TECHFLASH

Illuminating Evidence to Aid Decision Making – January 2012

ActiveCare+SFT® Portable Compression Device for Venous Thromboembolism Prevention After Joint Arthroplasty

Technology Overview and Status

The ActiveCare+SFT® (Medical Compression Systems, Inc., West Hills, Calif, www.mcsmed.com) is a portable, battery-powered intermittent pneumatic compression (IPC) device used for venous thromboembolism (VTE) prophylaxis following surgery. The system is intended to increase compliance in hospital by allowing use while ambulating; it may be prescribed for at-home use as well.

The ActiveCare device consists of a small (1.6 lb) controller unit, single- or multicelled disposable lower limb cuffs, and plastic hoses connecting the cuffs to the control unit. The controller unit can be worn on a shoulder strap during ambulation. Internal rechargeable batteries allow the device to be used for 5 to 7 hours without needing to be connected to an electrical outlet. Multiple-cuff designs allow various combinations of foot, calf, and/or thigh compression with single-cuff or sequential compression. Synchronized Flow Technology (SFT) uses an internal sensor to apply pressure in sync with respiratory-related changes in venous phasic flow to optimize peak venous velocity at lower applied pressures.[1] A typical cycle is 8 seconds of compression (peak pressure 50 mm Hg) followed by 36 to 56 seconds of decompression.

The cuffs may be placed immediately after the induction of anesthesia during total hip arthroplasty (THA) or total knee arthroplasty (TKA) procedures. The device is intended to be used 24 hours a day, or as much as possible, after surgery; it is typically removed only during bathing. An internal timer in the controller measures and displays the total amount of time the device is functioning to inform caregivers about compliance. With instruction, the cuffs, which attach with hook-and-loop fasteners, can be reapplied by the patient at home or in a rehabilitation setting. Use of the device may be prescribed for 8 to 12 days after surgery. Daily low-dose (e.g., 81 mg) aspirin may also be prescribed for select patients.

The ActiveCare device has been under development for about a decade. The first-generation product, called WizAir DVT or Continuous Enhanced Circulation Therapy (CECT), was developed in the late 1990s by an Israeli company (MCS, Or Akiva, Israel). Early clinical feasibility studies were mostly conducted in

Israel and at the University of Texas Medical Branch, Galveston. A second-generation device (ActiveCare ++) received 510(k) approval as a class II device (product code JOW) from the US Food and Drug Administration in March 2006.[2] After completion of clinical studies, widespread marketing of ActiveCare+SFT in the United States began in 2009. An additional software module for detecting venous obstruction was added to ActiveCare+SFT in 2011.[3] ActiveCare+SFT is labeled for ". . . preventing deep vein thrombosis, enhancing blood circulation, diminishing post-op pain and swelling, reducing edema, treatment and assistance in healing, reducing wound-healing time, and treatment of chronic venous insufficiency."

Technology Significance

Venous thromboembolism is a major health problem associated with significant patient morbidity and mortality and high utilization of health care resources.[4] Joint arthroplasty carries a particularly high risk for VTE because it may affect all points on Virchow's triad: hypercoagulability, venous stasis, and endothelial injury and dysfunction. The incidence of DVT can be as high as 40% to 60% in orthopedic knee and hip surgery if preventive measures are not taken, and fatal pulmonary embolism (PE) can occur in 1% to 5% of patients who do not receive prophylaxis.[5-7] Currently, more than 1 million joint arthroplasties are performed in the United States annually and the number of these procedures is expected to continue to rise rapidly over the next decade as the population ages.[8] Knee arthroplasties particularly are expected to undergo rapid growth, possibly doubling by 2015 and comprising the majority of lower limb arthroplasties in the future.

The actual incidence of VTE varies with individual patient characteristics, type of surgery, and use and type of prophylaxis. Mechanical methods have generally been shown to reduce DVT by 50% to 75% when used alone and may be even more effective in combination with other methods.[9] However, there is some controversy about the efficacy of mechanical methods compared with pharmacologic anticoagulation and there is little proof that mechanical methods reduce PE rates.[10] Despite this, mechanical methods of VTE prophylaxis are appealing to orthopedic surgeons because of the lower risk of postoperative bleeding compared with anticoagulants.[11] Major bleeding events occur at a rate of approximately 1% to 5% following joint surgery and may be associated with anemia-related complications, transfusion and transfusion-related adverse events, increased wound discharge, slowed wound healing, infection, prolonged hospitalization, rehospitalization, surgical intervention, delayed rehabilitation, and, rarely, death.[12]

The ActiveCare device is significant because it is the first highly portable mechanical device to show safety and efficacy in a randomized controlled trial (RCT) compared with conventional treatment with low-molecular-weight heparin (LMWH).[13] Further, the portability of the ActiveCare device may lead to higher usage compliance than comparable nonportable IPC devices—a distinct advantage because of the high expected correlation between the amount of time a mechanical device is used and the efficacy of prophylaxis.[14] Nonportable devices must be disconnected during ambulation, when the patient is moved for tests, or when the patient goes to the bathroom; one source of noncompliance arises when the patient does not promptly reconnect the IPC device when back in bed. The ability of ActiveCare to monitor and report usage time may also facilitate compliance.

