■ REVIEW ARTICLE

Current guidelines for total joint VTE prophylaxis

DAWN OF A NEW DAY

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Venous thromboembolism (VTE) remains an immediate threat to patients following total hip and knee replacement. While there is a strong consensus that steps should be taken to minimise the risk to patients by utilising some forms of prophylaxis for the vast majority of patients, the methods utilised have been extremely variable. Clinical practice guidelines (CPGs) have been published by various professional organisations for over 25 years to provide recommendations to standardise VTE prophylaxis. Historically, these recommendations have varied widely depending in underlying assumptions, goals, and methodology of the various groups. This effort has previously been exemplified by the American College of Chest Physicians (ACCP) and the American Academy of Orthopaedic Surgeons (AAOS). The former group of medical specialists targeted minimising venographically proven deep vein thrombosis (DVT) (the vast majority of which are asymptomatic) as their primary goal prior to 2012. The latter group of surgeons targeted minimising symptomatic VTE. As a result prior to 2012, the recommendations of the two groups were widely divergent. In the past year, both groups have reassessed the current literature with the principal goals of minimising symptomatic VTE events and bleeding complications. As a result, for the first time the CPGs of these two major subspecialty organisations are in close agreement.

Despite decades of clinical experience and hundreds of studies, the ideal method of venous thromboembolism (VTE) prophylaxis remains controversial. This has resulted in variability and inconsistency of prophylaxis for total joint replacement patients and a concern that many patients may be left at risk with no prophylaxis or suboptimal prophylaxis. This void has been filled to some degree by clinical practice guidelines (CPGs). Among the first subspecialty groups to take the lead in this subject were the American College of Chest Physicians (ACCP) who held their first conference in 1985 and published their findings the following year.[1] In 2001, their sixth conference refined the levels of risk and placed all patients undergoing total joint replacement in the highest risk category.[2] The seventh conference explicitly categorised levels of recommendation into 1A, 1B, 1C, and 2.[3] Grade 1 recommendations were defined as those having a strong basis to indicate that the benefit outweighs the risk, burden, and cost. 1A recommendations required the presence of randomised clinical trial with consistent results. 1B recommendations were based on randomised clinical trials with either inconsistent results or major methodological weaknesses. 1C recommendations come from observational studies or generalisations from groups of patients included in randomised trials to a different, but somewhat similar group of patients who did not participate in the trials. Grade 2 recommendations are based on studies that are of less certain magnitude of benefits, risks, burdens, and costs. The 1A recommendations for hip and knee replacement were the use of Warfarin with a target international normalised ratio (INR) of 2 to 3, Low Molecular Weight Heparin (LMWH), or Fondaparinux for all patients. The eighth conference of ACCP was published in 2008[4] and recommended the same 1A pharmacoprophylaxis for all total joint patients, but recommended a lower threshold for extended prophylaxis of 35 days, especially for total hip patients. During the same timeframe of the publication of the seventh and eighth conference recommendations, the Center for Medicare and Medicaid Services (CMS) mandated prophylaxis as a quality measure under the Surgical Care Improvement Program (SCIP).[5] This lead to the widespread promotion of use of a 1A protocol as the safest strategy for meeting SCIP guidelines. In the last two years there have been dramatic changes in CPGs of which total joint surgeons should be aware. These

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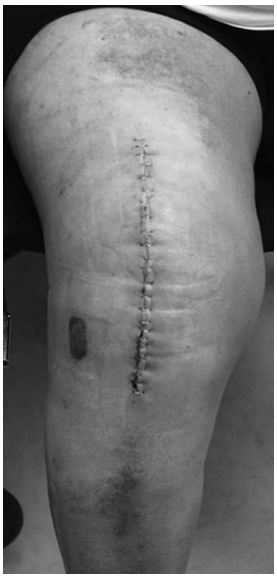

