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**Rapid Review 2015**

# Intermittent Pneumatic Compression and Graded Compression Stockings in Preventing Venous Thromboembolism with comment on pharmacological prophylaxis

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## Introduction

The Centre for Clinical Effectiveness received a request to review the evidence around Intermittent Pneumatic Compression and Graded Compression Stockings in preventing venous thromboembolism. The review was conducted with the aim of ascertaining whether disinvesting in the use of Intermittent Pneumatic Compression (IPC) at Monash Health is appropriate.

As a rapid review this report is not intended to be an exhaustive search of the evidence. With this in mind, reasonable effort has been made to search for and retrieve most recent evidence (since 2010) related to this topic.

## Objective

The purpose of this rapid review was to explore the evidence around the use of intermittent pneumatic compression (IPC) in addition to, or in place of, graduated compression stockings (GCS) in preventing venous thromboembolism. Evidence was also requested on the effectiveness of mechanical prophylaxis (i.e. IPC, GCS) with or without pharmacological prophylaxis in preventing venous thromboembolism.

## Methods

Google Scholar, Cochrane, Pubmed Clinical Queries, and the TRIP database were searched. Searches of the National Institute of Clinical Excellence (NICE) and the National Health and Medical Research Council (NHMRC) were also conducted to identify recent guidelines. Further details can be found in Appendix Table 3.

## Findings

Our database searches identified 891 publications (Appendix Table 4).

There was a paucity of recent systematic reviews (since 2010) investigating the use of IPCs in combination with, or as an adjunct to GCS.

We identified:

- One review that directly compares both treatments head-to-head [1],
- One meta-analysis comparing the risk of deep vein thrombosis between the two treatment modalities [2].
- A small number of recent guidelines relating to the use of mechanical prophylaxis (collective term for IPCs and GCS) in preventing thromboembolism [3, 4].

It may be worthwhile noting that the mechanism behind IPC is not clearly understood [5].

A summary of the findings is presented in Table 1 below.

**Table 1.** Summary of findings of IPCs and GCS

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| **Direct comparison of IPC and GCS**<br>(3 reviews) | • Recent research reviewed the evidence around IPC and GCS for deep vein thrombosis prophylaxis [1].<br>• It was shown that IPC produces significant lower deep vein thrombosis rates compared to GCS. Rates were reported as 2.5% for IPC and 5.9% for CGS.<br>• Included in this review were seven studies examining ICP and the prevention of deep vein thrombosis compared to 3 studies examining GCS suggesting limited evidence exists for both modes, but more evidence is available for ICP.<br>• Additionally, this review concluded that studies were too heterogeneous in their |