Further, the portability of the device suggests a new role for IPC devices in at-home VTE prophylaxis. The need for prolonged prophylaxis after surgery is widely accepted because VTE often occurs weeks after surgery.[15,16] Long-term prophylaxis is usually accomplished with pharmacologic agents, as the bleeding risk is usually lower by the time of discharge. However, when the bleeding risk remains significant, mechanical methods of VTE prophylaxis may play a role. Because this treatment strategy has only recently become available, the advantages and disadvan-

tages of prolonged at-home use of mechanical prophylaxis require additional study. There is some controversy about the need for continued mechanical prophylaxis once the patient is fully ambulatory.

Current Practice and Alternatives

There are a number of recently published evidence-based guidelines and reviews for VTE prophylaxis following joint arthroplasty from the American College of Chest Physicians (ACCP), the American Academy of Orthopaedic Surgeons (AAOS), the UK National Institute for Health and Clinical Excellence (NICE), and the Agency for Healthcare Research and Quality (AHRQ).[10,17-20] There are, however, some differences between the guidelines' recommendations; further studies are needed to reconcile these differences.[21]

Pharmacologic agents are commonly used for VTE prophylaxis, including antiplatelet drugs (aspirin), low-dose unfractionated heparin, LMWH, vitamin K antagonists (e.g., warfarin), and synthetic pentasaccharide factor Xa inhibitors (e.g., fondaparinux).[22,23] These drugs may differ in their mode of delivery (oral, parenteral, subcutaneous), dosing schedule, pharmacokinetics, costs (e.g., approximately $31/day for LMWH compared with < $1/day for warfarin or aspirin), proof of prophylactic efficacy, and side-effect profile. The most common complication of these agents is bleeding, which may be dose- and patient-related.

Subcutaneously administered LMWH is the most commonly used agent in the United States, although the ACCP suggests using any of the following: LMWH, fondaparinux, apixaban, dabigatran, rivaroxaban, low-dose unfractionated heparin, aspirin, or warfarin (targeting an international normalized ratio [INR] of 2.0 to 3.0) beginning perioperatively and continuing for a minimum of 10 to 14 days (strong recommendation based on moderate-quality evidence).[10] Newer oral agents under development (e.g., apixaban, rivaroxaban, and dabigatran) are promising but have less clinical evidence to date.[13] Potential advantages of these newer agents include ease of administration with predictable pharmacokinetics that minimize the need for monitoring and dosage adjustment. These agents are, however, still awaiting approval from the US Food and Drug Administration for use as VTE prophylaxis in the United States.

Mechanical devices for VTE prophylaxis include graduated compression stockings (GCS) and various IPC devices. GCS are often used because they are inexpensive and relatively easy to apply.[24,25] GCS are available in calf or thigh length; the choice of one or the other may depend on the type of surgery, but there is little evidence that either has greater efficacy.[26] Efficacy may be dependent on proper fitting, which is more likely with calf-length GCS.[27,28] The mechanism of action for GCS remains somewhat uncertain; potential mechanisms include increased venous flow velocity secondary to decreased venous diameter and the prevention of the vein distention that leads to venous blood pooling.[29]

There are many types of IPC devices.[30] Cuffs can be placed on the foot, calf, foot and calf, or calf and thigh. Some cuffs contain multiple bladders that are inflated consecutively from distal to proximal to create a "milking" action (sequential IPC) or use different pressures in each bladder (graded sequential IPC); others have only 1 bladder that is uniformly inflated. Air bladders can wrap completely around the limb (circumferential) or compress only a limited area (asymmetric). Asymmetric configurations require the least amount of air and therefore can use smaller pumps. Compression devices have a good safety profile, with skin irritation being the most commonly reported complication. Rare adverse events include compartment syndrome and peroneal nerve palsy.

Inflation cycle times and pressures vary among IPC devices and may be preset or configurable.[30]

Rapid compression times (e.g., < 15 s) may be used to increase blood flow velocity. Long (e.g., > 40 s) uninflated cycles are used to allow for complete venous refilling between compressions. Higher pressures tend to pump more blood through the veins, but may be more uncomfortable and decrease patient compliance. Because of the relatively small volume of blood in the foot (20 to 30 mL), higher pressures (> 130 mm Hg) are used in venous foot pumps than in calf pumps (about 40 mm Hg).

As with GCS, IPC devices' mechanism of DVT prevention is not entirely understood.[30] The primary mechanism is believed to be prevention of venous stasis. That is, pneumatic compression of the limb mimics the compression caused by muscle contraction when walking. Assuming the venous valves are competent, compression results in proximal displacement of the blood and venous refilling when compression is released. Different IPC systems may be designed to maximize venous blood flow velocity or flow volume.[31] Theoretically, higher velocities may be more effective at breaking down thrombi in valve pockets and more flow could reduce local concentrations of procoagulants. However, it is not known what hemodynamic parameter, if any, is important to optimize VTE outcomes.[32] Thus, there is no definitive evidence regarding the selection of thigh-length or knee-length cuffs or foot pumps, or sequential or uniform compression or varied pressure-timing cycles.[29]

Intermittent pneumatic compression may have significant hematological effects, including localized or systemic effects on blood coagulability. For example, IPC may stimulate endogenous fibrinolytic activity through actions on vascular endothelial cells or via rheologic mechanisms.[33,34] Further study is needed to better define and optimize these hematologic effects.

