

GUIDELINES

European guidelines on perioperative venous thromboembolism prophylaxis

Mechanical prophylaxis

Arash Afshari, Christian Fenger-Eriksen, Manuel Monreal and Peter Verhamme, for the ESA VTE Guidelines Task Force

Institutional protocols need to address the indications for pharmacological and mechanical thromboprophylaxis. The use of graduated compression stockings (GCS) and intermittent pneumatic compression (IPC) strongly differs between institutions. As a consequence, no strong recommendations can be made based on the contemporary high-level evidence. Although different clinical practices can be supported, such approaches should be part of an institutional strategy to reduce the burden of venous thromboembolism (VTE). We recommend against the use of GCS alone without pharmacological thromboprophylaxis for prevention of VTE in patients at intermediate and high risk. For patients

at high risk of VTE with contraindications for pharmacological thromboprophylaxis, we recommend the use of mechanical prophylaxis and suggest the use of IPC over GCS. However, for those patients receiving pharmacological thromboprophylaxis who are without a very high risk of VTE prophylaxis, we recommend against the routine use of mechanical thromboprophylaxis either with GCS or IPC. We suggest combined mechanical and pharmacological prophylaxis in selected patients at very high risk of VTE prophylaxis and suggest IPC rather than GCS in these selected patients.

Published online 6 November 2017

This article is part of the European guidelines on perioperative venous thromboembolism prophylaxis. For details concerning background, methods, and members of the ESA VTE Guidelines Task Force, please, refer to:

Samama CM, Afshari A, for the ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis. *Eur J Anaesthesiol* 2018; 35:73–76.

A synopsis of all recommendations can be found in the following accompanying article:

Afshari A, Ageno W, Ahmed A, *et al.*, for the ESA VTE Guidelines Task Force. European Guidelines on perioperative venous thromboembolism prophylaxis. Executive summary. *Eur J Anaesthesiol* 2018; 35:77–83.

Introduction

Since Virchow, the pathophysiology of venous thrombosis has consisted of hypercoagulability, stasis and vascular injury. Hence, to prevent venous thromboembolism (VTE), early ambulation, pharmacological thromboprophylaxis using anticoagulants and mechanical thromboprophylaxis by means of graduated compression stockings (GCS) and intermittent pneumatic compression (IPC) have been advocated.

In comparison with the numerous high-quality studies of anticoagulants, fewer studies have addressed the effect of mechanical thromboprophylaxis with GCS and IPC, and these studies were not powered to evaluate an impact on pulmonary embolism (PE). Furthermore, considerable ongoing debate and uncertainty remain on any potential benefit and improvement of clinically meaningful outcomes if pharmacological thromboprophylaxis is combined with GCS or IPC.

From the Department of Anesthesia, Juliane Marie Centre, University of Copenhagen, Rigshospitalet, Blegdamsvej (AA), Department of Anaesthesiology, Aarhus University Hospital, Aarhus, Denmark (CFE), Internal Medicine Department, Hospital Universitari Germans Trias i Pujol, Badalona, Spain (MM) and Vascular Medicine and Haemostasis, University of Leuven, Leuven, Belgium (PV)

Correspondence to Arash Afshari, MD, PhD, Department of Anesthesia, Juliane Marie Centre, University of Copenhagen, Rigshospitalet, 4013-4014, Blegdamsvej 9, 2100, CPH Ø, Denmark
Tel: +45 35458749; e-mail: arash.afshari@regionh.dk

The use of GCS and IPC varies widely in different institutions and no strong recommendations can be made based on high-level evidence. However, different clinical practices can be supported based on the current evidence and expertise, and there should be an institutional strategy to reduce the burden of VTE. Hence, institutional protocols should not only address pharmacological prophylaxis with anticoagulants but should also encompass the indications for mechanical thromboprophylaxis (GCS, IPC), both in addition to anticoagulation and for patients with contraindications against anticoagulation.^{1–4}

Thromboprophylaxis with graduated compression stockings

Mechanical thromboprophylaxis or compression therapy reduces the risk of deep venous thrombosis (DVT) but its impact on symptomatic VTE and in particular PE remains unclear and varies in different clinical settings. Evidence points to a reduction of DVT by GCS in surgical patients, whereas little evidence supports any indication for GCS in medical patients or patients in ICUs.^{5,6}