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| | methods and questionable study quality.<br>• Patient cohorts included in this review were, total hip and knee arthroplasty, craniotomy, prostatectomy, abdominal or urological surgical procedures, myocardial infarction and unstable angina.<br>• The evidence around the direct comparison of IPC to GCS is concluded to be weak. [1] |
| | • A systematic review with meta-analysis revealed that lower limb IPC is effective in reducing venous thromboembolism in combination with pharmacologic thromboprophylaxis when compared to IPC alone [2].<br>• Comparisons were made between IPC: (a) no IPC prophylaxis; (b) TEDS; (c) pharmacologic thromboprophylaxis; and (d) a combination of IPC and pharmacologic thromboprophylaxis.<br>• Comparisons of IPC and thromboembolic deterrent stockings (i.e. GCS) indicated that IPCs were associated with a greater reduced risk of DVT when compared to stockings (Appendix Figure 1).<br>• Patient cohorts included, total hip and knee arthroplasty, craniotomy, prostatectomy, abdominal or urological surgical procedures, myocardial infarction or unstable angina, all types of surgical and orthopaedic or vascular. [2]<br>• The protective effect of IPC appeared to be comparable to pharmacologic thromboprophylaxis.<br>• A further protective effect on venous thromboembolism could be enhanced by combining IPC with a pharmacologic thromboprophylaxis.<br>• In this review the authors also state that "Given the cost of the disposable component of IPC is relatively low ($180), the estimated cost to reduce one symptomatic PE is estimated to be $10,600 and this is cost-effective compared to the total costs associated with the treatment of PE and its complications ($20,000).<br>• As such, this data strongly supports the American College of Chest Physicians latest clinical practice guidelines on prevention of thrombosis that "IPC should be used as early as possible for hospitalised patients who have contraindications to pharmacologic thromboprophylaxis, and pharmacologic thromboprophylaxis should be added to the IPC instead of replacing it when the risk of bleeding subsides for patients who are at high-risk of venous thromboembolism." [2]<br>• It must be noted that that the authors state that given the data is limited on IPC and GCS and pulmonary embolism, findings that IPC is superior to GCS in reducing pulmonary embolism remains largely unproven. |
| **Cochrane Collaboration Evidence**<br>(2 reviews) | • There is evidence from Cochrane reviews that evaluate the use of mechanical prophylaxis in thromboembolism. For example, when compared with mechanical prophylaxis alone, the use of combined modalities, such as pharmacological prophylaxis and mechanical prophylaxis, reduced the incidence of both symptomatic pulmonary embolism and deep vein thrombosis in high risk patients [9].<br>• Compared with pharmacological prophylaxis alone, the use of combined modalities significantly reduced the incidence of deep vein thrombosis. However, again, no direct comparisons of IPC and GCS are made. [9] |
| | In stroke patients, the evidence does not support the use of GCS to reduce the risk of deep vein thrombosis after an acute stroke, and there is insufficient evidence to support the routine use of IPC to reduce the risk of deep vein thrombosis in acute stroke patients [10]. |
| **Other Systematic Reviews**<br>(3 reviews) | In patients that are undergoing hip or knee joint replacement mechanical prophylaxis enhances the efficacy of anticoagulation in preventing deep vein thrombosis, however, no effect is seen when anticoagulation is added to mechanical prophylaxis [11]. |
| | • A recent systematic review concluded that IPC devices are appropriate for orthopaedic and non-orthopaedic patients at high risk of bleeding [7].<br>• Additionally, the combination of IPC and anticoagulation may be more effective at |

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| | preventing venous thromboembolism than anticoagulation on its own.<br>• This review only looked at IPC devices and only included studies published in the United States [7]. |
| | • A systematic review explored the combination of compression and anticoagulation in surgical patients [8].<br>• It was concluded that post-surgical patients at high risk of venous thromboembolism there is a benefit of the combination of compression and anticoagulation.<br>• For those post-surgical patients at moderate or high risk of venous thromboembolism and anticoagulation is contraindicated, compression therapy should be employed.<br>• This review concluded that, although there is limited evidence, IPC is more effective than CGS even though deep vein thrombosis risk did not differ between IPC and GSC when comparing combination prophylaxis to anticoagulation alone.<br>• It must also be noted that the compression studies were of low quality. [8] |
| **Recent Experimental Studies**<br>(6 studies) | • Research also suggests that up to 25% of patients are non-adherent to mechanical prophylaxis while hospitalised, and there is no evidence regarding compliance after discharge [6].<br>• Additionally, there is some evidence from systematic reviews on the use of mechanical prophylaxis in various disciplines of medicine such as, orthopaedics [5], high risk surgical patients [7], and surgical patients [8].<br>• There are additional recent studies that have shown that CGS did not reduce the risk of deep vein thrombosis in patients after stroke [12] however, IPC did reduce the risk of proximal deep vein thrombosis [13]. Again, these modalities were not directly compared. |
| **Guidelines**<br>(2 Guidelines) | **Australian Guidelines [4]**<br>• The most recent Australian and New Zealand guideline was in 2007.<br>• The guideline recommends the use of IPC and CGS however, states that IPC is more effective than GCS in reducing the incidence of deep vein thrombosis in high risk patients in combination with anticoagulants or when anticoagulated are contraindicated. |
| | **The National Institute for Heal and Care Excellence (NICE) [3]**<br>• NICE recently updated their 2010 guidelines on reducing the risk of venous thromboembolism in hospitalised patients to include recent information regarding stroke patients.<br>• These guidelines suggest the use of any one of anti-embolism stockings, foot impulse devices or IPCs.<br>• Anti-embolism stockings are not recommended for patients who have suspected or proven peripheral arterial disease, peripheral arterial bypass grafting, peripheral neuropathy or other causes of sensory impairment, any local conditions in which stockings may cause damage, for example fragile 'tissue paper' skin, dermatitis, gangrene or recent skin graft, known allergy to material of manufacture, cardiac failure, severe leg oedema or pulmonary oedema from congestive heart failure unusual leg size or shape major limb deformity preventing correct fit, and to use caution and clinical judgement when applying anti-embolism stockings over venous ulcers or wounds.<br>• Do not offer anti-embolism stockings for venous thromboembolism prophylaxis to patients who are admitted for stroke.<br>• IPC and foot impulse devices are not recommended to patients with a known allergy to the material of manufacture.<br>• IPCs should be consider for venous thromboembolism prophylaxis in immobile patients who are admitted within 3 days of acute stroke and provide it for 30 days or until the patient is mobile or discharged, whichever is sooner.<br>• Do not offer mechanical venous thromboembolism prophylaxis to patients who are taking vitamin K antagonists and who are within their therapeutic range, providing anticoagulant therapy is continued, or patients who are having full anticoagulant therapy. |

