

DERİN VEN TROMBOZU PROFİLAKSİSİ

Özkan ÖZLER¹

Derin ven trombozu vücudun derin venlerinde kan pıhtısı oluşumu ile meydana gelir. Derin ven trombozu (DVT) çoğunlukla alt ekstremitelerde derin venlerinde meydana gelir, daha nadir olarak üst ekstremitelerde, pelvis ve diğer venlerde görülür. Bu venlerdeki trombüsün bir kısmı koparak akciğerlere gelir ve yaşamı tehdit eden en önemli komplikasyonu olan pulmoner embolizmi (PE) oluşturur.⁽¹⁾ Derin ven trombozu multifaktöryel bir hastalıktır ve hastalarda birden fazla risk faktörü bulunabilir.⁽²⁾ Derin ven trombozu gelişimini kolaylaştıran üç temel mekanizma bulunmaktadır. Alman patolog Rudolf Virchow tarafından tanımlanmış olan Virchow triadında “Staz, endotel hasarı, hiperkoagülabilité” patogenetik mekanizmalar olarak yer almaktadır (Tablo 1).⁽³⁾

¹ Op. Dr., Amasya Üniversitesi Sabuncuoğlu Şerefeddin Eğitim ve Araştırma Hastanesi, Kalp Damar Cerrahisi Kliniği, ozkan_ozl@yahoo.com

Tablo 7. Gebelikle ilgili venöz tromboembolizm risk faktörleri

İleri anne yaşı
Ailesinde ya da kendisinde geçirilmiş tromboz öyküsü
Obezite
Malignansi
Overyan hiperstimülasyon
Kalıtsal trombofilik hastalık öyküsü (Faktör V Leiden, protrombin G20210A, protein C/S eksikliği, antitrombin eksikliği, aktive protein C rezistansı)

Farmakolojik profilaksi amacıyla DMAH ve unfraksiyone heparin kullanılmaktadır.^(212,213)

Düşük molekül ağırlıklı heparin

- Enoksaparin	Profilaktik	1x40 mg/gün sc
	Terapotik	2x1 mg/kg/gün sc
- Dalteparin	Profilaktik	1x5000 ünite/gün sc
	Terapotik	2x100 ünite/kg/gün sc

Unfraksiyone heparin Profilaktik 2x5000 ünite/gün sc

Terapotik aPTT düzeyine göre titre edilip intravenöz infüzyon şeklinde ya da 12 saatte bir kez subkutan olarak verilir.^(212,213)

Mekanik profilaksi amacıyla basınçlı elastik çorap ve aralıklı pnömatik kompresyon uygulanabilir.⁽²¹²⁻²¹⁴⁾

Ek öneriler olarak erken mobilizasyon, hidrasyon verilebilir.

Kaynaklar

1. Segal JB, Eng J, Jenckes MW, et al. Diagnosis and treatment of deep venous thrombosis and pulmonary embolism. Evid Rep Technol Assess (Summ) 2003;1-6.
2. Gerotziapas GT, Samama MM. Prophylaxis of venous thromboembolism in medical patients. Curr Opin Pulm Med 2004;10:356-65.
3. Michota FA. Venous thromboembolism prophylaxis in medical patients. Curr Opin Cardiol 2004;19:570-4.

4. Anderson FA, Jr., Zayaruzny M, Heit JA, Fidan D, Cohen AT. Estimated annual numbers of US acute-care hospital patients at risk for venous thromboembolism. *Am J Hematol* 2007;82:777-82.
5. Lindblad B, Eriksson A, Bergqvist D. Autopsy-verified pulmonary embolism in a surgical department: analysis of the period from 1951 to 1988. *Br J Surg* 1991;78:849-52.
6. Stein PD, Henry JW. Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy. *Chest* 1995;108:978-81.
7. White RH, Zhou H, Romano PS. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. *Thromb Haemost* 2003;90:446-55.
8. Sandler DA, Martin JF. Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis? *J R Soc Med* 1989;82:203-5.
9. Martino MA, Borges E, Williamson E, et al. Pulmonary embolism after major abdominal surgery in gynecologic oncology. *Obstet Gynecol* 2006;107:666-71.
10. Dismuke SE, Wagner EH. Pulmonary embolism as a cause of death. The changing mortality in hospitalized patients. *JAMA* 1986;255:2039-42.
11. Horlander KT, Mannino DM, Leeper KV. Pulmonary embolism mortality in the United States, 1979-1998: an analysis using multiple-cause mortality data. *Arch Intern Med* 2003;163:1711-7.
12. Collins R, Scrimgeour A, Yusuf S, Peto R. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. *N Engl J Med* 1988;318:1162-73.
13. Prevention of fatal postoperative pulmonary embolism by low doses of heparin. An international multicentre trial. *Lancet* 1975;2:45-51.
14. Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. *N Engl J Med* 1999;341:793-800.
15. Hull RD, Schellong SM, Tapson VF, et al. Extended-duration venous thromboembolism prophylaxis in acutely ill medical patients with recently reduced mobility: a randomized trial. *Ann Intern Med* 2010;153:8-18.
16. Halkin H, Goldberg J, Modan M, Modan B. Reduction of mortality in general medical in-patients by low-dose heparin prophylaxis. *Ann Intern Med* 1982;96:561-5.
17. Gardlund B. Randomised, controlled trial of low-dose heparin for prevention of fatal pulmonary embolism in patients with infectious diseases. The Heparin Prophylaxis Study Group. *Lancet* 1996;347:1357-61.
18. Mahe I, Bergmann JF, d'Azemar P, Vaissie JJ, Caulin C. Lack of effect of a low-molecular-weight heparin (nadroparin) on mortality in bedridden medical in-patients: a prospective randomised double-blind study. *Eur J Clin Pharmacol* 2005;61:347-51.
19. Kakkar AK, Cimminiello C, Goldhaber SZ, et al. Low-molecular-weight heparin and mortality in acutely ill medical patients. *N Engl J Med* 2011;365:2463-72.
20. Lederle FA, Zylla D, MacDonald R, Wilt TJ. Venous thromboembolism prophylaxis in hospitalized medical patients and those with stroke: a background review for an American College of Physicians Clinical Practice Guideline. *Ann Intern Med* 2011;155:602-15.
21. Lester W, Freemantle N, Begaj I, Ray D, Wood J, Pagano D. Fatal venous thromboembolism associated with hospital admission: a cohort study to assess the impact of a national risk assessment target. *Heart* 2013;99:1734-9.
22. Heit JA, Crusan DJ, Ashrani AA, Petterson TM, Bailey KR. Effect of a near-universal hospitalization-based prophylaxis regimen on annual number of venous thromboembolism events in the US. *Blood* 2017;130:109-14.