The many limitations of these studies have been addressed and discussed in recent systematic reviews. A pooled analysis of nine trials was unable to reach any conclusions on the impact of GCS on PE [relative risk (RR) 0.63, 95% confidence intervals (CI) 0.32 to 1.25] but demonstrated a reduction of DVT (RR 0.51, 95% CI 0.36 to 0.73), including asymptomatic DVT found on venography.⁷

In patients undergoing major orthopaedic surgery, GCS is often used in conjunction with pharmacological prophylaxis, even though the impact of GCS on VTE prevention has not been properly studied in contemporary trials.⁸

In immobilised stroke patients, thigh-length GCS did not reduce the risk of DVT.⁹ Another trial in immobilised stroke patients observed a reduced incidence of DVT (symptomatic and asymptomatic) when comparing thigh-length stockings with knee-length stockings (6.3 vs. 8.3%, RR 0.71, 95% CI 0.56 to 0.92) without observing differences in the risk of PE.¹⁰ However, stockings seemed to increase the risk of skin complications.

In patients at high risk of VTE, there is insufficient evidence to recommend GCS as a stand-alone measure to prevent VTE or as an alternative for pharmacological prophylaxis. Consequently, we do not recommend the routine use of GCS to prevent VTE without pharmacological thromboprophylaxis. In patients at low risk of VTE, no prophylaxis is preferred over GCS.

Thromboprophylaxis with intermittent pneumatic compression

Two previously published reviews with meta-analyses have highlighted that IPC appears to reduce the risk of DVT by approximately 50% but considerable

heterogeneity exists in the choice of device, with most of the included studies combining IPC with GCS. Thus, there is currently no conclusive evidence on the impact of IPC for prevention of PE.^{11,12}

The majority of studies in surgical patients indicate that IPC reduces the risk of postoperative DVT.^{13,14} IPC also seems to reduce the risk of DVT in immobile stroke patients,¹⁵ with IPC being more effective than GCS in critically ill patients.¹⁶ Consequently, particularly in the surgical setting, IPC is to be considered as an alternative to pharmacological thromboprophylaxis.^{3,4} When compared with anticoagulants, IPC may not increase the risk of bleeding. Therefore, IPC remains an attractive method to prevent VTE in patients with active bleeding or those at high risk of bleeding, both in surgical and nonsurgical settings. The Compression pneumatique Intermittente en REAnimation (CIREA1) trial compared IPC with GCS versus GCS alone in patients at high risk of bleeding in ICUs. There was a nonsignificant reduction of VTE from 9.2% (17 of 184 patients) in the GCS group to 5.6% (10 of 179) in the IPC + GCS group.¹⁷ Among patients with intracranial bleeding, and thus at a high risk of re-bleeding, asymptomatic deep vein thrombosis (DVT) was present in 15.9% with a significant reduction to 4.7% when IPC was added.¹⁸

Combining pharmacological prophylaxis with mechanical prophylaxis

For prevention of postoperative DVT, a combination of compression and pharmacological prophylaxis is more effective than either modality alone. In a systematic review of 19 randomised clinical trials involving GCS alone or GCS used on a background of any other prophylactic method, 126 patients (9%) with GCS vs. 282 (21%) without GCS developed DVT [Peto odds ratio 0.33 (95% CI 0.26 to 0.41)]. The incidence of PE was 2% in the GCS group and 5% in the non-GCS group [Peto odds ratio 0.38 (95% CI 0.15 to 0.96)].⁵ However, for prevention of VTE in critically ill medical–surgical patients of whom 80% also received pharmacological prophylaxis, the use of IPC but not compression stockings was associated with a significantly lower risk of VTE.¹⁶

Among 11 studies with 7431 high-risk patients, combined therapy compared with intermittent compression significantly reduced the incidence of both PE [3 to 1%; odds ratio (OR) 0.39] and DVT (4 to 1%; OR 0.43). Additionally, combined therapy compared with pharmacological prophylaxis alone significantly reduced the incidence of DVT (4.2 to 0.65%; OR 0.16) but the included studies were underpowered with regard to PE.¹⁹ A recent systematic review compared a strategy of combined therapy with compression alone and found a reduced risk of DVT by 44% when applying combined prophylaxis (RR 0.56; OR 0.45 to 0.69) while the risk of PE was not significantly affected; the risk of any bleeding was increased by 74% (RR 1.74; OR 1.29 to 2.34) when anticoagulant therapy

was added to mechanical compression.¹³ The quality of evidence of adding compression to anticoagulation for further reduction of VTE risk was judged to be low.

