Title: Sequential Compression Devices for the Prevention of Venous Thromboembolism following Abdominal Surgery

Date: June 15, 2007

Context and policy issues:

a. Clinical context

Venous thromboembolism (VTE) is the formation within a vein of a clot (thrombus) that breaks free, travels through the vascular system, and lodges in a vessel in another part of the body (embolus). An embolus in the lungs, a pulmonary embolus (PE), is one of the leading causes of post-operative death, often occurring in patients with otherwise good prognoses.\(^1\) The term VTE encompasses both the clot formation, deep vein thrombosis (DVT), and PE. As first noted in the mid-19\(^{th}\) Century, VTE results from “Virchow’s triad”, a combination of venous stasis (stagnant blood flow), vein injury, and increased coagulation (clotting).\(^2\) It has been described as “the most common preventable cause of death in surgical patients”.\(^3\)

VTE has been measured in 15% to 30% and fatal PE in 0.2% to 0.9% of general surgery patients, these numbers coming from the 1970s and 1980s before fairly routine prophylaxis to prevent VTE was common.\(^1,4,5\) In addition to the significant morbidity and mortality that can result from VTE, other long-term consequences are possible such as post-thrombotic venous insufficiency, venous ulceration, and chronic PE with pulmonary hypertension.\(^1\)
A common complication in patients undergoing surgery, VTE is often asymptomatic. Only about one in eight venographically detected DVTs will become symptomatic, with a higher proportion of those that embolize being proximal deep venous system clots (originating in the upper leg or pelvis) versus distal vein clots (originating in the calf). Because the condition is generally asymptomatic, early diagnosis is seldom possible and in addition non-invasive testing has limited sensitivity. In general, routine screening of patients for asymptomatic VTE is logistically difficult and is not felt to prevent disease or be cost-effective.

Many VTE risk factors as complications of general surgery have been identified, e.g., advanced age, prolonged immobility, major (versus minor) surgery, underlying cancer, associated trauma, previous VTE, leg varicosities, heart failure, hematological disorders, pregnancy or estrogen use, and obesity. Bariatric (gastric bypass) surgery is particularly difficult because the patients are obese by definition (often morbidly obese), and most are have many risk factors for VTE.

b. VTE prophylaxis

Rather than seeking to diagnose VTE when it has occurred, the approach to VTE prevention has been thromboprophylaxis on the basis of VTE risk stratification. In particular, the criteria established by the American College of Chest Physicians (ACCP), as outlined in Table 1, have seen wide uptake. These classify patient risk based on age, type of surgery, and presence or absence of additional risk factors.

**TABLE 1: Risk stratification for thromboembolism after surgery (from Geerts et al., 2004)**

<table>
<thead>
<tr>
<th>Level of risk</th>
<th>Age (yrs)</th>
<th>Surgery type</th>
<th>Additional risk factors</th>
<th>Incidence of proximal DVT (%)</th>
<th>Incidence of PE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>&lt;40</td>
<td>Minor</td>
<td>None</td>
<td>0.4</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Moderate</td>
<td>Any</td>
<td>Minor</td>
<td>Present</td>
<td>2-4</td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>&lt;40</td>
<td>Major</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40-60</td>
<td>Non-major</td>
<td>Present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>&gt;60</td>
<td>Non-major</td>
<td>Present</td>
<td>4-8</td>
<td>2-4</td>
</tr>
<tr>
<td></td>
<td>&gt;40</td>
<td>Major</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;40</td>
<td>Major</td>
<td>Present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest</td>
<td>&gt;40</td>
<td>Hip or knee arthroplasty/hip fracture surgery/major trauma/spinal cord injury Major</td>
<td>Prior VTE Cancer Hypercoagulable state</td>
<td>10-20</td>
<td>4-10</td>
</tr>
<tr>
<td></td>
<td>&gt;40</td>
<td></td>
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</table>
VTE prophylaxis can involve pharmacological and/or non-pharmacological interventions. Pharmacological management, which is beyond the scope of this report, includes the use of anticoagulants such as heparin. Non-pharmacological management includes early ambulation, various types of elastic stockings, inferior vena cava filters, and intermittent pneumatic compression (IPC) devices. IPC devices are further divided into foot pumps and sequential compression devices (SCDs). The latter are the focus of this report.

c. The technology

An SCD is a knee-high or thigh-high device made up of series of disposable air-filled sleeves. Pumped air from an external electrical control unit follows a compression-relaxation cycle, filling chambers sequentially through separate tubes from the ankle up to the knee or thigh. One reference listed the sequential pressures as 45-50 mm Hg at the ankle, 35 mm at the calf, and 30 mm at the thigh, the duration of compression as 11 seconds and the relaxation period as 60 seconds. The control unit regulates chamber pressures by repeatedly independently measuring and adjusting them as necessary and different pressures and durations of cycles can be used.