23. Hull RD, Hirsh J, Sackett DL, Stoddart GL. Cost-effectiveness of primary and secondary prevention of fatal pulmonary embolism in high-risk surgical patients. *Can Med Assoc J* 1982;127:990-5.
24. Geerts WH, Bergqvist D, Pineo GF, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008;133:381S-453S.
25. Meyer CS, Blebea J, Davis K, Jr., Fowl RJ, Kempczinski RE. Surveillance venous scans for deep venous thrombosis in multiple trauma patients. *Ann Vasc Surg* 1995;9:109-14.
26. Schellong SM, Beyer J, Kakkar AK, et al. Ultrasound screening for asymptomatic deep vein thrombosis after major orthopaedic surgery: the VENUS study. *J Thromb Haemost* 2007;5:1431-7.
27. Chopard P, Spirik D, Bounameaux H. Identifying acutely ill medical patients requiring thromboprophylaxis. *J Thromb Haemost* 2006;4:915-6.
28. Spyropoulos AC, Anderson FA, Jr., FitzGerald G, et al. Predictive and associative models to identify hospitalized medical patients at risk for VTE. *Chest* 2011;140:706-14.
29. Khouli H, Shapiro J, Pham VP, et al. Efficacy of deep venous thrombosis prophylaxis in the medical intensive care unit. *J Intensive Care Med* 2006;21:352-8.
30. Laporte S, Mismetti P. Epidemiology of thrombotic risk factors: the difficulty in using clinical trials to develop a risk assessment model. *Crit Care Med* 2010;38:S10-7.
31. Hill J, Treasure T, National Clinical Guideline Centre for A, Chronic C. Reducing the risk of venous thromboembolism in patients admitted to hospital: summary of NICE guidance. *BMJ* 2010;340:c95.
32. Leizorovicz A, Cohen AT, Turpie AG, et al. Randomized, placebo-controlled trial of dalteparin for the prevention of venous thromboembolism in acutely ill medical patients. *Circulation* 2004;110:874-9.
33. Cohen AT, Davidson BL, Gallus AS, et al. Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial. *BMJ* 2006;332:325-9.
34. Alikhan R, Cohen AT. A safety analysis of thromboprophylaxis in acute medical illness. *Thromb Haemost* 2003;89:590-1.
35. Jois-Bilowich P, Michota F, Bartholomew JR, et al. Venous thromboembolism prophylaxis in hospitalized heart failure patients. *J Card Fail* 2008;14:127-32.
36. Dentali F, Douketis JD, Gianni M, Lim W, Crowther MA. Meta-analysis: anticoagulant prophylaxis to prevent symptomatic venous thromboembolism in hospitalized medical patients. *Ann Intern Med* 2007;146:278-88.
37. Wein L, Wein S, Haas SJ, Shaw J, Krum H. Pharmacological venous thromboembolism prophylaxis in hospitalized medical patients: a meta-analysis of randomized controlled trials. *Arch Intern Med* 2007;167:1476-86.
38. Sjalander A, Jansson JH, Bergqvist D, Eriksson H, Carlberg B, Svensson P. Efficacy and safety of anticoagulant prophylaxis to prevent venous thromboembolism in acutely ill medical inpatients: a meta-analysis. *J Intern Med* 2008;263:52-60.
39. Lentine KL, Flavin KE, Gould MK. Variability in the use of thromboprophylaxis and outcomes in critically ill medical patients. *Am J Med* 2005;118:1373-80.
40. Kanaan AO, Silva MA, Donovan JL, Roy T, Al-Homsi AS. Meta-analysis of venous thromboembolism prophylaxis in medically ill patients. *Clin Ther* 2007;29:2395-405.
41. Dunn AS, Brenner A, Halm EA. The magnitude of an iatrogenic disorder: a systematic review of the incidence of venous thromboembolism for general medical inpatients. *Thromb Haemost* 2006;95:758-62.