In general, evidence-based guidelines have not identified any particular mechanical method of VTE prophylaxis that works better than others. Guidelines have also noted that comparative data are limited and suggest that optimization of hemodynamic parameters has not been definitively linked to outcomes.[35] Because of the dearth of comparative clinical data, different mechanical devices are often assumed to be equally effective. It should be emphasized that there is little or no evidence to support this assumption, as equivalence has not been shown in comparative trials. Meta-analyses have generally shown similar rates of DVT reduction for different device classes compared with placebo. Heterogeneity in enrolled patient populations, however, makes direct interstudy comparisons difficult. Other criteria used in selecting a method of prophylaxis include patient comfort and compliance, nursing concerns, and costs.

Clinical Evidence Summary

Clinical studies involving the ActiveCare device were identified via a search of the PubMed (MEDLINE+) database (www.ncbi.nlm.nih.gov/pubmed) conducted in January 2012. The literature search used combinations of the keywords *mobile, portable, intermittent pneumatic compression, venous thromboembol*, VTE or DVT, continuous enhanced circulation therapy, WizAir,* and *ActiveCare*. Retrieved articles were limited to clinical trials on human subjects in English and with abstracts. No restrictions were placed on the publication date. The bibliographies of key references and recent review articles were searched for relevant studies not uncovered in the PubMed search. Manufacturer-sponsored clinical studies and reports of interim results were also identified on the manufacturer Web site.[36]

Six published clinical studies were identified, including 5 RCTs (Table 1).[37-42] Abstracts of these studies are included for reference in the Appendix. All randomized trials to date appear to have been sponsored by the manufacturer. The pivotal trial, known as the SAFE study, was a multicenter (9 US sites) trial randomizing 410 patients undergoing THA to either ActiveCare or LMWH.[38] There was also a comparative trial of combination therapy that randomized 277 patients undergoing THA or TKA at a single US center to either LMWH or LMWH plus the ActiveCare device.[39]

The remaining studies may be classified as early feasibility studies of the first-generation device. These include a small study conducted in 2000-2001 and involving 121 patients undergoing joint arthroplasty at a single Israeli center who were randomized to either WizAir or LMWH,[41] and another single-center (Israeli) comparative study of WizAir and a conventional IPC device in 50 patients undergoing joint arthroplasty in 1999-2000.[37] A small randomized feasibility study was conducted at the University of Texas Medical Branch, Galveston, studying IPC device compliance in 33 trauma patients.[42] The final study was a retrospective review using comparative data from a product conversion to the ActiveCare device in joint arthroplasty procedures; the study was conducted at a single US center (The Cleveland Clinic).[40]

The SAFE study was a comparison of the ActiveCare device used for 10 days (63% of patients also had an optional 81-mg aspirin daily) vs. LMWH (enoxaparin, 40 mg daily for 10 days) in patients undergoing THA.[38,43] There were 392 evaluable patients (395 hips) in the safety cohort out of 410 enrolled patients; 198 of these patients used the ActiveCare device and 194 received LMWH. Major bleeding—defined as bleeding requiring rehospitalization or prolonged hospitalization, any intervention to prevent serious complications, endangering critical organs, or of a life-threatening nature—occurred in 5.6% (11 of 196 hips) of LMWH cases; there were no cases of major bleeding in the ActiveCare group (P = .0004). There was no statistically significant difference between the groups in the number of minor bleeds or other indices of bleeding. Efficacy analyses noted 10 VTE diagnoses (established by occurrence of clinical events within 3 months, follow-up duplex ultrasonography at 10 to 12 days postoperatively, or spiral computed tomography) in 197 patients using compression (rate, 5.1%; 4.1% DVT and 1.0% PE) and 10 VTE diagnoses in 192 patients receiving LMWH (rate, 5.2%; 4.2% DVT and 1.0% PE); the difference was not significant (P = .953). All acute VTE events were successfully treated. Compliance in the compression arm averaged 20.9 hours of device wear per day (87% of maximum possible time). Limitations of the SAFE trial included a lack of blinding, use of duplex ultrasound to measure occult DVT, and inadequate power to identify differences in efficacy. There are also concerns about the definitions of major bleeding used in the trial, the apparent lack of consistency between diagnosis of major and minor bleeding events, and the absence of any major bleeding in the compression arm.[44]

In a prospective, single-center RCT, 277 patients undergoing lower limb joint arthroplasty (153 TKA, 124 THA) were assigned to either LMWH alone (enoxaparin, 30 mg every 12 h for 7 to 8 days) or an LMWH regimen combined with ActiveCare compression during the hospital stay.[39] Incidence of VTE was assessed using duplex ultrasound at discharge; patients were also observed clinically for signs and symptoms of VTE for 3 months after discharge. Overall, the rate of DVT was 4.3% in the combination-therapy group compared with 12.5% in the group receiving LMWH alone (P = .016); there was no discernible difference between the 2 groups in the rate of PE. For TKA patients, the rate of DVT was 6.6% in the combination-therapy group compared with 19.5% in those receiving LMWH alone (P = .018). The difference in DVT rates between groups in THA patients was not statistically significant (combination therapy, 1.5%, LMWH alone, 3.4%; P = .60). Rates of blood loss and transfusions for the 2 groups were similar. Compliance with mechanical compression was 85% of the possible time.