Fig. 1a

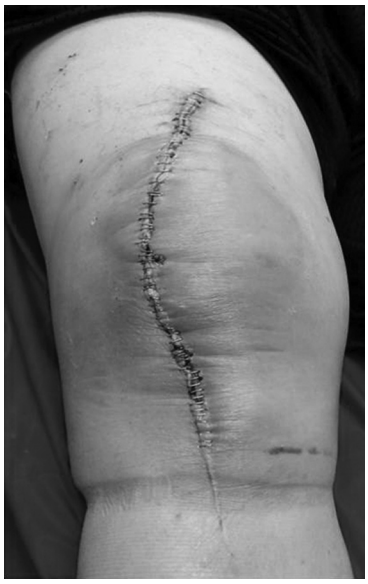

Fig. 1b

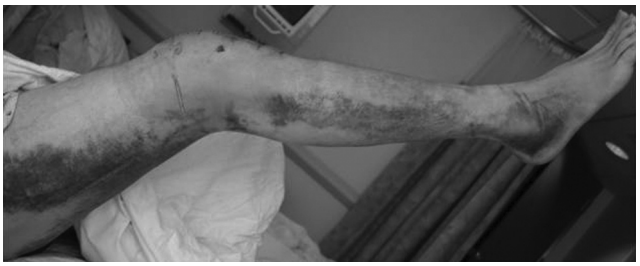

Fig. 1c

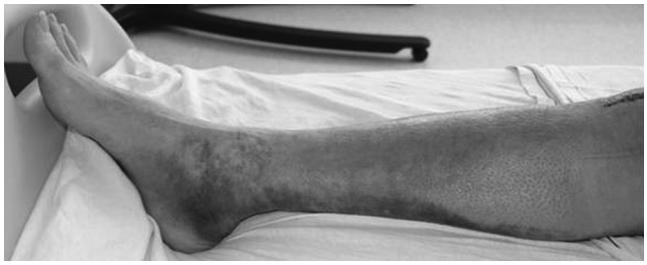

Fig. 1d

Clinical photographs of patients readmitted to hospital with wound drainage and hematoma with elevated INR (> 3.0) yet not meeting ACCP definition of major bleed.

represent 'sea change' in the approach to VTE prophylaxis. These changes were based largely on concerns for the methodology and recommendations of the ACCP. This review will focus on issues that were identified with the ACCP guidelines, how and why changes occurred, and the current status of VTE prophylaxis recommendations of two of the major subspecialty organisations dealing with this issue, the ACCP and the American Academy of Orthopaedic Surgeons (AAOS).

Concerns with prior CPGs

A number of issues have been identified with the ACCP guidelines up through the eighth conference in 2008. The methodology emphasised multicenter, randomised clinical trials with the end point of venographically proven deep vein thrombosis (DVT), the vast majority of which are asymptomatic. Venography is rarely used at most major medical centers and has been largely supplanted by ultrasonography. Virtually all studies performed with venography as an endpoint to are pharmaceutical sponsored FDA investigational device exemption (IDE) studies. The FDA does recognise venographically proven DVT as a valid endpoint for efficacy of drugs for VTE prophylaxis. This methodology, however, is enormously expensive and weighted towards pharmaceutical sponsored studies. The resources to study low cost, generic options such as Aspirin, Warfarin, and intermittent pneumatic compression devices (IPC) is limited and rarely, if ever, would reach the 1A level. There is also concern that the target INR of 2 to 3 is high by the standards of most orthopaedic surgeons and the use of a relatively high dose Coumadin, LMWH, or Fondaparinux for *all* patients regardless of risk profile may be placing a high population of patients at risk for bleeding that are at relatively low risk for VTE.