42. Sherman DG, Albers GW, Bladin C, et al. The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous thromboembolism after acute ischaemic stroke (PREVAIL Study): an open-label randomised comparison. *Lancet* 2007;369:1347-55.
43. Bergmann JF, Neuhart E. A multicenter randomized double-blind study of enoxaparin compared with unfractionated heparin in the prevention of venous thromboembolic disease in elderly in-patients bedridden for an acute medical illness. The Enoxaparin in Medicine Study Group. *Thromb Haemost* 1996;76:529-34.
44. Ananthakrishnan AN, Cagan A, Gainer VS, et al. Thromboprophylaxis is associated with reduced post-hospitalization venous thromboembolic events in patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol* 2014;12:1905-10.
45. Cohen AT, Spiro TE, Spyropoulos AC, et al. D-dimer as a predictor of venous thromboembolism in acutely ill, hospitalized patients: a subanalysis of the randomized controlled MAGELLAN trial. *J Thromb Haemost* 2014;12:479-87.
46. Farge D, Frere C, Connors JM, et al. 2019 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer. *Lancet Oncol* 2019;20:e566-e81.
47. Spyropoulos AC, Mahan C. Venous thromboembolism prophylaxis in the medical patient: controversies and perspectives. *Am J Med* 2009;122:1077-84.
48. Mismetti P, Laporte-Simitsidis S, Tardy B, et al. Prevention of venous thromboembolism in internal medicine with unfractionated or low-molecular-weight heparins: a meta-analysis of randomised clinical trials. *Thromb Haemost* 2000;83:14-9.
49. Hull RD, Schellong SM, Tapson VF, et al. Extended-duration thromboprophylaxis in acutely ill medical patients with recent reduced mobility: methodology for the EXCLAIM study. *J Thromb Thrombolysis* 2006;22:31-8.
50. Bump GM, Dandu M, Kaufman SR, Shojania KG, Flanders SA. How complete is the evidence for thromboembolism prophylaxis in general medicine patients? A meta-analysis of randomized controlled trials. *J Hosp Med* 2009;4:289-97.
51. McGarry LJ, Stokes ME, Thompson D. Outcomes of thromboprophylaxis with enoxaparin vs. unfractionated heparin in medical inpatients. *Thromb J* 2006;4:17.
52. Laporte S, Liotier J, Bertoletti L, et al. Individual patient data meta-analysis of enoxaparin vs. unfractionated heparin for venous thromboembolism prevention in medical patients. *J Thromb Haemost* 2011;9:464-72.
53. Greig MF, Rochow SB, Crilly MA, Mangoni AA. Routine pharmacological venous thromboembolism prophylaxis in frail older hospitalised patients: where is the evidence? *Age Ageing* 2013;42:428-34.
54. Alikhan R, Bedenis R, Cohen AT. Heparin for the prevention of venous thromboembolism in acutely ill medical patients (excluding stroke and myocardial infarction). *Cochrane Database Syst Rev* 2014:CD003747.
55. Lilly CM, Liu X, Badawi O, Franey CS, Zuckerman IH. Thrombosis prophylaxis and mortality risk among critically ill adults. *Chest* 2014;146:51-7.
56. Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. London 2019.
57. Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. *J Thromb Haemost* 2007;5:632-4.
58. Timp JF, Braekkan SK, Versteeg HH, Cannegieter SC. Epidemiology of cancer-associated venous thrombosis. *Blood* 2013;122:1712-23.
59. Pabinger I, Thaler J, Ay C. Biomarkers for prediction of venous thromboembolism in cancer. *Blood* 2013;122:2011-8.

60. Barsam SJ, Patel R, Arya R. Anticoagulation for prevention and treatment of cancer-related venous thromboembolism. *Br J Haematol* 2013;161:764-77.
61. Falanga A, Marchetti M, Vignoli A. Coagulation and cancer: biological and clinical aspects. *J Thromb Haemost* 2013;11:223-33.
62. Buijs JT, Laghmani EH, van den Akker RFP, et al. The direct oral anticoagulants rivaroxaban and dabigatran do not inhibit orthotopic growth and metastasis of human breast cancer in mice. *J Thromb Haemost* 2019;17:951-63.
63. Blom JW, Doggen CJ, Osanto S, Rosendaal FR. Malignancies, prothrombotic mutations, and the risk of venous thrombosis. *JAMA* 2005;293:715-22.
64. Chew HK, Wun T, Harvey D, Zhou H, White RH. Incidence of venous thromboembolism and its effect on survival among patients with common cancers. *Arch Intern Med* 2006;166:458-64.
65. Alcalay A, Wun T, Khatri V, et al. Venous thromboembolism in patients with colorectal cancer: incidence and effect on survival. *J Clin Oncol* 2006;24:1112-8.
66. Cronin-Fenton DP, Sondergaard F, Pedersen LA, et al. Hospitalisation for venous thromboembolism in cancer patients and the general population: a population-based cohort study in Denmark, 1997-2006. *Br J Cancer* 2010;103:947-53.
67. Anderson LA, Moore SC, Gridley G, Stone BJ, Landgren O. Concomitant and antecedent deep venous thrombosis and cancer survival in male US veterans. *Leuk Lymphoma* 2011;52:764-70.
68. De Martino RR, Goodney PP, Spangler EL, et al. Variation in thromboembolic complications among patients undergoing commonly performed cancer operations. *J Vasc Surg* 2012;55:1035-40 e4.
69. Hultcrantz M, Bjorkholm M, Dickman PW, et al. Risk for Arterial and Venous Thrombosis in Patients With Myeloproliferative Neoplasms: A Population-Based Cohort Study. *Ann Intern Med* 2018;168:317-25.
70. Hedderich GS, O'Connor RJ, Reid EC, Mulder DS. Caval tumor thrombus complicating renal cell carcinoma: a surgical challenge. *Surgery* 1987;102:614-21.
71. Srikanthan A, Tran B, Beausoleil M, et al. Large retroperitoneal lymphadenopathy as a predictor of venous thromboembolism in patients with disseminated germ cell tumors treated with chemotherapy. *J Clin Oncol* 2015;33:582-7.
72. Greco PS, Bazzi AA, McLean K, et al. Incidence and Timing of Thromboembolic Events in Patients With Ovarian Cancer Undergoing Neoadjuvant Chemotherapy. *Obstet Gynecol* 2017;129:979-85.
73. Mandala M, Barni S, Floriani I, et al. Incidence and clinical implications of venous thromboembolism in advanced colorectal cancer patients: the 'GISCAD-alternating schedule' study findings. *Eur J Cancer* 2009;45:65-73.
74. Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Frequency, risk factors, and trends for venous thromboembolism among hospitalized cancer patients. *Cancer* 2007;110:2339-46.
75. Prandoni P, Samama MM. Risk stratification and venous thromboprophylaxis in hospitalized medical and cancer patients. *Br J Haematol* 2008;141:587-97.
76. Khorana AA, Francis CW, Blumberg N, Culakova E, Refaai MA, Lyman GH. Blood transfusions, thrombosis, and mortality in hospitalized patients with cancer. *Arch Intern Med* 2008;168:2377-81.
77. Jacobson G, Lamml J, Zamba G, Hua L, Goodheart MJ. Thromboembolic events in patients with cervical carcinoma: Incidence and effect on survival. *Gynecol Oncol* 2009;113:240-4.
78. Pihusch R, Danzl G, Scholz M, et al. Impact of thrombophilic gene mutations on thrombosis risk in patients with gastrointestinal carcinoma. *Cancer* 2002;94:3120-6.