SCDs are believed to exert their effect by reducing stasis through the direct effect of pumping venous blood, thereby reducing the blood pooling that is present when patients are under anaesthesia or immobilized post-operatively. An additional mechanism of action may be promotion of the clearance of prothrombotic clotting factors and an increase in local plasminogen activators leading to enhanced fibrolysis, although these additional effects are controversial. They must be worn continuously while patients are non-ambulatory (up to 15 hours/day) and not worn when patients are ambulatory, therefore compliance is an issue and management is time-consuming for nursing staff.

Several SCD products are manufactured by the Kendall Medical Division of the Tyco Healthcare Group (Mansfield, Massachusetts): the Kendall 5325 SCD, the Kendall 6325 SCD and the Kendall 7325 SCD. These devices have been approved for use to help prevent DVT in patients at risk with the currently marketed versions being approved in Canada and the United States in 1999. A similar device is the KCI (formerly Jobst) Extremity Pump 7500 Sequential System which, although similar in design to the Kendall products, is marketed only for the treatment of peripheral edema caused by chronic venous insufficiency, lymphedema, etc., not for DVT prevention.

Of interest to policy-makers are the efficacy/effectiveness, safety, and cost of SCDs for VTE prophylaxis in patients undergoing abdominal/general surgery, particularly with respect to other devices or strategies that can be employed for this purpose. Also relevant are the patient populations most likely to benefit from SCD use and mention of these devices in evidence-based professional guidelines. Note that SCDs are used for other types of surgery including gynecologic, orthopedic, and urological, but the gathering and description of that material is beyond the scope of this report.
Research questions

1. What is the clinical effectiveness of SCDs for the prevention of VTE following abdominal/general surgery?

2. What is its cost effectiveness?

3. What do evidence-based guidelines state regarding the use of SCDs for the prevention of VTE following abdominal/general surgery?

Methods:

A limited literature search was conducted on key health technology assessment (HTA) resources, including PubMed, CINAHL, The Cochrane Library (Issue 2, 2007), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI's HTAIS, EuroScan, international HTA agencies, and a focused Internet search. Results include English language publications from 2002 to May 2007.

Summary of findings:

The search of the published literature identified 114 articles of potential relevance. Of these, 20 were obtained in full text for detailed analysis. Included were four systematic reviews (SRs), four clinical studies, two guideline documents, and ten narrative reviews related to the topic. A number of additional resources were located through grey literature sources, including manufacturers’ information.

a. Clinical effectiveness of SCDs for the prevention of DVT following abdominal surgery

i. Systematic review evidence:

Four SRs that made reference to SCDs for VTE prophylaxis in surgical patients were identified and are described below, chronologically ordered from oldest to most recent:

- Danish researchers performed an SR of thromboprophylaxis in colorectal surgery (benign or malignant disease), including heparin and mechanical compression devices. They employed an extensive search of literature up to August 2003 and selected only RCTs and controlled clinical trials for review. Trial authors and six pharmaceutical firms were also contacted for information. Trials were required to be comparative (two or more interventions and/or placebos) and the outcomes of interest were DVT, PE, and 30-day mortality. References were not assessed as to quality although note was made of blinding, allocation concealment, and intention-to-treat analysis. Of the 558 potential references identified, only 19 met the inclusion criteria. Ultimately, although the authors were able to form conclusions about heparin...
use (i.e., “any kind of heparin is better than no treatment or placebo”), they felt that the data were not sufficient to allow conclusions to be drawn about use of IPCs as compared with heparin or no treatment.20

