

## Thromboprophylaxis in Knee Arthroscopy Patients: Revisiting Values and Preferences

The most common orthopedic operation worldwide is knee arthroscopy. The best-practice guidelines for thromboprophylaxis for knee arthroscopy patients remain to be determined. Because of uncertainty about the perioperative and postoperative risk for deep venous thrombosis (DVT), physicians have been noncommittal about the need for thromboprophylaxis in such patients, especially because diagnostic arthroscopy and arthroscopy-assisted knee surgery are mostly performed in young patients. This debate about the need for thromboprophylaxis is important, because approximately 3.5 million knee arthroscopies are performed per year globally (1, 2). Although clinical venous thromboembolism (VTE) is uncommon and deaths are rare, this huge volume of surgery has the potential to substantially increase the burden of VTE in young patients.

Guidelines for thromboprophylaxis with knee arthroscopy are ambiguous, reflecting the gap between the potential for aggregate harm and the slender body of evidence. In 2004, the American College of Chest Physicians guidelines (3) recommended that “clinicians do not use routine thromboprophylaxis in these patients, other than early mobilization (Grade 2B). . . . For patients undergoing arthroscopic knee surgery who are at a higher than usual risk, based on preexisting VTE risk factors or following a prolonged or complicated procedure, [they] suggest thromboprophylaxis with LMWH [low-molecular-weight heparin] (Grade 2B).” The 2006 International Consensus Statement guidelines (4) state that for simple diagnostic arthroscopy, “routine prophylaxis is not recommended unless other risk factors are present (Grade C).” For patients undergoing arthroscopic knee surgery, such as ligament reconstructions, “LMWH starting before or after surgery (Grade B) or IPC [intermittent pneumatic compression] in the presence of contraindications to LMWH are recommended (Grade C) until full ambulation.” The B and C ratings of these recommendations reflect the limited available data at that time.

Randomized trials published in 2001 (5), 2002 (6), and 2007 (7) suggest that LMWH thromboprophylaxis reduces the frequency of DVT to an extent that is both statistically and clinically significant. In this issue, Camporese and colleagues (8) report the findings of a large randomized trial of LMWH prophylaxis and full-length graduated compression stockings in adults undergoing knee arthroscopy. This large, clinically relevant trial provides pertinent information about the need for thromboprophylaxis in patients undergoing knee arthroscopy; 1761 consecutive patients were enrolled. Patients were randomly assigned to wear full-length graduated compression stockings for 7 days (660 patients) or to receive once-daily subcuta-

neous LMWH for 7 days (657 patients) or 14 days (444 patients). To detect asymptomatic DVT, the authors did bilateral whole-leg ultrasonography at the end of the allocated prophylactic course or earlier if indicated.

The primary efficacy end point showed a 3-month cumulative incidence of VTE of 3.2% (21 of 660 patients) in the stockings group and 0.9% (6 of 657 patients) in the 7-day LMWH group (absolute reduction, 2.3 percentage points [95% CI, 0.7 to 4.0 percentage points];  $P = 0.005$ ). The data safety monitoring board stopped the 14-day LMWH group early, when the cumulative incidence of VTE was 0.9% (4 of 444 patients). The cumulative incidence of major or clinically relevant bleeding was 0.3% (2 of 660 patients) in the stockings group, 0.9% (6 of 657 patients) in the 7-day LMWH group (absolute difference,  $-0.6$  percentage point [95% CI,  $-1.5$  to 0.2 percentage points]), and 0.5% (2 of 444 patients) in the discontinued 14-day LMWH group. The authors reported that meniscectomy was independently associated with the development of the composite primary efficacy end point (VTE, death). Deep venous thrombosis occurred infrequently in nonmeniscectomy arthroscopy patients in both the 7-day LMWH group and the stockings group.

This study (8) confirms the findings of 3 previous knee arthroscopy trials, adding substantive information underpinning the efficacy and safety of LMWH prophylaxis. The authors discuss the balance of benefit to harm articulately, pointing out that the bleeding was clinically relevant but not life-threatening. The authors recommend offering a short course of LMWH prophylaxis to all patients undergoing knee arthroscopy.

The authors acknowledge several limitations that may affect the internal and external validity (generalizability) of the study results. First, the clinical team was not blinded to the intervention a patient received; however, the authors minimized bias by using a central, blinded adjudication committee to decide the study outcomes. Second, ultrasonography is an imperfect test that will underestimate the actual incidence of DVT. Third, the authors excluded patients who had prolonged arthroscopic procedures or had risk factors for VTE. Fourth, and most important, nearly half of the symptomatic, confirmed events that made up the primary composite outcome measure were distal DVT, which some argue is a less clinically relevant disorder because of the low embolic risk (9, 10). However, none of these potential limitations negate the authors' conclusion that “withholding prophylaxis after knee arthroscopy exposes these predominately young patients to a small but definite risk” for VTE (8).