Following joint replacement surgery, combined therapy also significantly reduced the rate of DVT (from 18.7 to 3.7% after elective knee arthroplasty and from 9.7% with anticoagulation alone to 0.9% with additional mechanical compression after hip replacement surgery). Adding pharmacological prophylaxis to intermittent mechanical compression caused a nonsignificant reduction in DVT from 8.7 to 7.2% after hip replacement. Once again, the included trials were not powered to conclude on a reduction of PE, and bleeding events were not adequately or consistently reported.²⁰ When fondaparinux in addition to IPC was compared with IPC alone in surgical patients, fondaparinux appeared to reduce the risk of VTE (including asymptomatic VTE) while increasing the risk of bleeding.²¹

Thus, there is insufficient evidence that the routine use of compression stockings in patients who receive pharmacological prophylaxis reduces clinically relevant outcomes and the routine use of combining GCS with anticoagulation is not recommended. In patients at very high-risk of VTE, a combination of mechanical and pharmacological prophylaxis further reduces DVT and IPC appears to be more effective than GCS. However, the patient population that benefit from combining different modalities is not well defined. Consequently, there is insufficient evidence that clinically meaningful outcomes are significantly reduced to recommend the routine use of combined pharmacological and mechanical prophylaxis²² and its use should be restricted to selected high-risk patients.

Recommendations

- We recommend an institution-wide protocol for the prevention of VTE that integrates early ambulation, pharmacological thromboprophylaxis with anticoagulants and mechanical thromboprophylaxis (Grade IB).
- We recommend against the routine use of GCS without pharmacological thromboprophylaxis to prevent VTE in patients at intermediate and high risk (Grade IB).
- In patients with contraindications to pharmacological thromboprophylaxis, we recommend the use of mechanical prophylaxis with IPC or GCS (Grade IB) and suggest the use of IPC over GCS (Grade 2B).
- In patients with contraindications to pharmacological thromboprophylaxis who are not at high-risk for VTE, we suggest no prophylaxis over GCS alone (Grade 2C).
- In patients receiving pharmacological thromboprophylaxis who are not at very high risk for VTE we recommend against the routine use of mechanical thromboprophylaxis with GCS or IPC (Grade IB).
- We suggest combined mechanical and pharmacological prophylaxis in selected patients at very high-risk for

VTE (grade 2B). We suggest the use of IPC rather than GCS in selected high-risk patients in addition to pharmacological thromboprophylaxis (Grade 2B).

Acknowledgements relating to this article

Assistance with the guideline chapter: none.

Financial support and sponsorship: expenses of two meetings of the VTE Task Force (Brussels and Berlin) were covered by the ESA for the ESA members.

Conflicts of interest: CFE has received honoraria, consulting fee or unrestricted grants for academic research from CSL Behring, TEM International, LEO Pharma, LFB and Novo Nordisk. PV has received honoraria for lectures and advisory boards from Bayer-Healthcare, Boehringer-Ingelheim, Pfizer, Daiichi-Sankyo, Medtronic, Portola and Bristol-Myers-Squibb and received research support from Bayer-Healthcare, Boehringer-Ingelheim, Leo-Pharma, Sanofi and Daiichi-Sankyo.