In a randomized, prospective, single-center RCT of 121 patients undergoing either unilateral THA (77 patients) or TKA (48 patients), 60 patients were assigned to receive enoxaparin (40 mg once daily) and 61 received mechanical compression plus aspirin (100 mg daily).[41] Prophylaxis was continued throughout hospitalization, which averaged 9 to 10 days. The incidence of DVT was assessed by venogram of both legs on postoperative day 5 to 8; patients were also followed clinically for VTE events for 3 months postoperatively. Deep vein thrombosis was detected in

28.3% of patients receiving enoxaparin vs. 6.6% of IPC patients (P = .002). Only 1 PE was detected, in the enoxaparin group. Most DVTs occurred in patients who had had THA (13 of 21); DVT rates in this subgroup were 32.5% (13 of 40) in the enoxaparin group and 0% in the IPC group (P < .012). Rates of DVT were similar in patients undergoing TKA (4 occurrences in each study group). There were no significant differences in incidence of bleeding events in the 2 groups.

Comparison of the ActiveCare mechanical device with other mechanical devices appears to show at least comparable safety and efficacy. In an early study of the first-generation ActiveCare device, testing in healthy volunteers showed ultrasound-determined femoral vein peak velocities that were similar to those of other mechanical devices.[37] The same group conducted a preliminary trial that randomized 50 patients undergoing joint arthroplasty (THA or TKA) to 1 or the other of 2 sequential mechanical devices and found no incidence of DVT in either group.[37] Another retrospective, single-center, before-and-after study evaluated conversion from one mechanical compression device (calf-length, single bladder) to the ActiveCare device (calf-length, sequential ICP).[40] Devices were used, per hospital protocol, in combination with LMWH for the duration of hospitalization. Cumulative VTE rates were 4.3% for the standard IPC device (58 of 1,354 cases) and 1.3% (3 of 223) for the ActiveCare device (P < .05). Compliance for the ActiveCare device was 83% of possible hours compared with a nurse-estimated 49% with the standard device.

Table 1. Summary of Randomized Clinical Trials of ActiveCare Device

Study	Design	Results
Coldwell et al. 2010[38] (*SAFE study*)	Multicenter, THA: ActiveCare (n = 198) vs. LMWH (n = 194) for 10 d	*Major bleeding:* ActiveCare, 0% vs. LMWH, 5.6%; P = .0004 *VTE diagnoses at 3 mo:* ActiveCare, 5.1% (4.1% DVT and 1% PE) vs. LMWH, 5.2% (4.2% DVT and 1% PE); P = .953 *ActiveCare compliance:* 87% (20.9 hrs/day)
Edwards et al. 2008[39]	Single-center, THA (n = 124) or TKA (n = 153) ActiveCare during hospitalization + LMWH (n = 141) vs. LMWH only (n = 136) for 7-8 d	*DVT diagnoses at 3 mo:* ActiveCare + LMWH, 4.3% vs. LMWH, 12.5%; P = .016 For TKA only: ActiveCare + LMWH, 6.6% vs. LMWH, 19.5%; P = .018 For THA only: ActiveCare + LMWH, 1.5% vs. LMWH, 3.4%; NS *Bleeding:* No difference reported *ActiveCare compliance:* 85%
Gelfer et al. 2006[41]	Single-center THA (n = 77) or TKA (n = 48) N = 121: 61 ActiveCare + aspirin vs. 60 LMWH for 9-10 d	*DVT diagnoses at 3 mo:* ActiveCare, 6.6% vs. LMWH, 28.3%; P = .002 For THA only: ActiveCare, 0% vs. LMWH, 32.5%; P < .012 For TKA only: no difference in DVT rate *Bleeding:* Differences NS
Ben-Galim et al. 2004[37]	Single-center, THA or TKA (N = 50) 25 ActiveCare vs. 25 Kendall SCD for ~ 6 d Both groups received heparin (5,000 units BID)	*DVT diagnoses at 6 d:* None reported in either group Similar comparative peak vein velocity achieved Feasibility shown
Murakami et al. 2003[42]	Single-center, trauma patients ActiveCare (n = 17) vs. SCD (n = 16) during hospitalization	*Compliance:* ActiveCare, 78% vs. SCD, 59%; P = .004 Compliance for ActiveCare was significantly higher for use in the ED and units, but not in the OR or ICU Other outcomes not reported

DVT = deep vein thrombosis; ED = emergency department; ICU = intensive care unit LMWH = low-molecular-weight heparin; NS = not significant; OR = operating room; PE = pulmonary embolism; SCD = sequential compression device; THA = total hip arthroplasty; TKA = total knee arthroplasty; VTE = venous thromboembolism.