## Comparison of Mechanical and Pharmacological Prophylaxis

From this review, a number of meta-analyses compared mechanical prophylaxis (i.e. compression caused by IPCs or GCS) either combined or instead of pharmacological prophylaxis in preventing DVT. The results of these meta-analyses have been extracted and tabulated below (Table 2). For a more detailed summary, see Appendix Table 5.

**Table 2.** Summary of meta-analysis findings comparing compression and pharmacological prophylaxis

| Patient group | (A) No compression | (B) Compression alone | (C) Compression + pharmacological prophylaxis | (D) Pharmacological Prophylaxis alone |
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| **DVT rates** | | | | |
| General high risk | | | Compared to B and D | |
| High risk surgical | | Favors D | Compared to D but favors C | No overall difference when results for B vs D and C vs D pooled. |
| Hospitalised | | Compared to D | | |
| Hospitalised* | | Compared to A / Compared to D | | |
| Joint replacement hip and knee | | | Compared to D | |
| Joint replacement knee | | | Compared to D | |
| Joint replacement hip | | Favors C | | |
| **PE rates** | | | | |
| General high risk | | | Compared to B / Compared to D | |
| Hospitalised | | Compared to D | | |
| Hospitalised* | Compared to B | Compared to D | | |
| Joint replacement knee | | | Compared to D | |
| **Major bleeding** | | | | |
| High risk surgical | | Compared to D but favors B | | |
| **Mortality** | | | | |
| Hospitalised | Compared to B | Compared to D and C | | |

| Legend: | Green = Difference - improved | Red = No difference | Orange = Unclear |
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Abbreviations: DVT = deep vein thrombosis, PE = pulmonary embolism, VTE = venous thromboembolism

Symbols: * Results after biased studies were removed.

## Conclusion – Implications for practice

It is apparent that a larger body of evidence exists supporting the efficacy of IPC than CGS.

The evidence comparing the use of IPC and/or CGS in preventing thromboembolism suggests that IPC is more effective however; caution must be exercised as only a small body of questionable quality evidence exists.

Given this caution, it must be noted that this must not be interpreted as meaning the modalities are equal.

In general high risk patients the use of combined compression and pharmacological prophylaxis reduce DVT and PE. In hospitalised patients, compression alone is better than no compression in reducing DVT. Combined compression and pharmacological prophylaxis does reduce PR compared to compression alone in hospitalised patients. In knee and hip replacement patients, combined compression and pharmacological prophylaxis reduces DVT incidence when compared to pharmacological prophylaxis alone.

It is clear nevertheless, that guidelines suggest that the use of mechanical prophylaxis in the prevention of thromboembolism be used as early as possible for hospitalised patients who have contraindications to pharmacologic prophylaxis, or in combination with pharmacologic prophylaxis.

Furthermore, this review has identified there is a research gap that currently exists around the direct head-to-head comparison of stockings and IPCs in a number of healthcare settings.

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## Appendices

The searches not limited to a specific medical discipline (i.e. Neurosurgery). The search development strategy and search terms are shown in Table 1 in Table 2. Only systematic review or meta-analyses published from 2010 until November 2015 were included. A brief search for the most recent guidelines was also conducted.

