

Graduated compression stockings to prevent venous thromboembolism in hospital

Evidence from patients with acute stroke

Clive Kearon¹, Martin O'Donnell²

¹ Department of Medicine, McMaster University, Ontario, Canada

² Department of Medicine, Galway University, Galway, Ireland

KEY WORDS

compression stockings, deep vein thrombosis, prevention, stroke, venous thromboembolism

ABSTRACT

Pulmonary embolism is the most common preventable cause of death in hospital patients and prevention of venous thromboembolism (VTE) is cost-saving in high-risk patients. Low-dose anticoagulation is very effective at preventing VTE but increases bleeding. Graduated compression stockings and intermittent pneumatic compression devices are also used to prevent VTE and do not increase bleeding, which makes their use appealing in patients who cannot tolerate bleeding, such as patients with acute stroke. Studies that evaluated mechanical methods of preventing VTE were small and mainly used asymptomatic deep vein thrombosis (DVT), detected using screening tests, as the study outcome. The recently published CLOTS Trial 1 (Clots in Legs Or sTockings after Stroke) compared thigh-level compression stockings with no stockings in about 2500 patients with stroke and immobility, and found that thigh-level stockings were not effective. Indirectly, the findings of this study question the ability of stockings to prevent VTE in other patient groups, including those after surgery. CLOTS 1 compared thigh-level and below-knee stockings in about 3000 patients with acute stroke. Given that thigh-level stockings were ineffective in CLOTS 1, it is surprising that they were more effective than below-knee stockings in CLOTS Trial 2. A possible explanation is that below-knee stockings increase DVT, although this seems unlikely. CLOTS 1 and CLOTS 2 question whether graduated compression stockings prevent VTE and suggest the need for further trials evaluating their efficacy in medical and surgical patients.

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a major cause of morbidity and mortality. After recurrent stroke and myocardial infarction, PE is the most common cause of vascular death, and PE is the most common cause of preventable death in hospitalized patients.¹ In addition, about one-third of patients with symptomatic DVT develop the post-thrombotic syndrome, which is often disabling and is associated with substantial costs to patients and to society. About half of all episodes of VTE are associated with hospitalization, with a similar number of patients having been admitted to surgical and medical wards.² Of these episodes of VTE, about half occur while patients are in hospital and half occur after discharge. Because most fatal PE are

either not associated with preceding symptoms, or such symptoms are not recognized, active prevention of VTE rather than clinical screening is the most effective way to prevent fatal PE. Prevention of VTE in hospitalized patients is therefore a high priority, because it has the potential to reduce the burden of VTE, including fatal episodes, by about one-third.

Virchow identified hypercoagulability, stasis, and vessel wall injury as the most important pathogenic mechanisms of thrombosis, and 2 components of this triad are targeted by methods to prevent VTE. Anticoagulant medications induce hypocoagulability, and mechanical methods of prophylaxis reduce venous stasis. Anticoagulants are the most widely used and effective way to prevent VTE; however, they have

Correspondence to:

Clive Kearon, MB MRCP(I) FRCP(C)
PhD, Hamilton Health Sciences,
Juravinski Hospital, 711 Concession
Street, Hamilton, Ontario, L8V 1C3,
Canada, phone: +1-905-383-2252,
fax: +1-905-574-7625,

e-mail: kearonc@mcmaster.ca

Received: December 14, 2010.

Accepted: December 14, 2010.

Conflict of interest: Dr. Kearon is
an advisor to Boehringer Ingelheim.
Pol Arch Med Wewn. 2011;

