

Prevention of Symptomatic Pulmonary Embolism in Patients Undergoing Total Hip or Knee Arthroplasty

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This clinical practice guideline was approved by the American Academy of Orthopaedic Surgeons. Approximately four AAOS Clinical Practice Guidelines will be developed per year, with summaries regularly presented in the *Journal of the American Academy of Orthopaedic Surgeons*. This guideline summary is first of the series.

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Abstract

This clinical practice guideline is based on a systematic review of published studies on the management of adult patients undergoing total hip replacement (THR) or total knee replacement (TKR) aimed specifically at preventing symptomatic pulmonary embolism (PE). The guideline emphasizes the need to assess the patient's risk for both PE and postoperative bleeding. Mechanical prophylaxis and early mobilization are recommended for all patients. Chemoprophylactic agents were evaluated using a systematic literature review. Forty-two studies met eligibility criteria, of which 23 included patients who had TKR and 25 included patients who had THR. The following statements summarize the recommendations for chemoprophylaxis:

Patients at standard risk of both PE and major bleeding should be considered for aspirin, low-molecular-weight heparin (LMWH), synthetic pentasaccharides, or warfarin with an international normalized ratio (INR) goal of ≤ 2.0 .

Patients at elevated (above standard) risk of PE and at standard risk of major bleeding should be considered for LMWH, synthetic pentasaccharides, or warfarin with an INR goal of ≤ 2.0 .

Patients at standard risk of PE and at elevated (above standard) risk of major bleeding should be considered for aspirin, warfarin with an INR goal of ≤ 2.0 , or none.

Patients at elevated (above standard) risk of both PE and major bleeding should be considered for aspirin, warfarin with an INR goal of ≤ 2.0 , or none.

Overview and Rationale

This clinical practice guideline was approved by the American Academy of Orthopaedic Surgeons (AAOS) on May 18, 2007. It is based on a systematic review of published studies on the management of adult patients undergoing total hip replacement (THR) or total knee replacement

(TKR) aimed specifically at preventing symptomatic pulmonary embolism (PE). In addition to providing practice recommendations, this guideline also highlights gaps in the literature and areas that require future research.

The purpose of this clinical practice guideline is to help improve treatment based on the current best evidence. Cur-

rent evidence-based practice standards demand that physicians use the best available evidence in their clinical decision making. To assist in this, this clinical practice guideline consists of a series of systematic reviews of the available literature regarding the prevention of PE in patients undergoing THR or TKR. These systematic reviews were conducted on August 28, 2006,

for pertinent articles published between 2000 and 2006 initially, and subsequently extended back to publications that included patient populations enrolled after the start of 1996. The results of the reviews show where there is good evidence, where evidence is lacking, and what topics future research must target to improve the treatment of patients with osteoarthritis of the knee.

The PE Guideline Work Group, with the assistance of an Evidence Review Team (ERT) from the Center for Clinical Evidence Synthesis at Tufts Medical Center, systematically reviewed the available literature and subsequently wrote the following recommendations based on a rigorous, standardized process. Of the 14 recommendations developed, only recommendations 3.3.1,

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3.3.2, 3.3.3, and 3.3.4 are based on the systematic review of the literature. The other recommendations contained in this guideline are based on consensus development methods only.

Musculoskeletal care is provided in many different settings by many different providers. The AAOS Research Department with the collaboration of a Physician Workgroup have created this guideline as an educational tool to guide qualified physicians through a series of treatment decisions in an effort to improve the quality and efficiency of care. By the introduction of new statistical methodology, which is discussed in the data summaries, we have moved ahead from previous efforts and have created state-of-the-art guideline recommendations. This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution.

These evidence-based Clinical Practice Guidelines, approximately four developed per year, will be regularly presented as summaries in the *Journal of the American Academy of Orthopaedic Surgeons*. They each represent work by AAOS staff and volunteer committee members of the Evidence-Based Practice Committee and the Guidelines and Technology Oversight Committee. While we recognize that the literature is imperfect and thus any guideline must be supplemented by experience, principles of good care, and other sources of information for decision support, these guidelines represent the best source of defense, based on the broadest literature search possible.

These guidelines also represent the definition of quality orthopaedic practice from an evidence-based view. There will be measureable improvements in patient care quality standards as evidence emerges and is summarized as future guidelines.

Potential Harms and Contraindications

Most treatments are associated with some known risks, especially invasive and surgical treatments. In addition, contraindications vary widely based on the treatment administered. Therefore, discussion of available treatments and procedures applicable to the individual patient rely on mutual communication between the patient and physician.

Methods

The methods used to develop this clinical practice guideline were designed to combat bias, enhance transparency, and promote reproducibility. Their purpose is to allow interested readers the ability to inspect all of the information the Workgroup used to reach all of its decisions, and to verify that these decisions are in accord with the best available evidence. The draft of this guideline was subject to peer review and public commentary, and it was approved by the AAOS's Evidence-Based Practice Committee; Guidelines and Technology Committee; Council on Research, Quality Assessment and Technology; and Board of Directors. The methods used to prepare this guideline as well as the references to the literature are detailed in the full clinical practice guideline, which is available at http://www.aaos.org/research/guidelines/PE_guideline.pdf.

Rating the Quality of Evidence

The quality of evidence was rated using an evidence hierarchy for each of four different study types: therapeutic, prognostic, diagnostic, and economic or decision modeling. These hierarchies were predefined by the AAOS and appear on the AAOS Website at www2.aaos.org/aaos/archives/bulletin/feb03/fline1.htm.

Grading the Recommendations

Each guideline recommendation was graded using the following system:

A: Good evidence (level I studies with consistent finding) for recommending intervention.

B: Fair evidence (level II or III studies with consistent findings) for recommending intervention.

C: Poor quality evidence (level IV or V) for recommending intervention.

Recommendations

Of the 14 recommendations listed below, only recommendations 3.3.1, 3.3.2, 3.3.3, and 3.3.4 are based on the systematic review of the literature conducted between August 2006 and March 2007 by the Center for Clinical Evidence Synthesis at Tufts Medical Center. The other recommendations contained in this guideline are based on consensus development methods only.