79. Mego M, De Giorgi U, Broglio K, et al. Circulating tumour cells are associated with increased risk of venous thromboembolism in metastatic breast cancer patients. *Br J Cancer* 2009;101:1813-6.
80. Simanek R, Vormittag R, Ay C, et al. High platelet count associated with venous thromboembolism in cancer patients: results from the Vienna Cancer and Thrombosis Study (CATS). *J Thromb Haemost* 2010;8:114-20.
81. Byrne M, Reynolds JV, O'Donnell JS, et al. Long-term activation of the pro-coagulant response after neoadjuvant chemoradiation and major cancer surgery. *Br J Cancer* 2010;102:73-9.
82. Dipasco PJ, Misra S, Koniaris LG, Moffat FL, Jr. Thrombophilic state in cancer, part I: biology, incidence, and risk factors. *J Surg Oncol* 2011;104:316-22.
83. Chavez-MacGregor M, Zhao H, Kroll M, et al. Risk factors and incidence of thromboembolic events (TEEs) in older men and women with breast cancer. *Ann Oncol* 2011;22:2394-402.
84. Ahlbrecht J, Dickmann B, Ay C, et al. Tumor grade is associated with venous thromboembolism in patients with cancer: results from the Vienna Cancer and Thrombosis Study. *J Clin Oncol* 2012;30:3870-5.
85. Merkow RP, Bilimoria KY, McCarter MD, et al. Post-discharge venous thromboembolism after cancer surgery: extending the case for extended prophylaxis. *Ann Surg* 2011;254:131-7.
86. Lyman GH, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2013;31:2189-204.
87. Lobastov K, Barinov V, Schastlivtsev I, Laberko L, Rodoman G, Boyarintsev V. Validation of the Caprini risk assessment model for venous thromboembolism in high-risk surgical patients in the background of standard prophylaxis. *J Vasc Surg Venous Lymphat Disord* 2016;4:153-60.
88. Ramanathan R, Lee N, Duane TM, et al. Correlation of venous thromboembolism prophylaxis and electronic medical record alerts with incidence among surgical patients. *Surgery* 2016;160:1202-10.
89. Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141:e278S-e325S.
90. Anderson DR, Morgano GP, Bennett C, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. *Blood Adv* 2019;3:3898-944.
91. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141:e227S-e277S.
92. Bahl V, Hu HM, Henke PK, Wakefield TW, Campbell DA, Jr., Caprini JA. A validation study of a retrospective venous thromboembolism risk scoring method. *Ann Surg* 2010;251:344-50.
93. Rogers SO, Jr., Kilaru RK, Hosokawa P, Henderson WG, Zinner MJ, Khuri SF. Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: results from the patient safety in surgery study. *J Am Coll Surg* 2007;204:1211-21.
94. Clarke-Pearson DL, Dodge RK, Synan I, McClelland RC, Maxwell GL. Venous thromboembolism prophylaxis: patients at high risk to fail intermittent pneumatic compression. *Obstet Gynecol* 2003;101:157-63.

95. Lijfering WM, Rosendaal FR, Cannegieter SC. Risk factors for venous thrombosis - current understanding from an epidemiological point of view. *Br J Haematol* 2010;149:824-33.
96. Goldhaber SZ. Risk factors for venous thromboembolism. *J Am Coll Cardiol* 2010;56:1-7.
97. Kakkos SK, Caprini JA, Geroulakos G, Nicolaides AN, Stansby GP, Reddy DJ. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients. *Cochrane Database Syst Rev* 2008:CD005258.
98. Hull R, Delmore TJ, Hirsh J, et al. Effectiveness of intermittent pulsatile elastic stockings for the prevention of calf and thigh vein thrombosis in patients undergoing elective knee surgery. *Thromb Res* 1979;16:37-45.
99. Morris RJ, Woodcock JP. Intermittent pneumatic compression or graduated compression stockings for deep vein thrombosis prophylaxis? A systematic review of direct clinical comparisons. *Ann Surg* 2010;251:393-6.
100. Mismetti P, Laporte S, Darmon JY, Buchmuller A, Decousus H. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. *Br J Surg* 2001;88:913-30.
101. Leonardi MJ, McGory ML, Ko CY. The rate of bleeding complications after pharmacologic deep venous thrombosis prophylaxis: a systematic review of 33 randomized controlled trials. *Arch Surg* 2006;141:790-7; discussion 7-9.
102. Clagett GP, Reisch JS. Prevention of venous thromboembolism in general surgical patients. Results of meta-analysis. *Ann Surg* 1988;208:227-40.
103. Bergqvist D. Low molecular weight heparin and unfractionated heparin in thrombosis prophylaxis after major surgical intervention: update of previous meta-analyses. *Br J Surg* 1998;85:872.
104. Agnelli G, Bergqvist D, Cohen AT, Gallus AS, Gent M, investigators P. Randomized clinical trial of postoperative fondaparinux versus perioperative dalteparin for prevention of venous thromboembolism in high-risk abdominal surgery. *Br J Surg* 2005;92:1212-20.
105. Di Nisio M, Peinemann F, Porreca E, Rutjes AW. Primary prophylaxis for venous thromboembolism in patients undergoing cardiac or thoracic surgery. *Cochrane Database Syst Rev* 2015:CD009658.
106. Kulik A, Rassen JA, Myers J, et al. Comparative effectiveness of preventative therapy for venous thromboembolism after coronary artery bypass graft surgery. *Circ Cardiovasc Interv* 2012;5:590-6.
107. Farkas JC, Chapuis C, Combe S, et al. A randomised controlled trial of a low-molecular-weight heparin (Enoxaparin) to prevent deep-vein thrombosis in patients undergoing vascular surgery. *Eur J Vasc Surg* 1993;7:554-60.
108. Harjola P, Meurala H, Frick MH. Prevention of deep venous thrombosis and thromboembolism by dipyridamole and acetylsalicylic acid after reconstructive arterial surgery. *J Cardiovasc Surg (Torino)* 1980;21:451-4.
109. Speziale F, Verardi S, Taurino M, et al. Low molecular weight heparin prevention of post-operative deep vein thrombosis in vascular surgery. *Pharmatherapeutica* 1988;5:261-8.
110. Lastoria S, Rollo HA, Yoshida WB, Giannini M, Moura R, Maffei FH. Prophylaxis of deep-vein thrombosis after lower extremity amputation: comparison of low molecular weight heparin with unfractionated heparin. *Acta Cir Bras* 2006;21:184-6.
111. de Maistre E, Terriat B, Lesne-Padieu AS, Abello N, Bouchot O, Steinmetz EF. High incidence of venous thrombosis after surgery for abdominal aortic aneurysm. *J Vasc Surg* 2009;49:596-601.
112. Scarborough JE, Cox MW, Mureebe L, Pappas TN, Shortell CK. A novel scoring system for predicting postoperative venous thromboembolic complications in patients after open aortic surgery. *J Am Coll Surg* 2012;214:620-6; discussion 7-8.

