EVIDENCE BASED STATEMENT

DOMAIN 06, Statement 03

TOPIC: "Thrombotic risk management in obese and CVD patients "

SEARCH TERMS & SOURCES

(("venous thrombosis" OR "venous thromboembolism" OR "VTE") AND
("obesity" OR "varicose" OR "chronic venous disease" OR "CVD")
AND ("risk") AND ("meta analysis" OR "Systematic Review")

INCLUSION CRITERIA

Systematic review or meta-analysis from 2012 to 2022
Focused on risk or prophylaxis associated with obesity or CVD

SEARCH RESULT BEFORE - AFTER SELECTION

107 - 8

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. Giorgi-Pierfranceschi M, López-Núñez JJ, Monreal M, et al. Morbid obesity and mortality in patients with VTE: findings from real-life clinical practice. Chest. 2020 Jun 1;157(6):1617-25.
2. Golemi I, Adum JP, Tafur A, Caprini J. Venous thromboembolism prophylaxis using the Caprini score. Disease-a-Month. 2019 Aug 1;65(8):249-98
3. Chang SL, Huang YL, Lee MC, et al. Association of varicose veins with incident venous thromboembolism and peripheral artery disease. Jama. 2018 Feb 27;319(8):807-17.
4. Cushman M, O'Meara ES, Heckbert SR, et al. Body size measures, hemostatic and inflammatory markers and risk of venous thrombosis: The Longitudinal Investigation of Thromboembolism Etiology. Thrombosis research. 2016 Aug 1;144:127-32.

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Domain 6; Statement 3

IDENTIFIED REFERENCES

1. Ceccato D, Di Vincenzo A, Pagano C, Pesavento R, Prandoni P, Vettor R. Weight-adjusted versus fixed dose heparin thromboprophylaxis in hospitalized obese patients: A systematic review and meta-analysis. European journal of internal medicine. 2021 Apr 19.
2. Rahmani J, Roudsari AH, Bawadi H, Thompson J, Fard RK, Clark C, Ryan PM, Ajami M, Sakak FR, Salehisahlabadi A, Abdulazeem HM. Relationship between body mass index, risk of venous thromboembolism and pulmonary embolism: a systematic review and dose-response meta-analysis of cohort studies among four million participants. Thrombosis Research. 2020 Aug 1;192:64-72.
3. Venclauskas L, Maleckas A, Arcelus JI. European guidelines on perioperative venous thromboembolism prophylaxis: surgery in the obese patient. European Journal of Anaesthesiology (EJA). 2018 Feb 1;35(2):147-53.
4. Baggen VJ, Chung K, Koole K, Sarneel MH, Rutten FH, Hajer GR. Association of varicosities and concomitant deep venous thrombosis in patients with superficial venous thrombosis, a systematic review. The European journal of general practice. 2015 Jan 2;21(1):70-6.
5. Ageno W, Di Minno MN, Ay C, Jang MJ, Hansen JB, Steffen LM, Vayà A, Rattazzi M, Pabinger I, Oh D, Di Minno G. Association between the metabolic syndrome, its individual components, and unprovoked venous thromboembolism: results of a patient-level meta-analysis. Arteriosclerosis, thrombosis, and vascular biology. 2014 Nov;34(11):2478-85.
6. Ikesaka R, Delluc A, Le Gal G, Carrier M. Efficacy and safety of weight-adjusted heparin prophylaxis for the prevention of acute venous thromboembolism among obese patients undergoing bariatric surgery: a systematic review and meta-analysis. Thrombosis research. 2014 Apr 1;133(4):682-7.
7. Kebede S, Prakasa KR, Shermock K, Shihab HM, Brotman DJ, Sharma R, Chelladurai Y, Haut ER, Singh S, Segal JB. A systematic review of venous thromboembolism prophylaxis strategies in patients with renal insufficiency, obesity, or on antiplatelet agents. Journal of hospital medicine. 2013 Jul;8(7):394-401.
8. Rocha AT, de Vasconcellos ÂG, da Luz Neto ER, Araújo DM, Alves ES, Lopes AA. Risk of venous thromboembolism and efficacy of thromboprophylaxis in hospitalized obese medical patients and in obese patients undergoing bariatric surgery. Obesity Surgery. 2006 Dec;16(12):1645-55.