Recommendation 1: Preoperative Care

Recommendation 1.1

All patients should be assessed preoperatively for elevated risk (greater than standard risk) of PE. The following patients are examples of

those considered to be at elevated risk:

- Hypercoagulable states
- Previous documented PE

Level of Evidence: III

Grade of Recommendation: B

Rationale for Recommendation 1.1

The risk of PE differs among different patients; however, there is currently no satisfactory evidence-based risk stratification system. There have been studies suggesting that the risk of PE is elevated in patients with previous history of cancer, thromboembolism, and hypercoagulable states such as polycythemia, as well as in spinal cord injury patients and multi-trauma patients.¹⁻³ It is also plausible that some patients may have genetic predisposition for development of PE.^{4,5} Currently no specific laboratory test can reliably identify patients at elevated risk of PE. Therefore, careful history taking and physical examination in combination with clinical judgment, which integrates knowledge of specific risk factors with the patient's clinical status, is the cornerstone of PE risk management for patients undergoing THR or TKR.

The identification of patients at elevated risk for PE is important in the selection process of appropriate thromboprophylactic regimens (see Recommendation 3.3).

Recommendation 1.2

All patients should be assessed preoperatively for elevated risk (greater than standard risk) of major bleeding. Patients with the following conditions are examples of those considered to be at elevated risk:

- History of a bleeding disorder
- History of recent gastrointestinal bleed
- History of recent hemorrhagic stroke

Level of Evidence: III

Grade of Recommendation: C

NB: This Grade of Recommendation was reduced from B to C because of the lack of consistent evidence in the literature on risk stratification of patient populations.

Rationale for Recommendation 1.2

The selection of a thromboprophylactic regimen should aim for a balance between efficacy and safety. All chemoprophylaxis agents, by virtue of their action, are associated with bleeding. Some agents may result in a higher incidence of bleeding following total joint arthroplasty,⁶ although the differences in bleeding rates with the currently used agents are unclear (see Recommendation 3.3).⁷⁻¹⁰ Patients on aspirin or mechanical prophylaxis alone, on the other hand, may have lower bleeding rates.^{6,11-13} Not only might the bleeding potential of different prophylactic agents vary, there may also be varying bleeding tendencies among individuals that may affect the bleeding risk with surgery.¹⁴ The intention of this recommendation is to identify patients who may be at elevated risk of major bleeding after THR or TKR. The type of prophylactic agent, the duration of prophylaxis, and the intensity of anticoagulation needs to be modulated based on the perceived bleeding risk in an individual patient. Some factors that may place a patient at an elevated risk of bleeding include a history of uncontrolled bleeding, and a known coagulation factor deficiency, a recent history of gastrointestinal bleeding, and recent hemorrhagic stroke. This recommendation highlights the central importance of careful history taking and physical examination for the purpose of risk stratification for bleeding. Although routine serological tests to screen patients for potential bleeding problems are not indicated, they may be useful in patients

for whom there is a high level of suspicion of a predisposition for bleeding.

Recommendation 1.3

Patients with known contraindications to anticoagulation should be considered for vena cava filter placement.

Level of Evidence: V

Grade of Recommendation: C

Rationale for Recommendation 1.3

A vena cava filter may reduce the risk of PE in a nonanticoagulated patient.¹⁵ The assumed ability of a filter to stop emboli originating in the lower extremities underlies the expected clinical usefulness of filters in selected total hip and knee patients. The very low level of evidence and strength of recommendation reflect the poor evidence base behind this decision-making process. The need for a filter is most commonly encountered when there is elevated preoperative risk of PE and a known contraindication for chemoprophylaxis, or if chemoprophylaxis becomes contraindicated in an elevated risk patient during the postoperative course. Similarly, if a patient with a known contraindication to chemoprophylaxis changes from standard to elevated PE risk in the postoperative period, a vena cava filter may be considered. Finally, in patients thought to be at elevated risk of major bleeding who develop symptomatic postoperative PE, a filter should be considered.

Recommendation 2: Intraoperative Care

Recommendation 2.1

Patients should be considered for intraoperative and/or immediate postoperative mechanical prophylaxis.

Level of Evidence: III

Grade of Recommendation: B

Rationale for Recommendation 2.1

Thrombogenesis activation begins during total hip arthroplasty through a variety of mechanisms. These include venous stasis due to anesthesia, immobilization, intimal injury (due to kinking of the femoral vein with dislocation of the hip and femoral canal preparation) and activation of the clotting cascade (by a variety of mechanisms).^{16,17} Mechanical venous compression ameliorates some of the factors involved in thrombogenesis and therefore should be considered intraoperatively, if practical and if there are no contraindications to use of the device.^{18,19} For THR, mechanical prophylaxis can easily be used on the nonsurgical limb, and there are sterile thigh-calf and calf-only pneumatic devices that can be used on the surgical limb.¹⁸⁻²⁰ In observational studies, the use of these devices (usually in combination with regional anesthesia and aspirin chemoprophylaxis) has been shown to result in a low rate of symptomatic PE.^{16,19} Alternatively, these pneumatic devices may be placed on the lower extremities in the recovery room after the procedure is completed.²¹ There is a variety of mechanical devices available, including thigh-calf, calf-only, and foot pumps.²² There are no prospective, randomized studies comparing the efficacy of these devices in the prevention of symptomatic PE.

The activation of thrombogenesis in TKR patients has been less well studied. Intraoperative mechanical compression can be used on the nonsurgical limb, but there is no effective sterile device for use on the surgical limb, especially if a tourniquet is used. Most studies begin use of a mechanical device on the surgical limb postoperatively in the recovery room.²³⁻²⁶

Recommendation 2.2

In consultation with the anesthesiologist, patients should be considered

for regional anesthesia.

Level of Evidence: IV

Grade of Recommendation: C

Rationale for Recommendation 2.2

Regional anesthesia (spinal, epidural or hypotensive epidural with cardiac monitoring) has been recommended over general endotracheal anesthesia for THR and TKR patients.^{16,17,27,28} Regional anesthesia has been shown to decrease venous flow less and result in fewer pulmonary complications. However, there is only circumstantial evidence that regional anesthesia, as part of a multimodal prophylaxis protocol, reduces the prevalence of symptomatic and fatal PE.^{18,19,27}

The choice of anesthetic technique for these patients is based on multiple factors, including thromboembolism prophylaxis. There should be close consultation between the surgeon and the anesthesiologist for the anesthetic technique.