113. Bush RL, Lumsden AB, Dodson TF, et al. Mid-term results after endovascular repair of the abdominal aortic aneurysm. *J Vasc Surg* 2001;33:S70-6.
114. Eagleton MJ, Grigoryants V, Peterson DA, et al. Endovascular treatment of abdominal aortic aneurysm is associated with a low incidence of deep venous thrombosis. *J Vasc Surg* 2002;36:912-6.
115. AbuRahma AF, Woodruff BA, Lucente FC. Edema after femoropopliteal bypass surgery: lymphatic and venous theories of causation. *J Vasc Surg* 1990;11:461-7.
116. Fletcher JP, Batiste P. Incidence of deep vein thrombosis following vascular surgery. *Int Angiol* 1997;16:65-8.
117. Hollyoak M, Woodruff P, Muller M, Daunt N, Weir P. Deep venous thrombosis in postoperative vascular surgical patients: a frequent finding without prophylaxis. *J Vasc Surg* 2001;34:656-60.
118. Hamer JD. Investigation of oedema of the lower limb following successful femoropopliteal by-pass surgery: the role of phlebography in demonstrating venous thrombosis. *Br J Surg* 1972;59:979-82.
119. Myhre HO, Storen EJ, Ongre A. The incidence of deep venous thrombosis in patients with leg oedema after arterial reconstruction. *Scand J Thorac Cardiovasc Surg* 1974;8:73-6.
120. Proebstle TM, Herdemann S. Early results and feasibility of incompetent perforator vein ablation by endovenous laser treatment. *Dermatol Surg* 2007;33:162-8.
121. Puggioni A, Kalra M, Carmo M, Mozes G, Gloviczki P. Endovenous laser therapy and radiofrequency ablation of the great saphenous vein: analysis of early efficacy and complications. *J Vasc Surg* 2005;42:488-93.
122. Marsh P, Price BA, Holdstock J, Harrison C, Whiteley MS. Deep vein thrombosis (DVT) after venous thermoablation techniques: rates of endovenous heat-induced thrombosis (EHIT) and classical DVT after radiofrequency and endovenous laser ablation in a single centre. *Eur J Vasc Endovasc Surg* 2010;40:521-7.
123. Lawrence PF, Chandra A, Wu M, et al. Classification of proximal endovenous closure levels and treatment algorithm. *J Vasc Surg* 2010;52:388-93.
124. de Medeiros CA, Luccas GC. Comparison of endovenous treatment with an 810 nm laser versus conventional stripping of the great saphenous vein in patients with primary varicose veins. *Dermatol Surg* 2005;31:1685-94; discussion 94.
125. Desmyttere J, Grard C, Wassmer B, Mordon S. Endovenous 980-nm laser treatment of saphenous veins in a series of 500 patients. *J Vasc Surg* 2007;46:1242-7.
126. Kalteis M, Berger I, Messie-Werndl S, et al. High ligation combined with stripping and endovenous laser ablation of the great saphenous vein: early results of a randomized controlled study. *J Vasc Surg* 2008;47:822-9; discussion 9.
127. Nwaejike N, Srodon PD, Kyriakides C. 5-years of endovenous laser ablation (EVLA) for the treatment of varicose veins--a prospective study. *Int J Surg* 2009;7:347-9.
128. Mozes G, Kalra M, Carmo M, Swenson L, Gloviczki P. Extension of saphenous thrombus into the femoral vein: a potential complication of new endovenous ablation techniques. *J Vasc Surg* 2005;41:130-5.
129. Merchant R, Jr, Kistner RL, Kabnick LS. Is there an increased risk for DVT with the VNUS closure procedure? *J Vasc Surg* 2003;38:628.
130. Hingorani AP, Ascher E, Markevich N, et al. Deep venous thrombosis after radiofrequency ablation of greater saphenous vein: a word of caution. *J Vasc Surg* 2004;40:500-4.
131. Burke B, Kumar R, Vickers V, Grant E, Scremin E. Deep vein thrombosis after lower limb amputation. *Am J Phys Med Rehabil* 2000;79:145-9.
132. Harper DR, Dhall DP, Woodruff PW. Prophylaxis in iliofemoral venous thrombosis. The major amputee as a clinical research model. *Br J Surg* 1973;60:831.