121 (1-2): 40-43

Copyright by Medycyna Praktyczna,
Kraków 2011

the disadvantage of increasing bleeding.^{1,3} Mechanical methods include graduated compression stockings, which reduce pooling of blood in the deep veins by applying greater pressure at the ankle than higher up the leg, and intermittent pneumatic compression devices, which actively promote venous return by cyclical inflation and deflation. The great advantage of graduated compression stockings and intermittent pneumatic compression devices is that they do not increase bleeding, which makes their use particularly appealing in patients who have a high risk of bleeding, or if any bleeding is poorly tolerated. Patients with acute disabling stroke fall into this category, especially those with intracerebral hemorrhage. While these patients have a high risk of developing VTE, there is a competing concern that anticoagulant therapies are associated with an increase in intracerebral hemorrhage in patients with ischemic stroke, and anticoagulants are contraindicated in patients with primary acute intracerebral hemorrhage (about 20% of stroke).⁴ Based on the evidence of their efficacy in surgical patients³ and on a single small study suggesting that they are effective in patients with stroke,⁵ graduated compression stockings are often used to prevent VTE in patients with stroke.^{6,7} However, the results of 2 large randomized trials,^{8,9} including CLOTS Trial 2 (Clots in Legs Or sTockings after Stroke),⁹ prompt a re-evaluation of the role of graduated compression stockings for the prevention of VTE in patients with acute stroke and, by implication, in other patient populations.

The CLOTS Trials are a series of 3 trials evaluating mechanical interventions to prevent VTE in patients with acute stroke. CLOTS Trial 1, which compared thigh-level compression stockings to control in about 2500 patients, found that thigh-level stockings did not appear to prevent the combined outcome of asymptomatic proximal DVT (detected by routine ultrasound examinations) and symptomatic VTE (odds ratio 0.98, 95% confidence interval [CI] 0.76 to 1.27).⁸ CLOTS Trial 2, which compared thigh-length stockings to below-knee stockings in about 3000 patients with acute stroke, found less VTE (same composite outcome as in CLOTS 1) with thigh-level than with below-knee stockings (odds ratio 0.69, 95% CI 0.53 to 0.91).⁹ CLOTS Trial 3, which is ongoing, is comparing intermittent pneumatic compression with control.

While interpretation of the findings of CLOTS 1 and, separately, of CLOTS 2 appears straightforward, the combined interpretation of the 2 studies is more difficult. If thigh-level stockings are ineffective (CLOTS 1), why are thigh-level stockings more effective than below-knee stockings (CLOTS 2)? One possibility considered by the CLOTS investigators is that below-knee stockings increase the risk of VTE. However, in the few studies that assessed below-knee stockings in surgical patients, and in long-distance air travellers, below-knee stockings appeared to be effective.^{3,10}

Another possible explanation for the findings of CLOTS 1 and 2 is that thigh-level stockings reduce VTE by about 20%. This modest reduction could have been missed in CLOTS 1 and would be consistent with the findings of CLOTS 2, if below-knee stockings neither increased nor decreased the risk of VTE.

It does not appear that differences in study design are likely to reconcile the findings of CLOTS 1 and 2. Although there were differences in the clinical centers that enrolled patients into CLOTS Trials 1 and 2, the patient populations in the 2 studies, the type of thigh-level stockings used, follow-up after enrollment, the primary outcome to assess efficacy, and how this was ascertained, were similar in the 2 studies. Also, it seems unlikely that, independently of a truly higher prevalence of thrombosis, a shorter stocking would result in more leg symptoms or signs that would prompt a search for DVT, or would result in more frequent diagnosis of DVT when ultrasound examination was performed (i.e., lead to an increase in ascertainment of DVT).

Given the findings of CLOTS 1 and 2, how should VTE be prevented in patients with acute stroke? CLOTS 1 and 2 suggest that graduated compression stockings are, at best, modestly effective at preventing venous thromboembolism in patients with stroke and immobility, and their use is associated with skin break down in about 5% of patients.^{8,9} Intermittent pneumatic compression may be an effective alternative that is also not associated with bleeding; however, this will not be known until completion of CLOTS Trial 3. Despite some concerns that low-dose unfractionated heparin and low-molecular-weight heparin increase intracerebral bleeding, as these agents reduce VTE by about 75%, guidelines from a number of organizations recommend their use in patients with acute ischemic stroke and immobility who do not have additional contraindications to anticoagulants.^{11,12} Lack of a clearly effective alternative to unfractionated heparin and low-molecular-weight heparin, in the form of graduated compression stockings or other mechanical methods, lends support to the use of these agents in patients with acute ischemic stroke. In patients with ischemic stroke who are considered unsuitable for anticoagulants (e.g., hemorrhagic transformation) and in those with acute intracerebral hemorrhage, it is reasonable to use thigh-level stockings or intermittent pneumatic compression, provided care is taken to avoid associated skin breakdown.