Recommendation 3: Postoperative/Inpatient Care

Recommendation 3.1

Postoperatively, patients should be considered for continued mechanical prophylaxis until discharge to home.

Level of Evidence: IV

Grade of Recommendation: C

Rationale for Recommendation 3.1

Unless contraindicated, mechanical compression should be used for both THR^{16,18-21,25} and TKR.²³⁻²⁶ for patients in the recovery room and during the hospital stay. The optimal number of hours daily that mechanical compression should be used is unknown. A team approach involving surgeons, nurses, aides, and therapists is required to optimize the amount of time the devices are on the patients' limbs. Many patients are transferred to "same site" reha-

bilitation floors or hospital services early postoperatively. It is recommended that mechanical prophylaxis continue at these locations if practical.

One prospective randomized study showed that rapid-inflation, asymmetric calf compression was superior to circumferential calf compression in total knee patients.²³ For total hip patients, the postoperative devices studied included thigh-calf compression,^{18,19} rapid-inflation calf,^{21,25} other calf compression, and foot pumps, usually part of a multimodal prophylaxis protocol. Patient preferences and comfort should be taken into account, when feasible. One study reported a high prevalence of patient intolerance and discontinuation of foot pumps postoperatively after THR.¹²

Recommendation 3.2

Postoperatively, patients should be mobilized as soon as feasible to the full extent of medical safety and comfort.

Level of Evidence: V

Grade of Recommendation: C

Rationale for Recommendation 3.2

At a minimum, patients should be taught to actively dorsiflex and plantar flex the ankle and toes. This exercise should be performed in sets of 10 to 20 every half hour when the patient is awake. A plan for pain management that allows control for the patient to be out of bed and subsequently ambulate should be in place before surgery. All patients should be out of bed to a sitting chair several times a day for several hours at a time to encourage deep breathing and avoid recumbency. All efforts should be made to have the patient stand and ambulate within the restrictions placed by the surgical surgeon. Practices should be in place to ensure that appropriate physical

therapy, ambulatory assistance, and support are provided by the first postoperative day. Patients who are treated with epidural catheters postoperatively should also be out of bed to a chair as soon as feasible. Standing and ambulation should begin for these patients when they are physically capable of it. During hospitalization, when patients are not ambulating, mechanical prophylaxis should remain in place at all times, even when the patient is out of bed.

Recommendation 3.3

Chemoprophylaxis of patients undergoing hip or knee replacement.

Recommendation 3.3.1 (based on systematic review)

Patients at standard risk of both PE and major bleeding should be considered for one of the chemoprophylactic agents evaluated in this guideline, including (in alphabetical order):

a. Aspirin, 325 mg 2×/d (reduce to 81 mg 1×/d if gastrointestinal symptoms develop), starting the day of surgery, for 6 weeks.

b. LMWH, dose per package insert, starting 12 to 24 hours postoperatively (or after an indwelling epidural catheter has been removed), for 7 to 12 days. (NB: The LMWHs have not been sufficiently evaluated for longer periods to allow recommendation beyond this period.)

c. Synthetic pentasaccharides, dose per package insert, starting 12 to 24 hours postoperatively (or after an indwelling epidural catheter has been removed), for 7 to 12 days. (NB: The synthetic pentasaccharides have not been sufficiently evaluated for longer periods to allow recommendation beyond this period.)

d. Warfarin, with an international normalized ratio (INR) goal of ≤ 2.0 , starting either the night before or the night after surgery, for 2 to 6 weeks.

Level of Evidence: III

Grade of Recommendation: B

(choice of prophylactic agent), C (dosage and timing)

NB: The Grade of Recommendation was reduced from B to C for dosage and timing because of the lack of consistent evidence in the literature defining a clearly superior regime.

Rationale for Recommendation 3.3.1

Patients with standard risk of PE and standard risk of major bleeding represent the majority of total joint arthroplasty patients. As noted in the introduction to this guideline orthopaedic surgery carries with it a higher level of risk for thromboembolic complications than for general surgical or medical patients. Therefore the term “standard” should be understood as a relative term specifically for hip and knee replacement. Since the incidence rates of symptomatic PE are low, it is not possible to make definitive recommendations on the occurrence of PE alone. To determine differences in current chemoprophylactic regimens, we would need at least 25,000 and 150,000 patients, respectively (calculated using a relative risk of 0.5 for the efficacy of prophylaxis). These low incidence rates of PE and fatal PE mean that we must look more closely at the opposite side of the risk equation and fully assess the adverse effects (primarily bleeding) that result from our recommendations.

The bleeding risk from chemoprophylactic agents may rise with increased effectiveness in reducing deep vein thrombosis (DVT).⁶ The incidence of major bleeding is <1% in patients without chemoprophylaxis and may be as high as about 3% to 5% in patients given chemoprophylactic agents.²⁹ Precise estimates of the true risk of bleeding are difficult to obtain since the definitions of major bleeds vary among different studies. In general, the defi-

nitions of a major bleed include life-threatening, intraocular, or intracerebral bleeds, or a bleed requiring more than a specified number of transfusions. Furthermore, most of the prospective data from drug comparison studies use selected populations, which exclude patients with prior gastrointestinal bleeds and noncompliant or frail patients. Also patients may not have been included within the major bleed definitions if they had bleeding events that did not immediately affect surgical outcomes. In general, clinical outcomes in patients with a defined major bleed or in the spectrum of patients with lesser bleeding have not been well studied.

The present recommendations reflect the Work Group’s concerns about increased bleeding associated with the use of chemoprophylactic agents without a demonstrated reduction in PE. The duration for the administration of chemoprophylactic agents has not been clearly established. The older literature notes that most postoperative PEs occurred within the first 6 weeks.³⁰⁻³⁴ Therefore, many regimens were established to conform to that experience. Some reports on the heparinlike drugs, show that it is not necessary to prolong the administration beyond the first 8 to 12 days.³⁵ The Work Group’s recommendations reflect these practices.

Combinations of agents may also be considered, such as a short course of LMWH followed by aspirin. However, there is no definitive evidence that demonstrates a reduction in PE using any of these regimens.