133. Huang ME, Johns JS, White J, Sanford K. Venous thromboembolism in a rehabilitation setting after major lower-extremity amputation. *Arch Phys Med Rehabil* 2005;86:73-8.
134. Yeager RA, Moneta GL, Edwards JM, Taylor LM, Jr., McConnell DB, Porter JM. Deep vein thrombosis associated with lower extremity amputation. *J Vasc Surg* 1995;22:612-5.
135. Matielo MF, Presti C, Casella IB, Netto BM, Puech-Leao P. Incidence of ipsilateral postoperative deep venous thrombosis in the amputated lower extremity of patients with peripheral obstructive arterial disease. *J Vasc Surg* 2008;48:1514-9.
136. Venturi ML, Davison SP, Caprini JA. Prevention of venous thromboembolism in the plastic surgery patient: current guidelines and recommendations. *Aesthet Surg J* 2009;29:421-8.
137. Liao EC, Taghinia AH, Nguyen LP, Yueh JH, May JW, Jr., Orgill DP. Incidence of hematoma complication with heparin venous thrombosis prophylaxis after TRAM flap breast reconstruction. *Plast Reconstr Surg* 2008;121:1101-7.
138. Hatef DA, Kenkel JM, Nguyen MQ, et al. Thromboembolic risk assessment and the efficacy of enoxaparin prophylaxis in excisional body contouring surgery. *Plast Reconstr Surg* 2008;122:269-79.
139. Kim EK, Eom JS, Ahn SH, Son BH, Lee TJ. The efficacy of prophylactic low-molecular-weight heparin to prevent pulmonary thromboembolism in immediate breast reconstruction using the TRAM flap. *Plast Reconstr Surg* 2009;123:9-12.
140. Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery: a metaanalysis. *Chest* 2008;134:237-49.
141. Iorio A, Agnelli G. Low-molecular-weight and unfractionated heparin for prevention of venous thromboembolism in neurosurgery: a meta-analysis. *Arch Intern Med* 2000;160:2327-32.
142. Taniguchi S, Fukuda I, Daitoku K, et al. Prevalence of venous thromboembolism in neurosurgical patients. *Heart Vessels* 2009;24:425-8.
143. Yoshioka K, Murakami H, Demura S, et al. Comparative study of the prevalence of venous thromboembolism after elective spinal surgery. *Orthopedics* 2013;36:e223-8.
144. Yoshioka K, Murakami H, Demura S, Kato S, Tsuchiya H. Prevalence and risk factors for development of venous thromboembolism after degenerative spinal surgery. *Spine (Phila Pa 1976)* 2015;40:E301-6.
145. Gruber UF, Rem J, Meisner C, Gratzl O. Prevention of thromboembolic complications with miniheparin-dihydroergotamine in patients undergoing lumbar disc operations. *Eur Arch Psychiatry Neurol Sci* 1984;234:157-61.
146. Rokito SE, Schwartz MC, Neuwirth MG. Deep vein thrombosis after major reconstructive spinal surgery. *Spine (Phila Pa 1976)* 1996;21:853-8; discussion 9.
147. Nelson LD, Jr., Montgomery SP, Dameron TB, Jr., Nelson RB. Deep vein thrombosis in lumbar spinal fusion: a prospective study of antiembolic and pneumatic compression stockings. *J South Orthop Assoc* 1996;5:181-4.
148. Wood KB, Kos PB, Abnet JK, Ista C. Prevention of deep-vein thrombosis after major spinal surgery: a comparison study of external devices. *J Spinal Disord* 1997;10:209-14.
149. Fiasconaro M, Poeran J, Liu J, Wilson LA, Memtsoudis SG. Venous thromboembolism and prophylaxis therapy after elective spine surgery: a population-based study. *Can J Anaesth* 2021;68:345-57.
150. Ho KM, Bham E, Pavey W. Incidence of Venous Thromboembolism and Benefits and Risks of Thromboprophylaxis After Cardiac Surgery: A Systematic Review and Meta-Analysis. *J Am Heart Assoc* 2015;4:e002652.
151. Venous Thromboembolism: Reducing the Risk of Venous Thromboembolism (Deep Vein Thrombosis and Pulmonary Embolism) in Patients Admitted to Hospital. London 2010.
152. Leizorovicz A, Haugh MC, Chapuis FR, Samama MM, Boissel JP. Low molecular weight heparin in prevention of perioperative thrombosis. *BMJ* 1992;305:913-20.