The unexpected finding from CLOTS 1 and 2 was that thigh-level stockings are not very effective at preventing VTE and that below-knee stockings might even increase thrombosis. It suggests that the efficacy of graduated compression stockings for the prevention of VTE in general (i.e., surgical and medical patients) needs to be re-evaluated. Most of the evidence supporting the efficacy of graduated compression stockings in high-risk situations was obtained in studies

of surgical patients.^{1,3} These studies usually assessed if stockings reduced the frequency of asymptomatic DVT detected by screening of post-operative patients with fibrinogen leg scanning. This outcome has a number of important limitations. First, fibrinogen leg scanning has limited accuracy for the diagnosis of postoperative DVT (i.e., associated with random error).¹³ Second, graduated compression stockings, by reducing venous stasis, may reduce the frequency of abnormal fibrinogen leg scans more than it reduces the presence of DVT (i.e., associated with systematic error or bias). Third, many of the DVT that were detected by fibrinogen leg scanning were confined to the distal veins. Fourth, asymptomatic DVT, unless it progresses to acute symptomatic DVT or PE, or causes the post thrombotic syndrome, is not of importance to patients. In order to overcome the limitations of previous studies, future studies evaluating graduated compression stockings should be large enough to assess the frequency of symptomatic VTE, an outcome that is clearly of importance to patients. Based on current evidence, anticoagulant therapies are preferred over mechanical methods for the prevention of VTE in most high-risk hospitalized patients.¹ If anticoagulants are contraindicated, or if graduated compression stockings are used in conjunction with an anticoagulant agent, CLOTS 2 suggests that thigh-level stockings are preferable to below-knee stockings.

Support Dr. Kearon is supported by the Heart and Stroke Foundation of Canada and a Canadian Institutes of Health Research Team Grant in Venous Thromboembolism (FRN 79 846).

REFERENCES

- 1 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 (6 Suppl): 381S-453S.
- 2 Naess IA, Christiansen SC, Romundstad P, et al. Incidence and mortality of venous thrombosis: a population-based study. *J Thromb Haemost*. 2007; 5: 692-699.
- 3 National Institute for Health and Clinical Excellence. Venous thromboembolism: reducing the risk. Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital. NICE clinical guideline 92. 2010. <http://guidance.nice.org.uk/CG92/Guidance/pdf/English>. Accessed February 1, 2011.
- 4 André C, de Freitas GR, Fukujima MM. Prevention of deep venous thrombosis and pulmonary embolism following stroke: a systematic review of published articles. *Eur J Neurol*. 2007; 14: 21-32.
- 5 Muir KW, Watt A, Baxter G, et al. Randomized trial of graded compression stockings for prevention of deep-vein thrombosis after acute stroke. *QJM*. 2000; 93: 359-364.
- 6 Naccarato M, Chiodo Grandi F, Dennis M, Sandercock PA. Physical methods for preventing deep vein thrombosis in stroke. *Cochrane Database Syst Rev*. 2010; 8: CD001922.
- 7 Bergmann JF, Cohen AT, Tapson VF, et al. Venous thromboembolism risk and prophylaxis in hospitalised medically ill patients. The ENDORSE Global Survey. *Thromb Haemost*. 2010; 103: 736-748.
- 8 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.
- 9 CLOTS (Clots in Legs Or sTockings after Stroke) Trial Collaboration. Thigh-length versus below-knee stockings for deep venous thrombosis prophylaxis after stroke: a randomized trial. *Ann Intern Med*. 2010; 153: 553-562.

- 10 Sajid MS, Tai NR, Goli G, et al. Knee versus thigh length graduated compression stockings for prevention of deep venous thrombosis: a systematic review. *Eur J Vasc Endovasc Surg*. 2006; 32: 730-736.
- 11 Albers GW, Amarenco P, Easton JD, et al. Antithrombotic and thrombolytic therapy for ischemic stroke: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest*. 2008; 133: 630S-669S.
- 12 Adams HP Jr, del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Stroke*. 2007; 38: 1655-1711.
- 13 Lensing AW, Hirsh J. 125I-fibrinogen leg scanning: reassessment of its role for the diagnosis of venous thrombosis in post-operative patients. *Thromb Haemost*. 1993; 69: 2-7.