Recommendation 3.2, which recommends that patients should be mobilized rapidly after surgery unless contraindicated, should be viewed as universally applicable, regardless of choice of chemical chemoprophylaxis. Mechanical devices have no inherent bleeding risk;

however, their effectiveness in reducing the incidence of PE has not been definitively demonstrated. Therefore, they remain an adjunct in the armamentarium for prophylaxis unless there is a contraindication for chemoprophylaxis, in which case they become the primary means of prevention.

Recommendation 3.3.2 (based on systematic review)

Patients at elevated (above standard) risk of PE and at standard risk of major bleeding should be considered for one of the following chemoprophylactic agents (in alphabetical order):

a. LMWH, dose per package insert, starting 12 to 24 hours postoperatively (or after an indwelling epidural catheter has been removed), for 7 to 12 days. (NB: The LMWHs have not been sufficiently evaluated for longer periods to allow recommendation beyond this period.)

b. Synthetic pentasaccharides, dose per package insert, starting 12 to 24 hours postoperatively (or after an indwelling epidural catheter has been removed), for 7 to 12 days. (NB: The synthetic pentasaccharides have not been sufficiently evaluated for longer periods to allow recommendation beyond this period.)

c. Warfarin, with an INR goal of ≤ 2.0 , starting either the night before or the night after surgery, for 2 to 6 weeks.

Level of Evidence: III

Grade of Recommendation: B (choice of prophylactic agent), C (dosage and timing)

NB: The grade of Recommendation was reduced from B to C for dosage and timing because of the lack of consistent evidence in the literature on risk stratification of patient populations. No studies currently include patients at elevated risk of major bleeding in study groups.

Rationale for Recommendation 3.3.2

Warfarin (INR ≤ 2.0), LMWH, or a synthetic pentasaccharide is recommended as chemoprophylaxis for patients known or suspected to be at increased risk of PE after total hip or knee arthroplasty. In this clinical setting, the customary risk-benefit balance between therapeutic anticoagulation and bleeding risk is tipped in favor of the most effective prophylaxis while acknowledging a potentially higher bleeding risk as a tradeoff for optimal efficacy in prevention of PE.

The data presented in Figures 1 and 2 do not demonstrate differentiation of effectiveness among any of the chemoprophylactic agents in the prevention of PE. This is in clear contrast to the results of DVT oriented studies, where there is evidence to support distinctions. For example, the efficacy in prevention of DVT has been shown, in declining order, for the synthetic pentasaccharide (fondaparinux), LMWH (enoxaparin, dalteparin),^{7,36-38} and low intensity warfarin (INR 2.0).³⁹

Although the incidence of major bleeding after THR appears to be higher than TKR (Figures 3 and 4), the clinical tolerance for major bleeding may be less after TKR owing to the more superficial nature of the knee and the tenuous character of its soft-tissue envelope. Therefore, a higher level of concern for postoperative bleeding in TKR is prevalent among most surgeons in light of a theoretically higher potential for a bleed to compromise the clinical outcome.

In addition to the use of chemoprophylactic agents it is prudent to employ other adjunctive measures as outlined in Recommendations 2.1, 2.2, and 3.1.

Recommendation 3.3.3 (based on systematic review)

Patients at standard risk of PE and at elevated (above standard) risk of major bleeding should be considered for one of the following chemoprophylactic agents (in alphabetical order):

a. Aspirin, 325 mg 2 \times /d (reduce to 81 mg 1 \times /d if gastrointestinal symptoms develop), starting the day of surgery, for 6 weeks.

b. Warfarin, with an INR goal of ≤ 2.0 , starting either the night before or the night after surgery, for 2 to 6 weeks.

c. None.

Level of Evidence: III

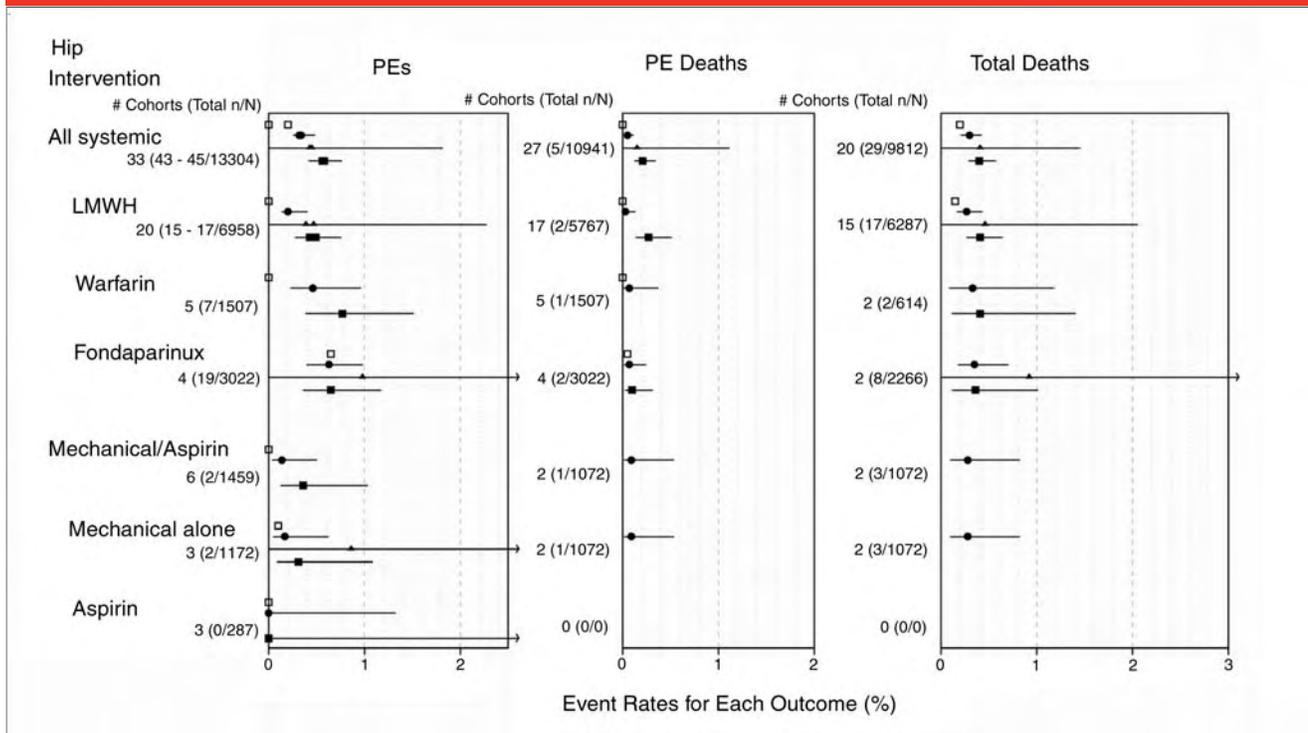
Grade of Recommendation: C

NB: This Grade of Recommendation was reduced from B to C because of the lack of consistent evidence in the literature on risk stratification of patient populations. No studies currently include patients at elevated risk of major bleeding in study groups.