153. Nurmohamed MT, Rosendaal FR, Buller HR, et al. Low-molecular-weight heparin versus standard heparin in general and orthopaedic surgery: a meta-analysis. *Lancet* 1992;340:152-6.
154. Kakkar VV, Cohen AT, Edmonson RA, et al. Low molecular weight versus standard heparin for prevention of venous thromboembolism after major abdominal surgery. The Thromboprophylaxis Collaborative Group. *Lancet* 1993;341:259-65.
155. Bergqvist D, Agnelli G, Cohen AT, et al. Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. *N Engl J Med* 2002;346:975-80.
156. Rasmussen MS. Preventing thromboembolic complications in cancer patients after surgery: a role for prolonged thromboprophylaxis. *Cancer Treat Rev* 2002;28:141-4.
157. Rasmussen MS, Jorgensen LN, Wille-Jorgensen P, et al. Prolonged prophylaxis with dalteparin to prevent late thromboembolic complications in patients undergoing major abdominal surgery: a multicenter randomized open-label study. *J Thromb Haemost* 2006;4:2384-90.
158. Akl EA, Terrenato I, Barba M, et al. Low-molecular-weight heparin vs unfractionated heparin for perioperative thromboprophylaxis in patients with cancer: a systematic review and meta-analysis. *Arch Intern Med* 2008;168:1261-9.
159. Efficacy and safety of enoxaparin versus unfractionated heparin for prevention of deep vein thrombosis in elective cancer surgery: a double-blind randomized multicentre trial with venographic assessment. ENOXACAN Study Group. *Br J Surg* 1997;84:1099-103.
160. Andtbacka RH, Babiera G, Singletary SE, et al. Incidence and prevention of venous thromboembolism in patients undergoing breast cancer surgery and treated according to clinical pathways. *Ann Surg* 2006;243:96-101.
161. McLeod RS, Geerts WH, Sniderman KW, et al. Subcutaneous heparin versus low-molecular-weight heparin as thromboprophylaxis in patients undergoing colorectal surgery: results of the canadian colorectal DVT prophylaxis trial: a randomized, double-blind trial. *Ann Surg* 2001;233:438-44.
162. Kalweit G, Huwer H, Volkmer I, Petzold T, Gams E. Pulmonary embolism: a frequent cause of acute fatality after lung resection. *Eur J Cardiothorac Surg* 1996;10:242-6; discussion 6-7.
163. Nagahiro I, Andou A, Aoe M, Sano Y, Date H, Shimizu N. Intermittent pneumatic compression is effective in preventing symptomatic pulmonary embolism after thoracic surgery. *Surg Today* 2004;34:6-10.
164. Gomez-Hernandez MT, Rodriguez-Perez M, Novoa-Valentin N, Jimenez-Lopez M, Aranda-Alcaide JL, Varela-Simo G. Prevalence of venous thromboembolism in elective thoracic surgery. *Arch Bronconeumol* 2013;49:297-302.
165. Johanson NA, Lachiewicz PF, Lieberman JR, et al. American academy of orthopaedic surgeons clinical practice guideline on. Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. *J Bone Joint Surg Am* 2009;91:1756-7.
166. Kwon S, Meissner M, Symons R, et al. Perioperative pharmacologic prophylaxis for venous thromboembolism in colorectal surgery. *J Am Coll Surg* 2011;213:596-603, e1.
167. Homoncik M, Gessl A, Ferlitsch A, Jilma B, Vierhapper H. Altered platelet plug formation in hyperthyroidism and hypothyroidism. *J Clin Endocrinol Metab* 2007;92:3006-12.
168. Squizzato A, Romualdi E, Piantanida E, et al. Subclinical hypothyroidism and deep venous thrombosis. A pilot cross-sectional study. *Thromb Haemost* 2007;97:803-6.
169. Brenner B, Hoffman R, Carp H, Dulitsky M, Younis J, Investigators L-E. Efficacy and safety of two doses of enoxaparin in women with thrombophilia and recurrent pregnancy loss: the LIVE-ENOX study. *J Thromb Haemost* 2005;3:227-9.
170. Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. *N Engl J Med* 1994;331:1601-6.

171. Cothren CC, Smith WR, Moore EE, Morgan SJ. Utility of once-daily dose of low-molecular-weight heparin to prevent venous thromboembolism in multisystem trauma patients. *World J Surg* 2007;31:98-104.
172. Serin K, Yanar H, Ozdenkaya Y, Tugrul S, Kurtoglu M. (Venous thromboembolism prophylaxis methods in trauma and emergency surgery intensive care unit patients: low molecular weight heparin versus elastic stockings + intermittent pneumatic compression). *Ulus Travma Acil Cerrahi Derg* 2010;16:130-4.
173. Kurtoglu M, Yanar H, Bilsel Y, et al. Venous thromboembolism prophylaxis after head and spinal trauma: intermittent pneumatic compression devices versus low molecular weight heparin. *World J Surg* 2004;28:807-11.
174. Heit JA, O'Fallon WM, Petterson TM, et al. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population-based study. *Arch Intern Med* 2002;162:1245-8.
175. Caprini JA, Arcelus JJ, Reyna JJ. Effective risk stratification of surgical and nonsurgical patients for venous thromboembolic disease. *Semin Hematol* 2001;38:12-9.
176. Gangireddy C, Rectenwald JR, Upchurch GR, et al. Risk factors and clinical impact of postoperative symptomatic venous thromboembolism. *J Vasc Surg* 2007;45:335-41; discussion 41-2.
177. Anderson FA, Jr., Spencer FA. Risk factors for venous thromboembolism. *Circulation* 2003;107:19-16.
178. Samama MM. An epidemiologic study of risk factors for deep vein thrombosis in medical outpatients: the Sirius study. *Arch Intern Med* 2000;160:3415-20.
179. Memtsoudis SG, Della Valle AG, Besculides MC, Esposito M, Koulouvaris P, Salvati EA. Risk factors for perioperative mortality after lower extremity arthroplasty: a population-based study of 6,901,324 patient discharges. *J Arthroplasty* 2010;25:19-26.
180. Cook D, Crowther M, Meade M, et al. Deep venous thrombosis in medical-surgical critically ill patients: prevalence, incidence, and risk factors. *Crit Care Med* 2005;33:1565-71.
181. Osborne NH, Wakefield TW, Henke PK. Venous thromboembolism in cancer patients undergoing major surgery. *Ann Surg Oncol* 2008;15:3567-78.
182. Jorgensen CC, Jacobsen MK, Soeballe K, et al. Thromboprophylaxis only during hospitalisation in fast-track hip and knee arthroplasty, a prospective cohort study. *BMJ Open* 2013;3:e003965.
183. White RH, Gettner S, Newman JM, Trauner KB, Romano PS. Predictors of rehospitalization for symptomatic venous thromboembolism after total hip arthroplasty. *N Engl J Med* 2000;343:1758-64.
184. Pedersen AB, Sorensen HT, Mehnert F, Overgaard S, Johnsen SP. Risk factors for venous thromboembolism in patients undergoing total hip replacement and receiving routine thromboprophylaxis. *J Bone Joint Surg Am* 2010;92:2156-64.
185. Leizorovicz A, Turpie AG, Cohen AT, et al. Epidemiology of venous thromboembolism in Asian patients undergoing major orthopedic surgery without thromboprophylaxis. The SMART study. *J Thromb Haemost* 2005;3:28-34.
186. Mantilla CB, Horlocker TT, Schroeder DR, Berry DJ, Brown DL. Risk factors for clinically relevant pulmonary embolism and deep venous thrombosis in patients undergoing primary hip or knee arthroplasty. *Anesthesiology* 2003;99:552-60; discussion 5A.
187. Dattani R, Smith CD, Patel VR. The venous thromboembolic complications of shoulder and elbow surgery: a systematic review. *Bone Joint J* 2013;95-B:70-4.
188. Bjornara BT, Gudmundsen TE, Dahl OE. Frequency and timing of clinical venous thromboembolism after major joint surgery. *J Bone Joint Surg Br* 2006;88:386-91.