• The prevention of VTE following surgery was investigated via an extensive SR commissioned by the National Health Service HTA program in the United Kingdom, and performed by researchers at the Universities of Southampton and Oxford. The project commenced in 1997 and the literature search ended in December 2001. Only RCTs were eligible for review although all types of surgical procedures on adults were included, e.g., orthopedics, neurosurgery, etc. Primary outcomes were DVT and PE. Identified for review were 123 trials. Of these, 19 compared IPC devices to a control although only six were specific to SCDs; in addition, eight trials examined IPC combined methods of prophylaxis and four of these included SCDs within the combinations. Most trials were conducted in orthopedic surgery with only two being specific to general surgery. The SR authors found benefit from use of mechanical compression devices when used as monotherapy with a reduction in DVT from 22% in the control group to 10% in the intervention group (odds reduction 63%, 95% confidence interval 57-69%). When device use was added to drug therapy, there was also benefit with reduction in DVT by about half (odds reduction 53%). Benefits were similar regardless of type of device or type of surgery. The authors concluded that, in the absence of a clear contraindication, surgical patients would benefit from use of mechanical compression devices.13

• An international team of researchers performed an SR of the evidence on compression and pneumatic devices for thromboprophylaxis in intensive care unit (ICU) patients including surgical patients, although the latter were a distinct minority and not analyzed separately. Three roles for the devices were determined: as an alternative to drug prophylaxis when contraindications to drug therapy existed, as an interim measure until drug prophylaxis could be introduced, or combined with drug prophylaxis. Selected for review were 21 articles published between 1992 and 2005 including five RCTs, 13 observational studies, and three surveys. Surgical patients were only included in the observational studies and even then only in six of the 13. The report authors observed that use of mechanical devices for DVT prophylaxis was widespread but somewhat ad hoc as they stated that no guidelines existed for the use of mechanical devices for VTE prevention in ICU patients. They also expressed concern that mechanical devices appeared to suffer from improper and inadequate use. Ultimately they recommended the need for large RCTs to allow guidelines to be developed and promulgated.14

• The fourth SR, performed by Brazilian experts, focused specifically on VTE prevention in hospitalized obese medical and surgical patients, particularly those undergoing bariatric surgery. Literature up to 2005 was sought, with 37 articles ultimately meeting the inclusion criteria; only nine were specific to the efficacy of VTE prevention. Further, only two of these included SCDs among the treatment options, one being Gonzalez et al. (2004) which is described below. Once again, due to a lack of rigorous primary research, the authors concluded that the evidence was too
sparse to allow for recommendations to be made as to the optimal VTE prophylaxis for obese patients. They recommended the performance of RCTs.\textsuperscript{10}

In summary, four SRs were located that touched on use of SCDs for VTE prophylaxis in general surgery patients. Safety did not seem to be a concern with no reports of adverse effects in any of the SRs and a number of statements supporting the benign nature of the devices. Three were unable to draw conclusions about SCD efficacy due to the poor evidence base.\textsuperscript{10,14,20} However, the remaining SR, which was both rigorous and extensive, was more optimistic with reported benefit of mechanical compression devices in DVT prevention in surgical patients in the range of 63% as monotherapy and 53% when added to drug therapy. Benefits were similar regardless of type of mechanical compression device, therefore SCDs did not stand out as a superior option.\textsuperscript{13}

ii. Primary research evidence:

The four clinical studies of SCDs for VTE prophylaxis in surgical patients are briefly presented below, ordered from oldest to most recent:

- A retrospective review at the University of Southern California examined the records of 1281 high risk patients who had undergone major abdominal surgery for cancer or irritable bowel disease in the previous seven years with only SCDs as VTE prophylaxis (versus heparin therapy as recommended by the American Society of Colorectal Surgeons guidelines). Results showed that, by 90 days follow-up, 0.78% of these patients had developed clinically detectable VTEs, a rate that was similar to published VTE incidence rates for similar patient populations who had received treatment with SCDs plus heparin (0.74% in one study to 234,669 patients with colorectal cancer). The authors recommended SCDs alone to avoid the safety concerns associated with heparin.\textsuperscript{21}