References

- 1 Treasure T, Hill J. NICE guidance on reducing the risk of venous thromboembolism in patients admitted to hospital. *J R Soc Med* 2010; **103**:210–212.
- 2 Kahn SR, Lim W, Dunn AS, et al. Prevention of VTE in nonsurgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th edn: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; **141** (2 Suppl):e195S–e226S.
- 3 Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th edn: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; **141** (2 Suppl):e278S–e325S.
- 4 Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th edn: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; **141** (2 Suppl):e227S–e277S.
- 5 Sachdeva A, Dalton M, Amaragiri SV, Lees T. Graduated compression stockings for prevention of deep vein thrombosis. *Cochrane Database Syst Rev* (12):2014;CD001484.
- 6 Loomba RS, Arora RR, Chandrasekar S, Shah PH. Thigh-length versus knee-length compression stockings for deep vein thrombosis prophylaxis in the inpatient setting. *Blood Coagul Fibrinolysis* 2012; **23**:168–171.
- 7 Hill J, Treasure T, Guideline Development Group. Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital: summary of the NICE guideline. *Heart* 2010; **96**:879–882.
- 8 Hui AC, Heras-Palou C, Dunn I, et al. Graded compression stockings for prevention of deep-vein thrombosis after hip and knee replacement. *J Bone Joint Surg Br* 1996; **78**:550–554.
- 9 CLOTS Trials Collaboration, Dennis M, Sandercock PA, Reid J, et al. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. *Lancet* 2009; **373**:1958–1965.
- 10 CLOTS Trials Collaboration, Dennis M, Cranswick G, Deary A, et al. Thigh-length versus below-knee stockings for deep venous thrombosis prophylaxis after stroke: a randomized trial. *Ann Intern Med* 2010; **153**:553–562.
- 11 Vanek VW. Meta-analysis of effectiveness of intermittent pneumatic compression devices with a comparison of thigh-high to knee-high sleeves. *Am Surg* 1998; **64**:1050–1058.
- 12 Urbankova J, Quiroz R, Kucher N, Goldhaber SZ. Intermittent pneumatic compression and deep vein thrombosis prevention. A meta-analysis in postoperative patients. *Thromb Haemost* 2005; **94**:1181–1185.
- 13 Zareba P, Wu C, Agzarian J, et al. Meta-analysis of randomized trials comparing combined compression and anticoagulation with either modality alone for prevention of venous thromboembolism after surgery. *Br J Surg* 2014; **101**:1053–1062.
- 14 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**:393–396.

- 15 CLOTS Trials Collaboration, Dennis M, Sandercock P, Reid J, *et al*. Effectiveness of intermittent pneumatic compression in reduction of risk of deep vein thrombosis in patients who have had a stroke (CLOTS 3): a multicentre randomised controlled trial. *Lancet* 2013; **382**:516–524.
- 16 Arabi YM, Khedr M, Dara SI, *et al*. Use of intermittent pneumatic compression and not graduated compression stockings is associated with lower incident VTE in critically ill patients: a multiple propensity scores adjusted analysis. *Chest* 2013; **144**:152–159.
- 17 Vignon P, Dequin PF, Renault A, *et al*. Intermittent pneumatic compression to prevent venous thromboembolism in patients with high risk of bleeding hospitalized in intensive care units: the CIREA1 randomized trial. *Intensive Care Med* 2013; **39**:872–880.
- 18 Lacut K, Bressollette L, Le Gal G, *et al*. Prevention of venous thrombosis in patients with acute intracerebral hemorrhage. *Neurology* 2005; **65**: 865–869.
- 19 Kakkos SK, Caprini JA, Geroulakos G, *et al*. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients. *Cochrane Database Syst Rev* (4):2008;CD005258.
- 20 Kakkos SK, Warwick D, Nicolaides AN, *et al*. Combined (mechanical and pharmacological) modalities for the prevention of venous thromboembolism in joint replacement surgery. *J Bone Joint Surg Br* 2012; **94**:729–734.
- 21 Turpie AG, Bauer KA, Caprini JA, *et al*. Fondaparinux combined with intermittent pneumatic compression vs. intermittent pneumatic compression alone for prevention of venous thromboembolism after abdominal surgery: a randomized, double-blind comparison. *J Thromb Haemost* 2007; **5**:1854–1861.
- 22 Kakkos SK, Caprini JA, Geroulakos G, *et al*. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism. *Cochrane Database Syst Rev* (9):2016;CD005258.