Pończochy o stopniowanym ucisku w zapobieganiu żylnej chorobie zakrzepowo-zatorowej w szpitalu

Dane pochodzące z obserwacji pacjentów ze świeżym udarem mózgu

Clive Kearon¹, Martin O'Donnell²

¹ Department of Medicine, McMaster University, Ontario, Kanada

² Department of Medicine, Galway University, Galway, Irlandia

SŁOWA KLUCZOWE

pończochy uciskowe,
udar mózgu,
zakrzepica żył
głębokich,
zapobieganie, żylna
choroba
zakrzepowo-zatorowa

STRESZCZENIE

Zatorowość płucna jest najczęstszą przyczyną zgonów szpitalnych, której można zapobiegać, a prewencja żylnej choroby zakrzepowo-zatorowej (ŻChZZ) ogranicza koszty leczenia u pacjentów wysokiego ryzyka. Leki przeciwzakrzepowe stosowane w małej dawce są bardzo skuteczne w zapobieganiu ŻChZZ, zwiększają jednak ryzyko krwawienia. W zapobieganiu ŻChZZ stosowane są także pończochy o stopniowanym ucisku i urządzenia generujące przerywany ucisk, które nie zwiększają ryzyka krwawienia. Ich użycie jest korzystne w grupie pacjentów, u których krwawienie wiąże się z dużym ryzykiem zgonu, np.: u chorych ze świeżym udarem mózgu. Badania oceniające mechaniczne metody zapobiegania ŻChZZ są nieliczne, a ich punkt końcowy stanowi głównie bezobjawowa zakrzepica żył głębokich, potwierdzana za pomocą testów przesiewowych. Niedawno opublikowane badanie CLOTS 1 (Clots in Legs Or sTockings after Stroke), w którym wśród ok. 2500 unieruchomionych pacjentów z udarem mózgu porównano grupę stosującą udowe pończochy o stopniowanym ucisku z grupą niestosującą pończoch, nie wykazało ich skuteczności. Pośrednio wyniki tego badania budzą wątpliwość co do skuteczności pończoch uciskowych w zapobieganiu ŻChZZ u innych grup pacjentów, w tym u pacjentów po przebytych operacjach chirurgicznych. W badaniu CLOTS 2 oceniano zastosowanie pończoch uciskowych zakładanych na całą kończynę dolną i podkolanowych u ok. 3000 pacjentów ze świeżym udarem mózgu. Wobec wyników badania CLOTS 1 wskazujących, że pończochy uciskowe zakładane na całą kończynę dolną są nieskuteczne, wyniki badania CLOTS 2 dowodzące większej skuteczności pończoch zakładanych na całą kończynę dolną w porównaniu z podkolanowymi są zaskakujące. Chociaż wydaje się to mało prawdopodobne, możliwym wytłumaczeniem jest fakt, że pończochy podkolanowe zwiększają ryzyko ŻChZZ. Badania CLOTS 1 i CLOTS 2 podają w wątpliwość, czy pończochy o stopniowanym ucisku zapobiegają występowaniu ŻChZZ i wskazują na potrzebę prowadzenia kolejnych badań oceniających ich skuteczność u pacjentów internistycznych i chirurgicznych.

Adres do korespondencji:
Clive Kearon, MB MRCP(I) FRCP(C)
PhD, Hamilton Health Sciences,
Juravinski Hospital, 711 Concession
Street, Hamilton, Ontario, L8V 1C3,
Kanada, tel.: +1-905-383-2252,
fax: +1-905-574-7625,
e-mail: kearonc@mcmaster.ca
Praca wpłynęła: 14.12.2010.
Przyjęta do druku: 14.12.2010.
Zgłoszono sprzeczność interesów:
Dr Kearon jest doradcą w firmie
Boehringer Ingelheim.
Pol Arch Med Wewn. 2011;
121 (1-2): 40-43
Tłumaczył lek. Michał Terlecki
Copyright by Medycyna Praktyczna,
Kraków 2011