Extensive debate exists as to the clinical significance of asymptomatic DVT. A recent study by Parvizi et al[6] found a very low correlation between the presence of DVT and PE and questioned the significance of asymptomatic DVT. The effect of lowering the incidence of DVT has on the subsequent risk of symptomatic PE or death is therefore questionable. A final concern has been the under reporting of complications of VTE prophylaxis including persistent wound drainage, bleeding, and the subsequent morbidity associated with such complications particularly hematoma following total knee replacement. The methodology of the ACCP defined a major bleeding episode as overt bleeding associated with at least of the following: death or life threatening clinical event, bleeding confirmed to be retroperitoneal, intracranial or intraocular, transfusion of more than two units of packed blood cells or whole blood, or a decrease in hemoglobin greater than 20 g/l compared with the relevant post-operative level.[3] These criteria are generally not applicable to total joint replacement procedures particularly of the knee. Persistent wound drainage and bleeding into a joint great enough to result in serious clinical morbidity would frequently not have reached the level of a major bleed by this definition yet would have substantial clinical impact (Fig. 1). Galat et al[7] reported that patients with wound complications requiring reoperation within 30 days of total knee replacement were ten times more likely to have subsequent major surgery and associated morbidity than those that did not. Failure to meet these strict criteria of a major bleed has likely resulted in systematic underreporting of bleeding complications in studies utilising this definition.

Despite the issues and concerns with the ACCP guidelines, this particular CPG was rapidly embraced by numerous groups including hospital oversight committees, state and federal agencies, and lawyers as a *de facto* standard of care. There is a natural tendency to use a 1A protocol as the safest standard for compliance for the SCIP program and from a medical legal perspective. While it is true that a 1A protocol did meet the SCIP guidelines for hip and knee replacement, an IPC was also deemed acceptable for knee replacement. It should be noted, however, that the dose and duration of pharmacoprophylaxis, especially the use of Warfarin, is not specified and although aspirin alone is not recommended, it can be used with proper documentation.

The question remains as to whether there was substantial clinical concern with the widespread application of 1A protocols in hip and knee arthroplasty. A study was undertaken in 2005 at Barnes-Jewish Hospital[8] in which all hip and knee arthroplasty patients were standardised to a 1A protocol. Routine ultrasounds screening of asymptomatic patients prior to discharge was discontinued as per the ACCP recommendations and ten days of Lovenox was implemented. Prior to that time, patients had routinely been treated with a shorter course of low-dose Coumadin (target INR 2.0) with predischarge ultrasound screening. The results were excellent with one PE and no deaths out of over 700 total hip cases and less than 2% symptomatic VTE.[8] The results with a 1A protocol at the same hospital were poor and the study was discontinued prematurely due to a high number of complications. Major complications were observed in 9% of patients and the efficacy was also inferior to that reported with a non-approved protocol.[9] The experience at Barnes-Jewish Hospital was not unique to that institution. Novicoff, et al[10] reported similar results at the University of Virginia when they experienced a dramatic increase in bleeding complications after switching to a 1A protocol, again in an attempt to be in compliance with a 1A protocol per the ACCP. This brought to light a number of potential disadvantages of the ACCP guidelines. Not only did orthopaedic surgeons experience an increase in drainage and bleeding complications, but they were also precluded from utilising less-aggressive, less expensive, and more cost effective options. Excellent results have been reported with the use of aspirin with or without mechanical compression, especially in patients that did not have an above average risk following total joint replacement, especially total knee replacment.[11-13] Another modality that became available in that timeframe was the use of a mobile IPC. A multicenter RCT published by Colwell et al[14] in 2010 showed a mobile IPC achieved equivalent incidence of proximal and distal DVT and PE with no deaths and a much lower bleeding rate (1.3% *versus* 4.3%). A final concern with the ACCP guidelines up through 2008 was the issue of financial conflict of interest. All but one author listed numerous potential financial conflicts of interest. In this timeframe, the Institute of Medicine issued recommendations regarding guideline development that discouraged a financial conflict of interest among authors of CPGs, certainly not among a majority of the authors.[15]