189. Januel JM, Chen G, Ruffieux C, et al. Symptomatic in-hospital deep vein thrombosis and pulmonary embolism following hip and knee arthroplasty among patients receiving recommended prophylaxis: a systematic review. *JAMA* 2012;307:294-303.
190. Samama CM, Vray M, Barre J, et al. Extended venous thromboembolism prophylaxis after total hip replacement: a comparison of low-molecular-weight heparin with oral anticoagulant. *Arch Intern Med* 2002;162:2191-6.
191. Eriksson BI, Bauer KA, Lassen MR, Turpie AG, Steering Committee of the Pentasaccharide in Hip-Fracture Surgery S. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after hip-fracture surgery. *N Engl J Med* 2001;345:1298-304.
192. Planes A, Vochelle N, Darmon JY, Fagola M, Bellaud M, Huet Y. Risk of deep-venous thrombosis after hospital discharge in patients having undergone total hip replacement: double-blind randomised comparison of enoxaparin versus placebo. *Lancet* 1996;348:224-8.
193. Bergqvist D, Benoni G, Bjorgell O, et al. Low-molecular-weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med* 1996;335:696-700.
194. Dahl OE, Andreassen G, Aspelin T, et al. Prolonged thromboprophylaxis following hip replacement surgery--results of a double-blind, prospective, randomised, placebo-controlled study with dalteparin (Fragmin). *Thromb Haemost* 1997;77:26-31.
195. Lassen MR, Borris LC, Anderson BS, et al. Efficacy and safety of prolonged thromboprophylaxis with a low molecular weight heparin (dalteparin) after total hip arthroplasty--the Danish Prolonged Prophylaxis (DaPP) Study. *Thromb Res* 1998;89:281-7.
196. Comp PC, Spiro TE, Friedman RJ, et al. Prolonged enoxaparin therapy to prevent venous thromboembolism after primary hip or knee replacement. *Enoxaparin Clinical Trial Group. J Bone Joint Surg Am* 2001;83:336-45.
197. White RH, Romano PS, Zhou H, Rodrigo J, Bargar W. Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. *Arch Intern Med* 1998;158:1525-31.
198. Eikelboom JW, Quinlan DJ, Douketis JD. Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials. *Lancet* 2001;358:9-15.
199. Hull RD, Pineo GF, Stein PD, et al. Extended out-of-hospital low-molecular-weight heparin prophylaxis against deep venous thrombosis in patients after elective hip arthroplasty: a systematic review. *Ann Intern Med* 2001;135:858-69.
200. Sobieraj DM, Lee S, Coleman CI, et al. Prolonged versus standard-duration venous thromboprophylaxis in major orthopedic surgery: a systematic review. *Ann Intern Med* 2012;156:720-7.
201. Fisher WD, Agnelli G, George DJ, et al. Extended venous thromboembolism prophylaxis in patients undergoing hip fracture surgery - the SAVE-HIP3 study. *Bone Joint J* 2013;95-B:459-66.
202. O'Donnell M, Linkins LA, Kearon C, Julian J, Hirsh J. Reduction of out-of-hospital symptomatic venous thromboembolism by extended thromboprophylaxis with low-molecular-weight heparin following elective hip arthroplasty: a systematic review. *Arch Intern Med* 2003;163:1362-6.
203. Forster R, Stewart M. Anticoagulants (extended duration) for prevention of venous thromboembolism following total hip or knee replacement or hip fracture repair. *Cochrane Database Syst Rev* 2016;3:CD004179.
204. Anderson DR, Dunbar M, Murnaghan J, et al. Aspirin or Rivaroxaban for VTE Prophylaxis after Hip or Knee Arthroplasty. *N Engl J Med* 2018;378:699-707.

205. Marik PE, Plante LA. Venous thromboembolic disease and pregnancy. *N Engl J Med* 2008;359:2025-33.
206. Greer IA. Thrombosis in pregnancy: maternal and fetal issues. *Lancet* 1999;353:1258-65.
207. Goodrich SM, Wood JE. Peripheral Venous Distensibility and Velocity of Venous Blood Flow during Pregnancy or during Oral Contraceptive Therapy. *Am J Obstet Gynecol* 1964;90:740-4.
208. Macklon NS, Greer IA, Bowman AW. An ultrasound study of gestational and postural changes in the deep venous system of the leg in pregnancy. *Br J Obstet Gynaecol* 1997;104:191-7.
209. McColl MD, Ramsay JE, Tait RC, et al. Risk factors for pregnancy associated venous thromboembolism. *Thromb Haemost* 1997;78:1183-8.
210. Friederich PW, Sanson BJ, Simioni P, et al. Frequency of pregnancy-related venous thromboembolism in anticoagulant factor-deficient women: implications for prophylaxis. *Ann Intern Med* 1996;125:955-60.
211. Branch DW, Silver RM, Blackwell JL, Reading JC, Scott JR. Outcome of treated pregnancies in women with antiphospholipid syndrome: an update of the Utah experience. *Obstet Gynecol* 1992;80:614-20.
212. Bates SM, Greer IA, Middeldorp S, Veenstra DL, Prabulos AM, Vandvik PO. VTE, thrombophilia, antithrombotic therapy, and pregnancy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141:e691S-e736S.
213. American College of O, Gynecologists Women's Health Care P. ACOG Practice Bulletin No. 138: Inherited thrombophilias in pregnancy. *Obstet Gynecol* 2013;122:706-17.
214. Norgren L, Austrell C, Nilsson L. The effect of graduated elastic compression stockings on femoral blood flow velocity during late pregnancy. *Vasa* 1995;24:282-5.