- A 669-bed, not-for-profit, tertiary care hospital in Pennsylvania was the setting for a retrospective review of VTE prophylaxis in the form of subcutaneous heparin combined with knee-high SCDs, administered to 255 obese patients who had undergone laparoscopic gastric bypass surgery using the Roux-en-Y procedure. The catalyst for the study was the lack of consensus regarding VTE prophylaxis for this patient group, with national surveys showing that a minority of surgeons used a combination of two or more prophylactic modalities, i.e., presumably most were choosing drug therapy over mechanical devices although this detail was not provided. The authors sought to confirm that their VTE prophylactic regimen was at least as effective as those reported in the literature. Results showed that three patients (1.2%) were diagnosed with clinically symptomatic but treatable PE, this incidence being comparable to the 2% published VTE rates for bariatric surgery. The study authors concluded that their prophylactic regimen provided excellent results in this patient population although there was no information about what types of regimens other surgeons were using.\textsuperscript{8}
At the University of South Florida in Tampa, obese patients undergoing Roux-en-Y gastric bypass surgery (n=660) between 1998 and 2004, with subcutaneous heparin and SCD VTE prophylaxis, were studied prospectively. Thirteen patients (2%) developed PE about seven days post-operatively, with three dying. Multivariate analysis of risk factors revealed increased risk due to age >50 years, history of VTE or smoking, and post-operative anastomotic leaks. The study authors revised their VTE prophylactic regimen to replace subcutaneous heparin with low molecular weight heparin, although SCDs and were maintained and early ambulation was emphasized.9

The fourth study focused on SCD compliance. The study authors state at the outset that SCDs have become the most common form of prophylaxis against the formation of deep vein thrombosis (DVT) among surgical patients due to their ease of use and safety profile, particularly for those in whom anticoagulants are contraindicated. Because compliance with SCD use can be an issue (the authors cited previously published rates of 48%), gains were anticipated through education of nurses and patients. The prospective study at a single hospital blinded nurses and patients (n=365). For 2 months, surgical residents noted compliance with SCD use, measured as 62% on the surgical floor and 48% on nonsurgical floors. Following this, SCD educational sessions for nurses on the busiest surgical floor were held and pamphlets about SCD use were distributed to patients. Compliance over the following 2 months was again monitored but results were disappointing (65% on the surgical floor and 48% on nonsurgical floors). Several interesting observations were made by the study authors: the effectiveness that could be achieved by SCD is limited by poor compliance; nurses, patients, and physicians may not realize the importance of SCDs; there is no logging system for SCD compliance (in contrast to administration of drugs) therefore accountability is lacking; and with hospital beds at a premium surgical patients may increasingly be cared for on non-surgical floors where the expertise with SCD use is not inherent.22

An additional article provides information about the mechanisms of action of various different types of products available for peripheral venous compression. Welsh physicists/engineers investigated the venous flow effects of mechanical devices designed to prevent DVT. On the basis of literature retrieved via a 1970 to 2002 Medline search they concluded that all IPCs successfully empty the deep veins of the lower limbs and prevent stasis but there was no evidence that rapid inflation, high pressures, or graded sequential compression improved a system's prophylactic ability, rather patient compliance and appropriateness of the site of compression should be priorities.24

In summary, the primary research shows some promising results when SCDs were used for VTE prophylaxis although overall the literature is scant and seldom focused specifically on SCDs and their efficacy/effectiveness. Almost no comparative information was located. The source of study funding was not reported in any of the publications.
With respect to more research underway or planned, two SCD clinical trials are described in the clinical trials registry at ClinicalTrials.gov:

- SCDs and foot pumps will be compared in 200 obstetric patients who require VTE prophylaxis at Johns Hopkins University (Baltimore, Maryland) in a prospective, randomized, open-label safety/efficacy study. Outcome measures include DVT prevention, patient comfort, and compliance, and expected study completion is July 2007.\(^{26}\)

- Use of the device for patients with restless legs syndrome at the Sleep Disorders Clinic, Walter Reed Army Medical Center (Washington, DC), will be explored in a phase III, prospective, randomized, sham-controlled study that began recruiting 40 patients late in 2005. Expected study completion is late 2009. Outcomes of interest are symptoms, sleepiness, quality of life, and compliance.\(^{27}\)

b. **Cost effectiveness of SCDs for the prevention of DVT following abdominal surgery**

No cost-effectiveness information was located. With respect to device purchase costs, the products appear to be readily available through medical equipment suppliers and even as resale items through vehicles such as eBay, with prices in the $600 range.\(^{28}\) An additional consideration when costs are being considered is the reported poor compliance with these devices and the need for vigilance on the part of nursing staff. This could conceivably extend to higher nursing costs when patients are using the devices in hospital.\(^ {7,22}\)

c. **Information from evidence-based guidelines**

Three references to clinical practice guidelines were located that included SCDs for VTE prophylaxis, two identified through the literature search,\(^ {7,23}\) and an additional reference through internet searching:\(^ {29}\)