The AAOS responds

In response to the number of concerns regarding the ACCP recommendations, the AAOS formed the DVT/PE workgroup in 2007, which issued its first recommendations that were subsequently updated in 2011 to meet the CPG standards of the Agency for Healthcare Research and Quality (AHRQ). The available literature on VTE was reviewed with new methodology that focused on PE and death as endpoints with symptomatic DVT also considered as an end point in 2011.[16] The goal was to achieve more balance in minimising risk as well as maximising efficacy and eliminating or minimising conflict of interest in the guideline development. Patients were classified based on risk for VTE and risk for bleeding. When symptomatic events were utilised as an endpoint, the data was not sufficient to recommend any commonly utilised pharmacoprophylaxis, including aspirin, over another for total hip or knee replacement. More aggressive prophylaxis was recommended for those at high risk for VTE, but the only risk factor that was consistently supported in the literature was prior history of VTE. Less aggressive prophylaxis or no prophylaxis was recommended for those with a bleeding disorder, but again the only risk factor with strong supporting literature was severe liver disease or a bleeding disorder. This placed the AAOS in direct conflict with the ACCP in every major recommendation until the ninth edition of the ACCP was published in 2012, which largely resolved the conflict between the two groups (Tables I and II).

Current status of AAOS and ACCP

The ninth conference of the ACCP addressed virtually all of the previously described concerns with their CPG. The conflict of interest issue was addressed with most authors (five of nine) declaring no potential conflict of interest. The methodology changed dramatically with a focus placed on clinically important outcomes rather than asymptomatic VTE. More focus was placed on bleeding and wound drainage. The only IPC that was recommended was a mobile device with a compliance monitoring chip as supported by the recent level 1 publication by Colwell, et al.[14] Going forward, the ACCP recommended emphasis on clinically symptomatic events and avoiding bleeding while minimising the importance of asymptomatic events.

This dramatic change in methodology resulted in an equally dramatic change in recommendations. No intervention achieved a 1A status. Similar to the AAOS, the evidence did not support any of the major utilised drug interventions over another including aspirin and all were placed in the 1B category. IPC achieved a 1C recommendation and the length of treatment for all of these modalities was 10 to 14 days.[17] There are a number of lower level recommendations in the level 1B or 2 category (Table II).

Table I. Summary of AAOS 2011 CPG on Preventing VTE in Patients

Recommendation	Grade of Recommendation
Against routine post-operative duplex ultrasonography screening	Strong
Practitioner should further assess the risk of VTE	Weak
Factors other than a history of previous VTE don't have clear support as risk factor for VTE	Inconclusive
Assess for known bleeding disorders like hemophilia and for the presence of active liver disease	Consensus
Factors other than the presence of a known bleeding disorder or active liver disease don't have clear support as risk factor for bleeding	Inconclusive
Discontinue antiplatelet agents before undergoing elective hip or knee arthroplasty	Moderate
Use of pharmacologic agents and/or mechanical compressive devices for prevention of VTE	Moderate
Which prophylactic strategy is/are optimal or suboptimal	Inconclusive
Patients and physicians should discuss the duration of prophylaxis	Consensus
Patients who have also had a previous VTE, should receive pharmacologic prophylaxis AND mechanical compressive devices	Consensus
Patients who have a known bleeding disorder and/or active liver disease, use mechanical compressive devices for preventing VTE	Consensus
Early mobilization is of low cost, minimal risk to the patient, and consistent with current practice	Consensus
Use of neuraxial anesthesia to help limit blood loss, even though evidence suggests that neuraxial anesthesia does not affect the occurrence of VTE disease	Moderate
Unable to recommend for or against inferior vena cava (IVC) filter for patients with contraindication for chemoprophylaxis	Inconclusive

Table II. Summary of ACCP 9th, 2012 Edition Recommendations

Grade	Recommendation
All 1B*	Use of one of the following rather than no antithrombotic prophylaxis: LMWH; fondaparinux; dabigatran†, apixaban†, rivaroxaban (THA or TKA but not hip fracture surgery); low-dose unfractionated heparin; adjusted-dose vitamin K antagonist; aspirin
1C*,‡	Intermittent pneumatic compression device (IPCD)
2C/2B	Use of LMWH in preference to the other agents recommended as alternatives
2C	In patients receiving pharmacologic prophylaxis: adding an IPCD during the hospital stay
2B	Extending thromboprophylaxis for up to 35 days
2C	In patients at increased bleeding risk: an IPCD or no prophylaxis
All 1B	In patients who decline injections: using apixaban† or dabigatran†
2C	Suggest against using IVC filter placement for primary prevention in patients with contraindications to both pharmacologic and mechanical thromboprophylaxis
1B	Against Doppler (or duplex) ultrasonography screening before hospital discharge
2B	For patients with isolated lower extremity injuries requiring leg immobilization: no thromboprophylaxis
2B	For patients undergoing knee arthroscopy without a history of VTE: no thromboprophylaxis