How does Camporese and colleagues' study (8) advance our knowledge? I believe that the findings should change clinical practice in individual patients. At the very

least, the quality of evidence is now stronger because of the trial's large sample size, rigorous conduct, and subgroup analysis identifying the higher risk for DVT in patients undergoing arthroscopic meniscectomy surgery. Patients undergoing arthroscopic knee surgery have a largely avoidable increased risk for a negative outcome due to postoperative VTE. Of importance, the authors' found that 7 days of LMWH thromboprophylaxis is sufficient in these "low-risk" patients (8).

Because this study characterizes the harms of thromboprophylaxis in a large sample, we can form a qualitative judgment about the balance of harms and benefits. Although LMWH was more effective than stockings, it increases the frequency of clinically relevant—albeit mild—bleeding. On the basis of the relatively high incidence of VTE associated with arthroscopic meniscectomy and the substantial reduction in incidence with LMWH, I conclude that administering LMWH thromboprophylaxis to arthroscopic knee surgery patients undergoing meniscectomy is reasonable because of the substantial absolute reduction in risk for VTE—which presumably includes the rare tragedy of massive or fatal pulmonary embolism. Given the huge volume of surgery, this policy means that many patients worldwide will avoid this rare complication.

Camporese and colleagues show that the incidence of VTE was lower in the patients undergoing diagnostic arthroscopy without surgery, but these patients probably remain at risk for clinically relevant bleeding. Thus, the balance of harms and benefits is less clear for patients with diagnostic arthroscopy than for those undergoing arthroscopy with meniscectomy. The clinician and the consensus guideline maker face a conundrum. How should they decide whether the harms exceed the benefits in especially low-risk groups?

One way out of this dilemma is to use the principles of expected-value decision making, which assesses the balance of benefits and harm, considering the patients' values and preferences for the potential outcomes, as well as the probability of those outcomes. We may ask whether physicians—especially those who are writing the guidelines—are substituting their values for their patient's values, because current policy, which is not to give thromboprophylaxis, seems to place a relatively high value on minimizing bleeding complications and a relatively low value on preventing asymptomatic DVT (3). This philosophy reflects a high value placed on harm avoidance ("first do no harm"). Should we base decision making on the patient's values for the outcomes that they face, or on our values for the outcomes that we—the profession—face? The answer seems obvious. It is time to revisit policies that maximize bleeding avoidance and minimize thrombosis avoidance. Postoperative VTE may present without warning as fatal pulmonary embolism, a potentially avoidable tragedy. Thus, sudden death due to massive pulmonary embolism may well be the dominant harm rather than fatal bleeding due to thromboprophylaxis, but we will not know until we

learn our patients' preferences and measure the frequency of these outcomes.

These considerations underscore the need for a better understanding of the harms of prophylaxis. An immediate and important contribution to the understanding of values and preferences in the debate about thromboprophylaxis is to begin a prospective global registry of patients to evaluate harm due to symptomatic VTE and bleeding due to thromboprophylaxis using LMWH. Such a registry is feasible, particularly in Europe—where LMWH prophylaxis is more commonly used after arthroscopy. These studies should measure participants' utilities for the outcomes that they face, the costs of care, and the frequency of the outcomes of care, which are needed to perform a cost-effectiveness analysis on which to base future guidelines for thromboprophylaxis in knee arthroscopy.

The finding reported by Camporese and colleagues (8) encourages the use of LMWH thromboprophylaxis in knee arthroscopy patients undergoing meniscectomy. The aggregate evidence supports this recommendation. A clear answer about thromboprophylaxis in nonmeniscectomy patients—which includes diagnostic arthroscopy patients—awaits further research to precisely define the incidence of DVT according to the type of arthroscopic procedure.

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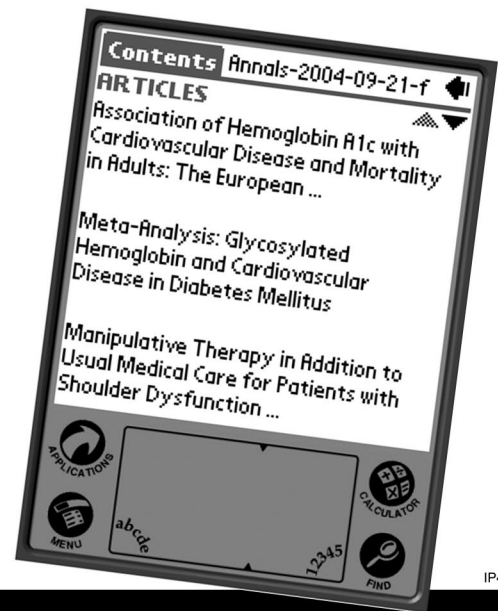
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