Patients who are at standard risk of PE but at an elevated risk of major bleeding are relatively uncommon. Examples of this include thrombocytopenia, bone marrow suppression, known hemophilia or other defined coagulation defects, recent radiation, and chemotherapy. The management of these patients should be individualized (perhaps in association with a hematologist). The first priority is to correct the clotting defect, if possible, before surgery, using transfusions of clotting factors, platelets, or frozen plasma. The use of a chemoprophylactic agent in a patient with a known diminished ability to clot must be considered judiciously, as there is currently no evidence base to assist in this decision.

In addition to the use of chemoprophylactic agents it is prudent to employ other adjunctive measures as outlined in Recommendations 2.1, 2.2, and 3.1.

Figure 1



Summary pulmonary embolism, pulmonary embolism death, and total death rates for patients after hip arthroplasty receiving different prophylaxis regimens. Dotted vertical lines represent 0.2% increments. Where there are ranges of total n's (events), one or more studies were unclear as to the total number of events (eg, whether pulmonary embolisms were confirmed or not, whether deaths were due to confirmed pulmonary embolism or not). Multiple medians or averages represent the range of estimates. These approaches do not adequately account for the heterogeneity of interventions, follow-up duration, quality, applicability, etc. These analyses do not include studies that excluded events that occurred in-hospital. PE = pulmonary embolism. All systemic = low-molecular-weight heparin (LMWH) + warfarin + fondaparinux studies combined (in addition to studies that combined these interventions). LMWH = LMWH alone and combination LMWH and mechanical; warfarin = warfarin alone and combination warfarin and mechanical; mechanical/aspirin = either mechanical alone, aspirin alone, or mechanical and aspirin; aspirin = aspirin and combination aspirin and mechanical. □ = median rate among studies (only determined if 3 cohorts of patients), • = simple average (total n/total N) and "exact" estimate of CI of that average, ▲ = random effects estimate and CI using Bayesian methodology, ■ = random effects estimate and CI using logit of proportions methodology. (Reprinted from Lachiewicz PF: Prevention of symptomatic pulmonary embolism in patients undergoing total hip and knee arthroplasty: Clinical guideline of the American Academy of Orthopaedic Surgeons. *Instr Course Lect* 2009;58:795-804.)

Recommendation 3.3.4 (based on systematic review)

Patients at elevated (above standard) risk of both PE and major bleeding should be considered for one of the following chemoprophylactic agents (in alphabetical order):

a. Aspirin, 325 mg 2×/d (reduce to 81 mg 1×/d if gastrointestinal symptoms develop), starting the day of surgery, for 6 weeks.

b. Warfarin, with an INR goal of ≤2.0, starting either the night before

or the night after surgery, for 2 to 6 weeks.

c. None.

Level of Evidence: III

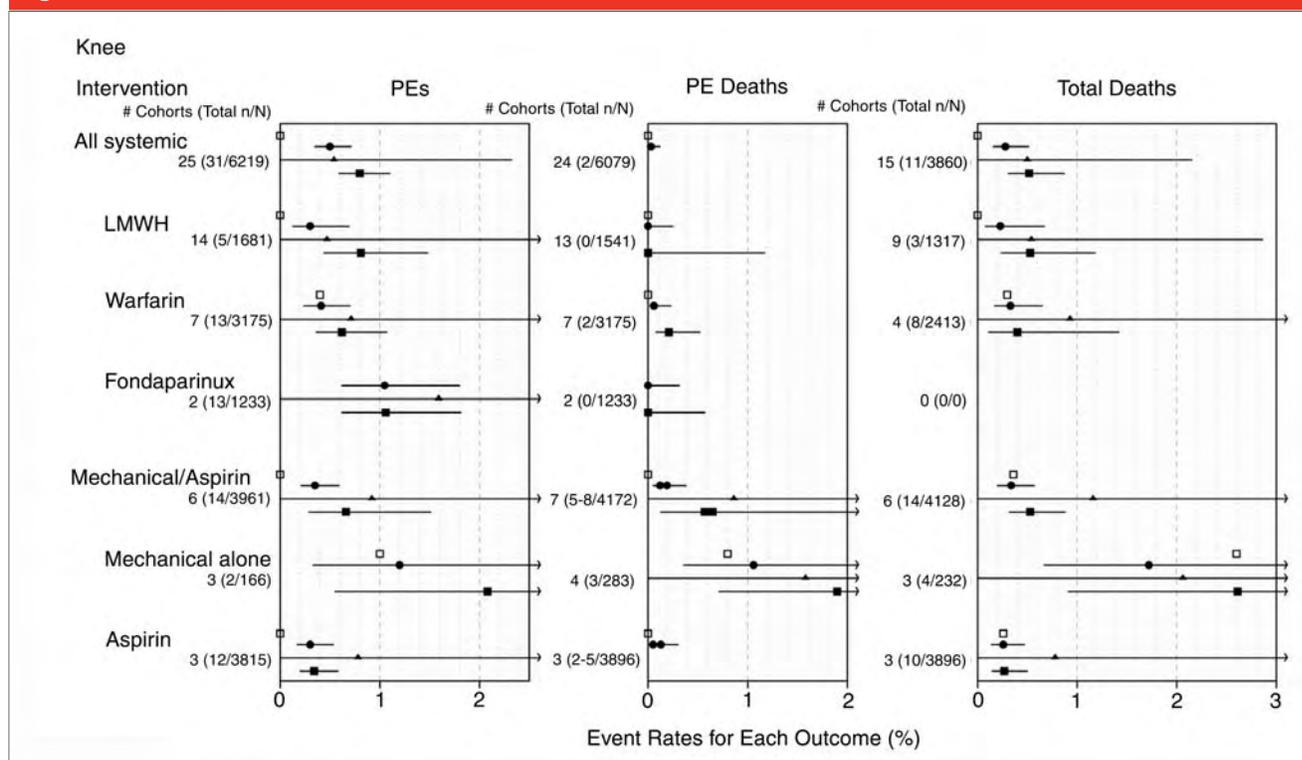
Grade of Recommendation: C

NB: This Grade of Recommendation was reduced from B to C because of the lack of consistent evidence in the literature on risk stratification of patient populations. No studies currently include patients at elevated risk of major bleeding and PE in study groups.