Financial Issues

The cost of the ActiveCare pump and controller is approximately $1,500; a pair of disposable leg cuffs cost approximately $30 to $50.[41] Typical charges for device use may be around $200 for in-hospital use and another $200 for at-home use. Thus, in one scenario, total usage may cost about $450 per patient. In a first-order approximation, this cost may be comparable to the total cost for in-hospital and at-home use of pharmacologic prophylaxis.[45] The approximate cost of other DVT prophylaxis strategies is shown in Table 2. Organizations should use their own costs and practices to determine financial comparability.

More in-depth cost-effectiveness calculations should also take into account any incremental costs associated with treatment of DVT complications, bleeding complications, and extended length of stay. For example, suspicion of DVT may lead to serial diagnostic testing with ultrasound (about $300 per test) or venography, increase hospital stays by 1 to 5 days, and result in excess costs of approximately $7,500.[47] Suspected PE may lead to ultrasound testing, ventilation/perfusion scans, computed tomography, or pulmonary angiography; treatment with LMWH or warfarin; an increased hospital length of stay of > 5 days and a potential ICU stay for a few patients; and excess costs, compared with patients with no VTE, of > $10,000.[47] It can readily be seen that in moderate- to high-risk patients in whom the incidence of DVT or PE is high, most prophylactic methods are both health improving and cost saving compared with no prophylaxis.[48-51] The cost-effectiveness of prophylaxis becomes more contentious as the rate of VTE goes down (i.e., in low-risk patients) and as prophylaxis costs increase (as with multimodal strategies). Cost-effectiveness calculations also depend on good comparative efficacy data to use in the models. At this time, there is little published cost-effectiveness data for the ActiveCare from which to draw conclusions.

Because of its relative newness, third-party reimbursement policies for home use of IPC for the prevention of postoperative VTE are evolving.[52-55] Some payers may consider this usage to be experimental and thus not covered. Others may stipulate selection criteria, such as a contraindications to anticoagulation medication or a prolonged inability to ambulate. Because of the inconsistency, preapproval may be necessary to ensure adequate coverage. Specific equipment models and rates may be defined in the durable medical equipment plans.

Table 2. Daily Cost of VTE Prophylactic Methods

Treatment	Cost/Day
Fondaparinux (once-daily injection, 2.5 mg)	$30
Enoxaparin (2 × 30 mg syringes)	$24
Dalteparin (5,000 units/d)	$13
Warfarin (per pill)	$0.30[a]
Compression stockings	$5 to $40[b]
Intermittent pneumatic compression	$26[c] to $100

Adapted from reference 46.

[a] Does not include cost of testing to measure international normalized ratio (INR).

[b] One-time cost.

[c] Recycled sterilized knee-high cuff (one-time cost) with daily leased pump.

Patient Selection Criteria

Appropriate patient selection criteria for the ActiveCare device are not yet well defined; the approved labeling does not include patient selection criteria. Specialty society guidelines differ significantly, only provide general guidance on the use of mechanical prophylaxis, and do not specify a particular device (Table 3).[21] However, both ACCP (2012) and AAOS (2011) agree that lower-limb arthroplasty is a major risk factor for VTE and that all patients require some form of prophylaxis.[10,17] This is consistent with the premise that at this time there are no good ways to identify the subset of arthroplasty patients who will go on to develop VTE; therefore, available ActiveCare clinical studies have generally included all patients undergoing THA or TKA.

The high risk of bleeding associated with pharmacologic prophylaxis is often cited by guidelines as a potential reason for selecting mechanical methods instead. Unfortunately, the criteria for quantifying bleeding risk are controversial and not well defined. The AAOS guidelines suggest that there is a consensus regarding high bleeding risk only in cases of known bleeding disorders like hemophilia and active liver disease.[17] AAOS recommendations for bleeding risk assessment based on other factors are inconclusive because they are not supported by clinical evidence. Likewise, recommendations regarding pharmacologic prophylaxis when bleeding risk is decreased are not well defined at this time.

The ACCP guidelines on VTE prophylaxis generally favor anticoagulant-based approaches over mechanical methods because the former have been studied more intensively. However, when IPC is selected, the ACCP guidelines favor the use of portable, battery-powered IPCs that are capable of recording daily wear time, such as the ActiveCare device. [10]

Table 3. ACCP Guidelines for VTE Prevention in Joint Arthroplasty[a]

In patients undergoing THA or TKA, we recommend use of one of the following for a minimum of 10 to 14 days rather than no antithrombotic prophylaxis: LMWH, fondaparinux, apixaban, dabigatran, rivaroxaban, LDUH, adjusted-dose VKA, aspirin (all Grade 1B), or an IPC device (Grade 1C).
In patients undergoing THA or TKA, irrespective of the concomitant use of an IPC device or length of treatment, we suggest the use of LMWH in preference to the other agents we have recommended as alternatives: fondaparinux, apixaban, dabigatran, rivaroxaban, LDUH (all Grade 2B), adjusted-dose VKA, or aspirin (all Grade 2C).
In patients undergoing major orthopedic surgery and who decline or are uncooperative with injections or an IPC device, we recommend using apixaban or dabigatran (alternatively rivaroxaban or adjusted-dose VKA if apixaban or dabigatran are unavailable) rather than alternative forms of prophylaxis (all Grade 1B).
For patients undergoing major orthopedic surgery, we suggest extending thromboprophylaxis in the outpatient period for up to 35 days from the day of surgery rather than for only 10 to 14 days (Grade 2B).
In patients undergoing major orthopedic surgery, we suggest using dual prophylaxis with an antithrombotic agent and an IPC device during the hospital stay (Grade 2C).
In patients undergoing major orthopedic surgery and increased risk of bleeding, we suggest using an IPC device or no prophylaxis rather than pharmacologic treatment (Grade 2C).