**Table 3.** Search development using PICOS

| Item | Description |
|---|---|
| Population/Setting | Undefined |
| Intervention | Mechanical prophylaxis (i.e. Intermittent pneumatic compression (IPC) and Graduated Compression Stockings (GCS) |
| Comparator | Graduated compression stockings (GCS);<br>IPC together with GCS |
| Outcomes | Prevention/risk reduction of DVT (a subset of venous thromboembolism (VTE) |
| Publication details | Systematic reviews and/or meta-analyses |
| Publication date | 2010 – current |
| Databases searched | Google Scholar; Cochrane; Pubmed Clinical Queries; Trip; NICE/NHMRC guidelines |
| Search terms | Graduated compression stockings<br>Intermittent pneumatic compression |

**Table 4.** Search results

| Database | Search terms | Results |
|---|---|---|
| TRIP | intermittent pneumatic compression | 56 |
| Cochrane | intermittent pneumatic compression | 14 |
| Pubmed Clinical Queries | systematic[sb] AND (intermittent pneumatic compression) (filter: 10 years) | 90 |
| Google Scholar | “intermittent pneumatic compression “ OR “”graduated compression stockings” AND "Deep Vein Thrombosis" OR thromboembolism AND review | 731 |
| Total | | 891 |

**Table 5.** Meta-analysis results summary of compression versus pharmacological prophylaxis

| Patient group | Summary |
|---|---|
| General high risk patients [9] | • Compared with compression alone, compression plus pharmacological prophylaxis decreased DVT and PE.<br>• Compared with pharmacological prophylaxis alone, compression plus pharmacological prophylaxis reduced the incidence of DVT, but the effect on PE is unknown. |

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| | • The comparison of compression plus pharmacological prophylaxis versus compression plus aspirin showed a non-significant reduction in PE and DVT in favor of the former group.<br>• High quality systematic review (low risk of bias) included studies with moderate to high risk of bias. |
| High risk surgical patients [7] | • IPCs compared with pharmacological prophylaxis, may decreased risk of major bleeding complications.<br>• No difference found in DVT events when pharmacological prophylaxis was compared with IPCs, or when IPC plus pharmacological prophylaxis was compared to pharmacological prophylaxis alone. However, IPCs alone may increase DVT events, and IPCs plus pharmacological prophylaxis may reduce DVT events.<br>• IPCs plus pharmacological prophylaxis was not different to pharmacological prophylaxis alone at preventing VTE. However, IPCs compared to pharmacological prophylaxis alone favors pharmacological prophylaxis only. Pooled results show no overall difference in IPC, or IPC plus pharmacological prophylaxis compared to pharmacological prophylaxis alone.<br>• Of note, no studies reported major bleeding as an adverse outcome, and all but one did not report mortality outcomes. One death occurred due to myocardial infarction.<br>• This review only included studies in the U.S. and studies that reported VTE outcomes at ≥ 4 weeks. Studies were high or moderate risk of bias and ~40% of studies had a conflict of interest or did not report their conflict. |
| Hospitalised patients [2] | • IPCs are as effective as pharmacological prophylaxis in reducing PE, and DVT.<br>• Of note, when only looking at studies that used blinding, IPC compared to no IPC remained effective in reducing DVT but not PE, ,<br>• and no difference in the risk of DVT and PE existed when comparing IPC to pharmacological prophylaxis.<br>• Pharmacological prophylaxis plus IPC further reduced the risk of DVT but not PE when compared to IPC alone. No difference in mortality was reported between the two.<br>• No difference in mortality exists between IPC and pharmacological prophylaxis. No difference in mortality exists between the combination of IPC and pharmacological prophylaxis versus IPC alone.<br>• Study quality was modest. No publication bias existed. No comment on conflict of interest. |
| Joint replacement patients [11] | • Compared with pharmacological prophylaxis alone the combination of compression with pharmacological prophylaxis is effective in preventing DVT in both hip and knee replacement patients.<br>• In hip replacement patients, there is no difference in DVT rates between compression plus pharmacological prophylaxis and compression alone. However, results favored combining the modalities.<br>• For knee replacement patients, there were no studies investigating DVT rates in compression plus |

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| | pharmacological prophylaxis versus compression alone. DVT rates were reduced in compression plus pharmacological prophylaxis versus pharmacological prophylaxis alone.<br>• For knee replacement patients, there was no difference in PE rates between compression plus pharmacological prophylaxis versus pharmacological prophylaxis alone.<br>• Study quality or conflict of interest not assessed. |

**Figure 1. Forest plot showing the effect of intermittent pneumatic compression (IPC) on risk of deep vein thrombosis compared to thromboembolic deterrent stockings (TEDS). Studies are listed according to their year of publication. [2]**