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TEXT FOR INCLUSION IN THE DOCUMENT

DOMAIN 06, Statement 03, TOPIC: "Thrombotic risk management in obese and CVD patients"

Patients with obesity (defined as a body mass index of ≥ 30 kg/m^2) are at significantly higher risk of VTE compared to patients at a normal BMI, and this risk increases linearly with increased BMI (***Rahmani J, Roudsari AH, Bawadi H, et al. Relationship between body mass index, risk of venous thromboembolism and pulmonary embolism: a systematic review and dose-response meta-analysis of cohort studies among four million participants. Thrombosis Research. 2020 Aug 1;192:64-72**). Women may also be at risk at a BMI of ≥ 25 kg/m^2, and are at much higher risk if they are taking oral contraceptive pills (**Golemi I, Adum JP, Tafur A, Caprini J. Venous thromboembolism prophylaxis using the Caprini score. Disease-a-Month. 2019 Aug 1;65(8):249-9**). Physiologic changes in obese patients, including impaired venous return, the inflammatory effects of adipose tissue, and vessel wall alterations, have all been shown to influence the formation of DVT (**Cushman M, O'Meara ES, Heckbert SR, et al. Body size measures, hemostatic and inflammatory markers and risk of venous thrombosis: The Longitudinal Investigation of Thromboembolism Etiology. Thrombosis research. 2016 Aug 1;144:127-32**). Obesity can also be associated with obstructive sleep apnea, another independent risk factor for VTE. Obesity is also a risk factor for VTE recurrence. Somewhat surprisingly, obesity does appear to be protective against mortality in patients who do suffer a PE, although this relationship has not been fully explained (**Golemi I, Adum JP, Tafur A, Caprini J. Venous thromboembolism prophylaxis using the Caprini score. Disease-a-Month. 2019 Aug 1;65(8):249-98**).

Patients with chronic venous disease, including varicose veins, spider telangiectasias, and reticular veins, have up to 7 times the risk of VTE. The associated valvular incompetence, venous hypertension, inflammatory changes, and vein wall alterations influence VTE formation via all three factors of Virchow's triad (**Golemi I, Adum JP, Tafur A, Caprini J. Venous thromboembolism prophylaxis using the Caprini score. Disease-a-Month. 2019 Aug 1;65(8):249-98**).

For hospitalized patients with obesity or venous insufficiency, individualized risk assessment should guide VTE risk stratification and prophylaxis approaches. Research has focused on identifying optimal prophylaxis strategies in obese patients; however, no clearly superior approaches have yet been identified in this patient group. Weight-based dosing of prophylactic unfractionated heparin does not appear to increase bleeding risk in obese patients and is associated with increases in factor Xa levels, but has not been shown to decrease VTE events (**Ceccato D, Di Vincenzo A, Pagano C, et al. Weight-adjusted versus fixed dose heparin thromboprophylaxis in hospitalized obese patients: A systematic review and meta-analysis. European journal of internal medicine. 2021 Apr 19**).

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STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 06, Statement 03

"Patients who are obese or who have varicose veins are at increased risk of blood clots"

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4 SELECTED REFEREENCES

1. Ceccato D, Di Vincenzo A, Pagano C, et al. Weight-adjusted versus fixed dose heparin thromboprophylaxis in hospitalized obese patients: A systematic review and meta-analysis. European journal of internal medicine. 2021 Apr 19.
2. *Rahmani J, Roudsari AH, Bawadi H, et al. Relationship between body mass index, risk of venous thromboembolism and pulmonary embolism: a systematic review and dose-response meta-analysis of cohort studies among four million participants. Thrombosis Research. 2020 Aug 1;192:64-72.
3. Golemi I, Adum JP, Tafur A, Caprini J. Venous thromboembolism prophylaxis using the Caprini score. Disease-a-Month. 2019 Aug 1;65(8):249-98.
4. Cushman M, O'Meara ES, Heckbert SR, et al. Body size measures, hemostatic and inflammatory markers and risk of venous thrombosis: The Longitudinal Investigation of Thromboembolism Etiology. Thrombosis research. 2016 Aug 1;144:127-32.

identified LITERATURE BIAS

Because there is no consensus approach for "weight-based" dosing among obese patients, there is significant heterogeneity between studies comparing weight-based to standard prophylactic dosing.

SUGGESTED NEXT LINES OF RESEARCH

More research is needed on optimal prophylaxis strategies in patients with obesity. In particular, studies should focus on the role of thrombodynamic testing to optimize dosing regimens. Studies on the pathophysiology behind the "obesity paradox," whereby obesity is protective against PE mortality.