GCS = graduated compression stockings; INR = international normalized ratio; IPC = intermittent pneumatic compression; LDUH = low dose unfractionated heparin; LMWH = low molecular weight heparin; THA = total hip arthroplasty; TKA = total knee arthroplasty; VFP = venous foot pump; VKA = vitamin K antagonist.

Adapted from reference 10.

[a] Evidence grading: Grade 1B = strong recommendation, moderate-quality evidence; Grade 1C = strong recommendation, low- or very-low quality evidence; Grade 2B = weak recommendation, moderate-quality evidence; Grade 2C = weak recommendation, low- or very-low quality evidence.

Future Developments

A next-generation ActiveCare device under development will use the SFT sensors to aid in the diagnosis of proximal DVT during prophylactic therapy.[56] This early detection may allow changes in thromboprophylaxis or more aggressive treatment to minimize potential complications. Further studies are needed, however, to determine the diagnostic efficacy of and outcomes associated with this approach. Further, other IPC device manufacturers may be expected to develop similar portable products if at-home mechanical thromboprophylaxis gains favor.

As with most emerging technology, additional clinical studies of safety and efficacy are needed to confirm and add to early results. Ideally, much larger RCTs (> 3,000 patients) are needed to determine equivalency in VTE rates between patients using ActiveCare therapy and those receiving anticoagulant medications.[38] Other studies are needed to better define the optimal use of this technology (e.g., the necessary duration of treatment) and to better define patient selection criteria. Well-designed economic studies are also needed to define the role of this technology.

The future role of this technology may be significantly affected by the continued development of new oral agents that are more convenient than current options in that they don't require subcutaneous injection and can be used with simple dosing without the need for monitoring. Results to date seem to indicate that these drugs (e.g., rivaroxaban, apixaban, and dabigatran) may be highly competitive with LMWH in joint arthroplasty.[57-66] If these agents gain approval and become more widely used, clinical trials of ActiveCare will need to compare VTE and bleeding rates with those associated with these drugs.

Conclusions and Recommendations

The following conclusions and recommendations are based on the material presented in this report:

- Patients undergoing total joint arthroplasty are at high risk for VTE and should receive prophylaxis against VTE. Current guidelines suggest that the optimal use of mechanical devices is a viable option in patients who have a high bleeding risk. However, criteria for assessing bleeding risk are not well defined. There is minimal high-quality clinical evidence to support the choice of optimal prophylactic strategy, use of specific devices or agents, or duration of therapy. In general, however, there is more and better evidence available for pharmacologic agents than for mechanical devices.

- The clinical evidence supporting use of the ActiveCare device in joint arthroplasty includes 5 published clinical studies prospectively assessing use of the device in about 425 patients and a retrospective review of its use in another 223 patients. As of January 2012, there were 4 RCTs of varying quality evaluating ActiveCare use in patients undergoing joint arthroplasty. Two of the RCTs were small, preliminary feasibility studies with limited outcomes analysis and conclusions. Another single-center RCT compared LMWH + ActiveCare with LMWH alone and found a lower incidence of DVT in the combination-therapy arm. This is consistent with other studies of combination VTE prophylaxis in the literature and suggests that the ActiveCare device is comparable to other mechanical IPC devices. There were few complications associated with use of the ActiveCare device, and they were similar to those reported for other IPC devices.

- The strongest available clinical evidence comes from the multicenter SAFE study comparing ActiveCare used as monotherapy with LMWH monotherapy in 410 patients undergoing THA, with both therapies used for 10 days. This study was well designed (Level I evidence) but was limited by the small number of patients and potential bias. However, its promising results suggest that further larger studies are warranted. Outcomes analyses showed that both methods of prophylaxis had similar rates of VTE (about 5%), but there were no major bleeding events in the ActiveCare arm while the LMWH arm had a 5.6% rate of bleeding events, which resulted in prolonged hospitalization or rehospitalization for these patients. No differences were reported in other clinical outcomes.

- Given the limited available evidence, the cost-effectiveness and appropriate patient selection criteria for ActiveCare usage are undetermined. Recent ACCP guidelines suggest that portable, battery-powered devices that can record wear time are the preferred type of IPC device when mechanical prophylaxis is selected. Anecdotal reports suggest that some institutions use ActiveCare in all patients undergoing elective joint arthroplasty; a majority, however, still use pharmacologic agents for thromboprophylaxis at some point.

- Resumption of normal ambulation is sometimes used as a cut-off point for discontinuation of mechanical VTE prophylaxis. As yet, there are no available studies comparing ActiveCare use in ambulating patients with placebo. This type of study may be needed to determine the optimal duration of ActiveCare therapy. It is clear, however, that VTE prophylaxis in some form should continue for some time after the patient is discharged. Based on the SAFE study, ActiveCare appears to be a viable alternative to LMWH. Assuming similar efficacy rates in the prevention of VTE, the choice of mechanical or pharmacologic methods of at-home prophylaxis may be based on patient and caregiver preference, as well as cost/reimbursement issues. ActiveCare may be particularly well-suited for patients deemed to be at high risk of bleeding after discharge.