Rationale for Recommendation 3.3.4

In the setting of elevated risk of both PE and major bleeding (above standard risk), the selection of the most appropriate prophylactic regimen is dependent on the clinical judgment of the surgeon and medical consultants. The final judgment is the result of integrating the knowledge of the severity of existent risk factors for PE and bleeding with the patient's current status. Although the recom-

Figure 2



Summary pulmonary embolism, pulmonary embolism death, and total death rates for patients after knee arthroplasty receiving different prophylaxis regimens. Dotted vertical lines represent 0.2% increments. Where there are ranges of total n's (events), one or more studies were unclear as to the total number of events (eg, whether pulmonary embolisms were confirmed or not, whether deaths were due to confirmed pulmonary embolism or not). Multiple medians or averages represent the range of estimates. These approaches do not adequately account for the heterogeneity of interventions, follow-up duration, quality, applicability, etc. These analyses do not include studies that excluded events that occurred in-hospital. PE = pulmonary embolism. All systemic = low-molecular-weight heparin (LMWH) + warfarin + fondaparinux studies combined (in addition to studies that combined these interventions). LMWH = LMWH alone and combination LMWH and mechanical; warfarin = warfarin alone and combination warfarin and mechanical; mechanical/aspirin = either mechanical alone, aspirin alone, or mechanical and aspirin; aspirin = aspirin and combination aspirin and mechanical. □ = median rate among studies (only determined if 3 cohorts of patients), • = simple average (total n/total N) and "exact" estimate of CI of that average, ▲ = random effects estimate and CI using Bayesian methodology, ■ = random effects estimate and CI using logit of proportions methodology. (Reprinted from Lachiewicz PF: Prevention of symptomatic pulmonary embolism in patients undergoing total hip and knee arthroplasty: Clinical guideline of the American Academy of Orthopaedic Surgeons. *Instr Course Lect* 2009;58:795-804.)

recommendations 3.3.3 and 3.3.4 regarding chemoprophylaxis contain identical agents, the range of options (from warfarin to no chemoprophylaxis) is wide. Particularly for patients at elevated risk of both PE and major bleeding, it is very important that the physician has as accurate an assessment as possible of the actual likelihood of a life-threatening PE. Aspirin, with its attendant very low risk of bleeding, and warfarin, which can be dosed to lower INRs in high-

risk bleeding situations, are the agents recommended if chemoprophylaxis is deemed necessary.

In addition to the use of chemoprophylactic agents it is prudent to employ other adjunctive measures as outlined in Recommendations 2.1, 2.2, and 3.1.

Recommendation 3.4

Routine screening for DVT or PE postoperatively in asymptomatic patients is not recommended.

