Mechanical prophylaxis for prevention of venous thromboembolism

Arash Afshari¹, Christian Fenger-Eriksen², Manuel Monreal³, Peter Verhamme⁴

Corresponding author: Arash Afshari, MD, PhD.
Address: Rigshospitalet, University of Copenhagen, Department of anesthesia, mother and children’s centre, 4013-4014. Blegdamsvej 9, 2100, CPH Ø. Denmark
Phone: +45 51948186 (private)
Phone: +45 35458749 (work)
Fax number: +45 35454525
E-mail: arash.afshari@regionh.dk

2: Christian Fenger-Eriksen, MD, PhD.
Department of Anaesthesiology, Aarhus University Hospital. Aarhus, Denmark

3: Manuel Monreal, MD, PhD.
Internal Medicine Department. Hospital Universitari Germans Trias i Pujol. 08916 Badalona. Spain.

4: Peter Verhamme, MD, PhD.
Vascular Medicine and Haemostasis, University of Leuven, Leuven, Belgium
Abstract

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.

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 contra-indications 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 that are without a very high risk of VTE, 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 and suggest IPC rather than GCS in these selected patients.

Key words: Thromboembolism, venous, mechanical prophylaxis, graduated compression stockings, intermittent pneumatic compression.
**Introduction**

Since Virchow, the pathophysiology of venous thrombosis consisted of hypercoagulability, stasis and vascular injury. Hence, to prevent venous thrombosis early ambulation, pharmacological thromboprophylaxis using anticoagulants and mechanical thromboprophylaxis by means of graduated compression stockings (GCS) and intermittent pneumatic compression (IPC) have been advocated. As compared to the numerous high-quality studies with 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. Furthermore, considerable ongoing debate and uncertainty remains on any potential benefit and improvement of clinically meaningful outcomes if pharmacological thromboprophylaxis is combined with GCS or IPC. The use of GCS and IPC strongly differs between many 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 but this should be part of an institutional strategy to reduce the burden of venous thromboembolism. 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 GCS**

Mechanical thromboprophylaxis or compression therapy reduces the risk of DVT but it’s impact on symptomatic VTE and in particular pulmonary embolism (PE) remains unclear and varies between different clinical settings. Evidence points to the reduction of deep venous thrombosis (DVT) in surgical patients with GCS, whereas little evidence supports any indication for GCS in medical patients or patients in the intensive care units (5, 6).

The many limitations of these studies have been addressed and discussed in recent systematic reviews. A pooled analysis of 9 trials was unable to conclude on the impact of GCS on PE (RR 0.63; 95% CI 0.32 – 1.25) but demonstrated a reduction of DVT (RR 0.51; 95% CI 0.36-0.73), including asymptomatic venographically documented DVT (7).
In patients undergoing major orthopedic 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 immobilized stroke patients, thigh-length GCS did not reduce the risk of DVT in hospitalized patients with stroke (9). Another trial comparing knee-length to thigh-length GCS in immobilized stroke patients observed reduced incidence of DVT (symptomatic and asymptomatic) when comparing thigh-length stockings to knee-length stockings (6.3% vs. 8.3%, RR 0.71, 95% CI 0.56-0.92) without observing differences in the risk of skin complications. However, stockings seemed to increase the risk of skin complications.

In patients at high risk for VTE, there is insufficient evidence to recommend GCS as a standalone measure to prevent VTE or as an alternative for pharmacological prophylaxis. Hence, 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 IPC**

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 post-operative DVT (13, 14). IPC equally seems to reduce the risk of DVT in immobile stroke patients (15) with IPC being more effective than GCS in critically ill patients (16).

Hence, particularly in the surgical setting, IPC is to be considered an alternative to pharmacological thromboprophylaxis (3, 4). When compared to 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 the surgical and non-surgical setting. The CIREA1 trial compared IPC with GCS versus GCS alone in patients at high risk of bleeding in intensive care units. There was a non-significant 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 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 randomized 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: 0.15-0.96) (5). However, for prevention of VTE in critically ill medical-surgical patients of whom 80% also received pharmacologic 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) while 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, 0·45 to 0·69) while risk of PE was not significantly affected; the risk of any bleeding was increased by 74 % (RR 1·74, 1·29 to 2·34) when anticoagulant therapy was added to mechanical compression (13). The quality evidence of adding compression to anticoagulation for further reduction of VTE risk was judged to be of low quality.
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 non-significant 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 pulmonary embolism, and bleeding events were not adequately or consistently reported (20). When fondaparinux plus IPC was compared to IPC alone in surgical patients, fondaparinux appeared to reduce the risk of VTE (including asymptomatic VTE) while increasing the risk of bleeding. (21)

Hence, 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, combination of mechanical and pharmacological prophylaxis further reduces DVT and IPC appears to be more effective than GCS also when added to pharmacological thromboprophylaxis. However, the patient population that benefit from combining different modalities is not well defined. Hence, there is insufficient evidence that clinically meaningful outcomes are significantly reduced to recommend the routine use of combined pharmacological and mechanical prophylaxis and its use should be restricted to selected high-risk patients.
Summary of 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 graduated compression stockings without pharmacological thromboprophylaxis to prevent VTE in patients at intermediate and high risk.
Grade IB

In patients with contra-indications for 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 contra-indications for 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).
Reference List