- Because of the emerging nature of the at-home mechanical VTE prophylaxis paradigm, organizations choosing to use it should proceed carefully. Early adopters may consider piloting its use in small trials with close monitoring of short- and long-term outcomes to ensure safety and provide a basis for further decisions regarding use of the device. The clinical literature should be evaluated periodically for new clinical findings. The informed consent process may be useful in educating the patient about safety and efficacy issues.

- New pharmacologic agents for VTE prophylaxis following joint arthroplasty are expected to be approved. The comparative safety, efficacy, cost-effectiveness, and patient/caregiver preference for these agents or the ActiveCare device are not yet known. However, an incremental improvement in outcomes may be expected with the new agents, as well as large improvements in dosing convenience. These developments could drastically change the VTE prophylaxis paradigm in the future

Related Links

VTE Prevention Guidelines

American Academy of Orthopedic Surgeons, 2011: www.aaos.org/research/guidelines/VTE/VTE_guideline.asp

American College of Chest Physicians, 2012: http://chestjournal.chestpubs.org/content/141/2_suppl

Agency for Healthcare Research and Quality, 2010: www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=496

UK National Institute for Health and Clinical Excellence, 2010: http://guidance.nice.org.uk/CG92

UHC Tech Flash

Mechanical Devices to Prevent Venous Thromboembolic Disease in Surgical Patients, 2009: www.uhc.edu/docs/003740792_MedDevicesPreVenousThromTechFlash2009.pdf

Appendix. Abstracts of Key Clinical Studies

Colwell CW, Jr., Froimson MI, Mont MA, et al. Thrombosis prevention after total hip arthroplasty: a prospective, randomized trial comparing a mobile compression device with low-molecular-weight heparin. *J Bone Joint Surg Am*. 2010;92(3):527-535.

BACKGROUND: Thromboembolic disease is a common complication of total hip arthroplasty. The purpose of this study was to compare a new mobile compression device with low-molecular-weight heparin with regard to their safety and effectiveness for the prevention of venous thromboembolic disease.

METHODS: Patients who had a total hip arthroplasty were randomized to receive prophylaxis with a mobile compression device or low-molecular-weight heparin for ten days. Use of the compression device began intraoperatively, and the patients in this group could receive 81 mg of aspirin daily after the surgery. The first injection of the low-molecular-weight heparin began between twelve and twenty-four hours after the surgery. After ten to twelve days, all patients underwent bilateral lower-extremity duplex ultrasonography to screen for deep venous thrombi in the calf and thigh. Any clinical symptoms of pulmonary embolism were evaluated with spiral computed tomography lung scans. Bleeding events and utilization of (i.e., compliance with) prophylactic treatment in both groups were documented. Clinical evaluation to look for evidence of deep venous thrombi and pulmonary emboli was performed at twelve weeks postoperatively.

RESULTS: Four hundred and ten patients (414 hips) were randomized; 392 of these patients (395 of the hips) were evaluable with regard to the safety of the intervention and 386 patients (389 hips) were evaluable with regard to its efficacy. Demographics were similar clinically between the groups. The rate of major bleeding events was 0% in the compression group and 6% in the low-molecular-weight heparin group. The rates of distal and proximal deep venous thrombosis were 3% and 2%, respectively, in the compression group compared with 3% and 1% in the heparin group. The rates of pulmonary embolism were 1% in the compression group and 1% in the heparin group, and there were no fatal pulmonary emboli. Within the twelve-week follow-up period, two events (one deep venous thrombosis and one pulmonary embolus) occurred in one patient in the compression group following negative findings on duplex ultrasonography on the twelfth postoperative day. There was no difference between the groups with regard to the prevalence of venous thromboembolism.

CONCLUSIONS: When compared with low-molecular-weight heparin, use of the mobile compression device for prophylaxis against venous thromboembolic events following total hip arthroplasty resulted in a significant decrease in major bleeding events.

Edwards JZ, Pulido PA, Ezzet KA, Copp SN, Walker RH, Colwell CW Jr. Portable compression device and low-molecular-weight heparin compared with low-molecular-weight heparin for thromboprophylaxis after total joint arthroplasty. *J Arthroplasty*. 2008;23(8):1122-1127.

This preliminary prospective study to determine the rate of deep venous thrombosis (DVT) examined 277 patients undergoing total knee or total hip arthroplasty (TKA or THA) who were randomized to use a portable, continuous enhanced circulation therapy (CECT) compression device and low-molecular-weight heparin (LMWH) or to receive LMWH alone. Patients were screened for DVT using duplex ultrasound at hospital discharge and followed clinically for 3 months. In TKA, 5 DVTs (6.6%) occurred in the CECT + LMWH group compared with one

pulmonary embolism and 14 DVTs (19.5%) in the LMWH group (P = .018). In THA, 1 DVT (1.5%) occurred in the CECT + LMWH group and 2 DVTs (3.4%) occurred in the LMWH group. This preliminary study demonstrated significant reduction in rate of DVT after TKA when the CECT device was combined with LMWH.