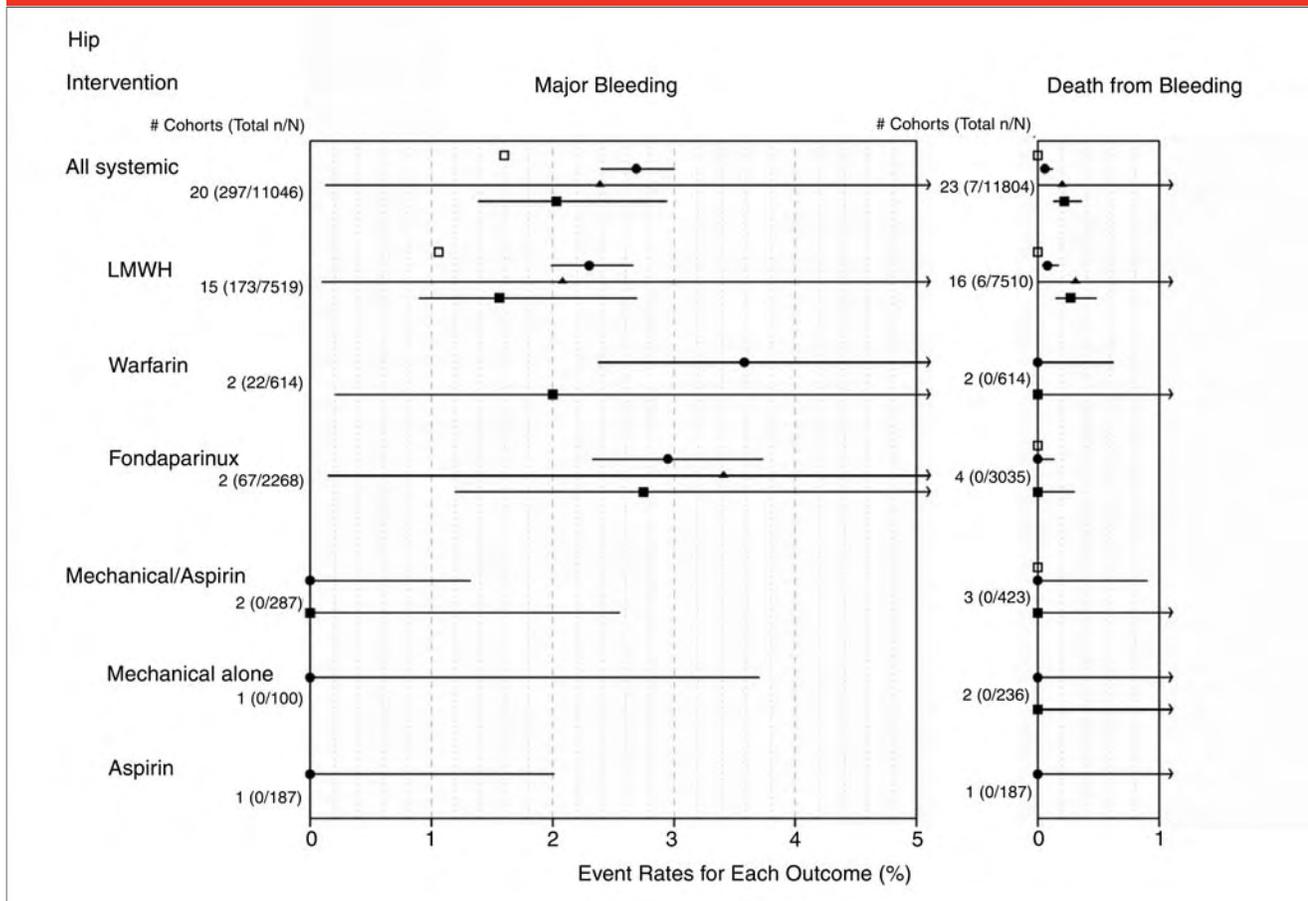
Level of Evidence: III

Grade of Recommendation: B

Rationale for Recommendation 3.4

Specific recommendation is made against routine surveillance for venous thromboembolism after THR or TKR. There is neither a sufficiently sensitive noninvasive screening tool nor a clearly established period of risk for venous thromboembolism as to make routine

Figure 3



Major bleeding and death from bleeding rates for patients after hip arthroplasty receiving different prophylaxis regimens. Dotted vertical lines represent 0.2% increments. Where there are ranges of total n's (events), one or more studies were unclear as to the total number of events (eg, whether pulmonary embolisms were confirmed or not, whether deaths were due to confirmed pulmonary embolism or not). Multiple medians or averages represent the range of estimates. These approaches do not adequately account for the heterogeneity of interventions, follow-up duration, quality, applicability, etc. These analyses do not include studies that excluded events that occurred in-hospital. PE = pulmonary embolism. All systemic = low-molecular-weight heparin (LMWH) + warfarin + fondaparinux studies combined (in addition to studies that combined these interventions). LMWH = LMWH alone and combination LMWH and mechanical; warfarin = warfarin alone and combination warfarin and mechanical; mechanical/aspirin = either mechanical alone, aspirin alone, or mechanical and aspirin; aspirin = aspirin and combination aspirin and mechanical. □ = median rate among studies (only determined if 3 cohorts of patients), • = simple average (total n/total N) and "exact" estimate of CI of that average, ▲ = random effects estimate and CI using Bayesian methodology, ■ = random effects estimate and CI using logit of proportions methodology. (Reprinted from Lachiewicz PF: Prevention of symptomatic pulmonary embolism in patients undergoing total hip and knee arthroplasty: Clinical guideline of the American Academy of Orthopaedic Surgeons. *Instr Course Lect* 2009;58:795-804.)

screening reliably predictive or cost-effective in preventing PE.

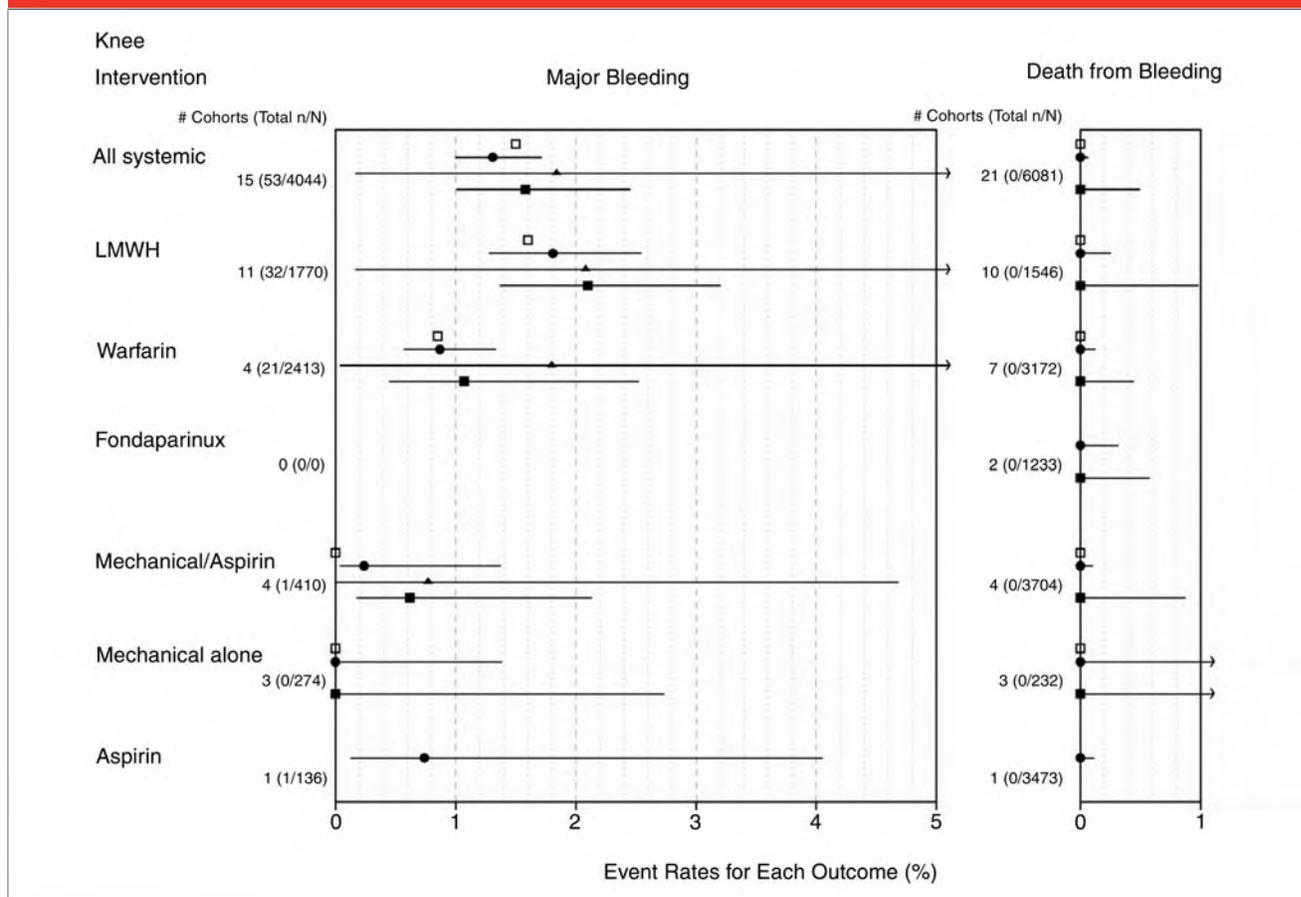
The premise that routine screening is an effective strategy to prevent PE is predicated upon the hypothesis that secondary prophylaxis, namely prevention of propagation and embolization of existing thrombi, is a valid approach to reducing the in-

