, prospective cohort study. *Wound Repair Regen* 2005; 13: 138-47
66. Wilson JR, Mills JG, Prather ID, et al. A toxicity index of skin and wound cleansers used on in vitro fibroblasts and keratinocytes. *Adv Skin Wound Care* 2005; 18: 373-8
67. Gilchrist B, Reed C. The bacteriology of chronic venous ulcers treated with hydrocolloid dressings. *Br J Dermatol* 1989; 121: 337-44