Froimson MI, Murray TG, Fazekas AF. Venous thromboembolic disease reduction with a portable pneumatic compression device. *J Arthroplasty*. 2009;24(2):310-316.

This study compares a miniaturized, portable, sequential, pneumatic compression device (ActiveCare continuous enhanced circulation therapy [CECT] system) (Medical Compression Systems Ltd, Or Aqiva, Israel), with a non-mobile, nonsequential device on the ability to prevent postoperative deep venous thrombosis (DVT) after joint arthroplasty. All patients were treated with low-molecular-weight heparin, application of 1 of the 2 devices perioperatively, and routine duplex screening. The CECT system had better compliance (83% of the time vs 49%), lower rates of DVT (1.3% compared with 3.6%), reduction in clinically important pulmonary embolism (0 compared to 0.66%), and shorter length of hospital stay (4.2 vs. 5.0 days). The portable CECT system proved significantly more effective than the standard intermittent pneumatic compression when used in conjunction with low-molecular-weight heparin for DVT prevention in high-risk orthopedic patients.

Gelfer Y, Tavor H, Oron A, Peer A, Halperin N, Robinson D. Deep vein thrombosis prevention in joint arthroplasties: continuous enhanced circulation therapy vs low molecular weight heparin. *J Arthroplasty*. 2006;21(2):206-214.

Deep vein thrombosis prevention efficacy using a new, miniature, mobile, battery-operated pneumatic system (continuous enhanced circulation therapy [CECT] system) combined with low-dose aspirin was compared to enoxaparin. One hundred twenty-one patients who underwent total hip or knee arthroplasty were prospectively randomized into 2 groups. The study group was treated by the CECT system starting immediately after the induction of anesthesia. Postoperatively, a daily 100-mg aspirin tablet was added. The control group received 40 mg of enoxaparin per day. Bilateral venography was performed at the fifth to eight postoperative day. In the CECT group, as compared to the enoxaparin group, there was a significantly lower overall rate of DVT and proximal DVT. Safety profiles were similar in both groups. The combination of the CECT device with low-dose aspirin is more effective than enoxaparin in preventing deep-vein thrombosis after lower limb arthroplasties.

Ben-Galim P, Steinberg EL, Rosenblatt Y, Parnes N, Menahem A, et al. A miniature and mobile intermittent pneumatic compression device for the prevention of deep-vein thrombosis after joint replacement. *Acta Orthop Scand*. 2004;75(5):584-587.

The WizAir-DVT is a miniature, lightweight (690 g), battery-operated and mobile intermittent pneumatic compression device (ICD), which enables continuous intraoperative use and immediate patient mobilization postoperatively. We compared its efficacy with a commonly used ICD, the Kendall SCD. Peak femoral vein flow velocity was measured in 20 apparently healthy volunteers at rest and with each device: we found no significant differences between them. A second prospective, randomized, clinical trial was used to compare the efficiency of the device in preventing deep venous thrombosis (DVT) after joint replacement in 50 patients (n=25/group). None developed DVT. Doppler ultrasonography revealed no significant differences. The WizAir-DVT antithrombotic compression device is as safe and effective as the Kendall SCD.

Murakami M, McDill TL, Cindrick-Pounds L, et al. Deep venous thrombosis prophylaxis in trauma: improved compliance with a novel miniatur-ized pneumatic compression device. *J Vasc Surg*. 2003;38(5):923-927.

OBJECTIVE: Intermittent pneumatic compression (IPC) devices prevent lower-extremity deep venous thrombosis (LEDVT) when used properly, but compliance remains an issue. Devices are frequently discontinued when patients are out of bed, and they are rarely used in emergency departments. Trauma patients are at high risk for LEDVT; however, IPCs are underused in this population because of compliance limitations. The hypothesis of this study was that a new miniaturized, portable, battery-powered pneumatic compression device improves compliance in trauma patients over that provided by a standard device.

METHODS: This was a prospective trial in which trauma patients (mean age, 46 years; revised trauma score, 11.7) were randomized to DVT prophylaxis with a standard calf-length sequential IPC device (SCD group) or a miniaturized sequential device (continuous enhanced-circulation therapy [CECT] group). The CECT device can be battery-operated for up to 6 hours and worn during ambulation. Timers attached to the devices, which recorded the time each device was applied to the legs and functioning, were used to quantify compliance. For each subject in each location during hospitalization, compliance rates were deter-mined by dividing the number of minutes the device was functioning by the total minutes in that location. Compliance rates for all subjects were averaged in each location: emergency department, operating room, intensive care unit, and nursing ward. RESULTS: Total compliance rate in the CECT group was significantly higher than in the SCD group (77.7% vs. 58.9%, P =.004). Compliance in the emergency department and nursing ward were also significantly greater with the CECT device (P =.002 and P =.008, respectively).

CONCLUSIONS: Previous studies have demonstrated that reduced compliance with IPC devices results in a higher incidence of LEDVT. Given its ability to improve compliance, the CECT may provide superior DVT prevention compared with that provided by standard devices.

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