cidence of PE. One study of more than 3,000 patients with 6-month follow-up of readmission for symptomatic proximal DVT or PE demonstrated a readmission rate in patients discharged without continued anticoagulation on the basis of negative screening contrast venography nearly 8 times greater than patients

who received 6 weeks of warfarin based on a positive screening venogram or empiric continuation of prophylaxis.^{40,41}

Other imaging modalities have been suggested for routine screening. Duplex ultrasound is highly operator dependent, test performance is variable from institution to institution, and the test is

Figure 4



Major bleeding and death from bleeding rates for patients after hip arthroplasty receiving different prophylaxis regimens. Dotted vertical lines represent 0.2% increments. Where there are ranges of total n's (events), one or more studies were unclear as to the total number of events (eg, whether pulmonary embolisms were confirmed or not, whether deaths were due to confirmed pulmonary embolism or not). Multiple medians or averages represent the range of estimates. These approaches do not adequately account for the heterogeneity of interventions, follow-up duration, quality, applicability, etc. These analyses do not include studies that excluded events that occurred in-hospital. PE = pulmonary embolism. All systemic = low-molecular-weight heparin (LMWH) + warfarin + fondaparinux studies combined (in addition to studies that combined these interventions). LMWH = LMWH alone and combination LMWH and mechanical; warfarin = warfarin alone and combination warfarin and mechanical; mechanical/aspirin = either mechanical alone, aspirin alone, or mechanical and aspirin; aspirin = aspirin and combination aspirin and mechanical. □ = median rate among studies (only determined if 3 cohorts of patients), • = simple average (total n/total N) and "exact" estimate of CI of that average, ▲ = random effects estimate and CI using Bayesian methodology, ■ = random effects estimate and CI using logit of proportions methodology. (Reprinted from Lachiewicz PF: Prevention of symptomatic pulmonary embolism in patients undergoing total hip and knee arthroplasty: Clinical guideline of the American Academy of Orthopaedic Surgeons. *Instr Course Lect* 2009;58:795-804.)

not sensitive to thrombus identification distal to the level of the adductor canal and in the pelvis. Magnetic resonance venography has been shown to be sensitive in imaging asymptomatic pelvic thrombi but remains costly and cumbersome to repeat on a regular basis.

Routine screening by genetic predisposition or identification of a single serum clotting factor has yet to demon-

strate a strong correlation with venous thromboembolic disease after THR or TKR.

Recommendation 4: Discharge to Home

Recommendation 4.1

Patients should be encouraged to progressively increase mobility after

discharge to home.

Level of Evidence: V

Grade of Recommendation: C

Recommendation 4.2

Patients should be educated about the common symptoms of DVT and PE.

Level of Evidence: V

Grade of Recommendation: B

NB: The level of evidence is level V, expert opinion, but the strength of recommendation was increased from C to B because patient education is consistent with the minimal expected standard of care for today's medical practices.

Rationale for Recommendations 4.1 and 4.2

During postoperative hospitalization, the team caring for the patient should collaborate with physical therapy, occupational therapy, and discharge planning to extend the hospital program to the home environment. The team should stress appropriate range of motion and appropriate conditioning programs, and encourage the patients to avoid prolonged immobility.

All patients should be educated regarding common symptoms of DVT and PE. DVT symptoms are usually localized to site and include: pain, swelling, tenderness and redness or discoloration of skin. PE symptoms include shortness of breath, rapid pulse, sweating, feeling of apprehension, chest pains worsening with deep breath, coughing up blood, decreased blood pressure, and lightheadedness.

These recommendations are an extension of the AAOS concept of patient-centered care encouraging patient education as part of the surgical process. The presumption is that patient participation and education will enhance awareness, improve outcomes, and potentially diminish the risk associated with the procedure specifically the potential for PE-related morbidity and mortality.

Future Research

Appropriately powered studies to detect the superiority of any preventive strategy for PE would be far more

costly than for DVT. Consequently DVT, which occurs much more frequently and seems to occur with a wider variability among treatment groups is a more attractive proxy measure. But the reduction of DVT does not appear to have a significant effect on the PE rate, and this calls into question the long-assumed epidemiologic if not pathophysiologic link between the two processes. Additional research, which better describes this relationship, would be helpful.

Postoperative bleeding in and around the surgical wound is an example of a complication that may be directly caused by prophylaxis. In contrast to an asymptomatic DVT, a postoperative bleed may lead to even more serious problems that significantly impact the surgical outcome. In this sense the expected benefit of prevention of one type of surgical complication may be overshadowed by the increased risk of another. The incidence of major postoperative bleeding should be addressed in a more uniform and standardized fashion to facilitate a more reliable comparison of different studies, and pooling of the results. The functional outcomes in patients with major bleeds should be followed in studies that are concerned primarily with thromboembolic events to fairly estimate the costs of treatment complications in comparison with those of fatal and nonfatal PE.

The issue of PE risk stratification in the preoperative assessment of THR and TKR patients is very important. By developing an evidence-based risk adjustment system it will be possible to use a more cost-effective individualized prophylactic strategy. Future research should be directed at the assessment of the incidence of PE following hip or knee replacement in large unselected populations in which the potential risk factors are reliably documented.

Large databases such as Medicare and those administered by states may provide some assistance, but currently do not include enough specific risk stratification and outcome variables. Hip and knee replacement registries present real opportunities to enhance the quality and applicability of the data. The AAOS has demonstrated a commitment to oversee the development of a national total joint registry which would facilitate an efficient and timely approach to preventing PE and postoperative bleeding complications. Successful implementation of this strategy would undoubtedly improve the quality of care for our patients and deliver value to the health care system.

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