- An important reference publication is a 60-page summary of the Seventh Conference on Antithrombotic and Thrombolytic Therapy held by the ACCP. An extensive preamble and presentation of evidence is followed by ACCP recommendations/guidelines including statements related to VTE prevention.\(^ {7}\)

Guideline classifications are:

| Grade 1: Strong recommendations indicating that benefits do (or do not) outweigh risks, burdens, and costs. |
| Grade 2: Individual patient values may lead to different choices. |
The relevant guidelines/recommendations with respect to mechanical methods of VTE prophylaxis are:

- The devices should be used primarily in patients at high risk of bleeding (Recommendation Grade 1), or as an adjunct to anticoagulant-based prophylaxis (Recommendation Grade 2).
- Careful attention should be directed toward ensuring the proper use of, and optimal compliance with, the mechanical device (Recommendation Grade 1).

Additional recommendations/guidelines refer specifically to use of these devices for general surgery patients (as per the risk categories described earlier in Table 1):

- Low risk: No VTE prophylaxis including mechanical devices (Recommendation Grade 1).
- Moderate risk: Heparin therapy only (Recommendation Grade 1).
- High-risk: Higher dose heparin therapy only (Recommendation Grade 1).
- Highest-risk with multiple risk factors such as age >40 years, cancer, priori VTE: Pharmacologic methods combined with mechanical devices such as IPCs or graduated compression stockings (Recommendation Grade 1).
- Patients with a risk of bleeding: Mechanical devices such as properly fitted IPCs or graduated compression stockings, at least until the bleeding risk decreases (Recommendation Grade 1).

- Laparoscopic surgeons from London, England, explored the principles guiding safe practice for preventing VTE in patients undergoing laparoscopic surgery. They noted that some researchers had documented VTE risks that were higher for patients undergoing laparoscopic versus open procedures whereas others had documented lower rates. Practice guidelines developed by the European Association for Endoscopic Surgery (EAES) were presented, including intraoperative use of IPCs for all prolonged laparoscopic procedures.\(^{23}\)

- The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) has web-posted a position statement on DVT prophylaxis during laparoscopic surgery.\(^{29}\) IPCs are listed as a choice in the situations shown in Table 2:

Table 2: Excerpt from SAGES position statement related to ICP use\(^{29}\)

<table>
<thead>
<tr>
<th>Procedure (all laparoscopic)</th>
<th>Patient risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholecystectomy</td>
<td>Any</td>
</tr>
<tr>
<td>Appendectomy</td>
<td>Any</td>
</tr>
<tr>
<td>Diagnostic appendectomy</td>
<td>2 or more</td>
</tr>
<tr>
<td>Inguinal hernia repair</td>
<td>2 or more</td>
</tr>
<tr>
<td>Nissen procedure (hiatus hernia repair)</td>
<td>0 or 1; combined with heparin for 2 or more</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>0 or 1; combined with heparin for 2 or more</td>
</tr>
<tr>
<td>Procedures such as Roux-en-Y</td>
<td>Combined with heparin for all patients</td>
</tr>
</tbody>
</table>
Conclusions and implications for decision or policy making:

SCDs have been available for several decades; the devices currently marketed were approved in 1999 in the United States and Canada for use in DVT prevention in patients at risk. Some studies have shown a benefit in terms of reductions in VTE overall (particularly DVT which is more common than PE), although there is a definite lack of high-quality evidence, at least within the five years covered by this review. In particular, there is a lack of evidence specific to SCD use in general surgical patients as more information has been published (although not reported here) in orthopedic and trauma patients. There is also a lack of information comparing SCDs to other types of mechanical devices and to pharmacological interventions or combination regimens for VTE prevention.

Based on the available evidence SCDs appear to be safe and may have a place in VTE prophylactic regimens for selected general surgery patients. Recent ACCP guidelines have supported SCD use in combination with anti-coagulation in the highest-risk patients and as monotherapy in patients when anti-coagulation is to be avoided or delayed.

The cost per device is affordable (about $600) although it appears that measures to optimize compliance on the part of nurses and patients are important. It might also be key to ensure that surgeons in an institution are interested and believe in SCD use prior to equipment purchase. It should be noted that indiscriminate use of SCDs based on perceived low cost and/or adoption of the technology without attention to compliance issues could undermine any health system benefit that might otherwise accrue.

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