* Length of treatment minimum 10 to 14 days
† Not FDA approved for DVT prophylaxis prior to total joint replacement
‡ Recommend the use of only portable, battery-powered IPCDs capable of recording and reporting proper wear time on a daily basis for inpatients and outpatients. Efforts should be made to achieve 18 hours of daily compliance

Both the AAOS and the ACCP do not find literature to support any specific indication for an IVC filter to prevent PE and the ACCP recommends against its use while the AAOS states there is lack of literature support for its use.

Conclusion

VTE remains an important complication following total hip and knee replacement. A 'sea change' has occurred in the recommendations of the CPGs of the AAOS and ACCP, which are now largely in agreement for the first time. Both now recognise all major options for prophylaxis including aspirin and IPCs. Both now focus on clinically symptomatic events and avoiding iatrogenic complications. Further research is needed to identify patients at risk for VTE and bleeding and the role of IVC filters remains to be established with stronger studies. The ultimate choice of prophylaxis, however, remains with the treating physician and his unique knowledge of a particular patient's medical history. The current CPGs, however, give orthopaedic surgeons more latitude in their choice of VTE prophylaxis with less impetus to apply aggressive pharmacoprophylaxis to all patients, less emphasis on asymptomatic VTE, and more emphasis on avoiding iatrogenic complications of prophylaxis. This seems particularly appropriate given the higher volume of arthroplasty procedures that are being performed, the shorter surgical times, more rapid mobilisation, large cohort of relatively healthy patients undergoing these procedures, and the apparent decline in risk of VTE due to these numerous factors. While much work remains to be done to refine these CPGs, the current situation has placed the AAOS and the ACCP in much closer alignment and seems to be a major step forward for both patients and surgeons.

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References

1. **Hull R, Raskob G, Pineo G, et al.** A comparison of subcutaneous low-molecular-weight heparin with warfarin sodium for prophylaxis against deep-vein thrombosis after hip or knee implantation. *N Engl J Med* 1993;329:1370–1376.
2. **Haas S.** Prevention of venous thromboembolism: recommendations based on the International Consensus and the American College of Chest Physicians Sixth Consensus Conference on Antithrombotic Therapy. *Clin Appl Thromb Hemost* 2001;7:171–177.
3. **Geerts WH, Pineo GF, Heit JA, et al.** Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126(Suppl):338S–400S.
4. **Geerts WH, Bergqvist D, Pineo GF, et al.** Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008;133(Suppl):381S–453S.
5. **No authors listed.** QualityNet. Specifications Manual for National Hospital Inpatient Quality Measures. http://www.qualitynet.org/dcs/ContentServer?c=Page&pagename=QnetPublic%2FPage%2FQnetTier2&cid=1141662756099 (date last accessed 5 September 2012).
6. **Parvizi J, Jacovides CL, Bican O, et al.** Is deep vein thrombosis a good proxy for pulmonary embolus? *J Arthroplasty* 2010;25:138–144.
7. **Galat DD, McGovern SC, Larson DR, et al.** Surgical treatment of early wound complications following primary total knee arthroplasty. *J Bone Joint Surg [Am]* 2009;91-A:48–54.
8. **Keeney JA, Clohisy JC, Curry MC, Maloney WJ.** Efficacy of combined modality prophylaxis including short-duration warfarin to prevent venous thromboembolism after total hip arthroplasty. *J Arthroplasty* 2006;21:469–475.
9. **Burnett RS, Clohisy JC, Wright RW, et al.** Failure of the American College of Chest Physicians-1A protocol for lovenox in clinical outcomes for thromboembolic prophylaxis. *J Arthroplasty* 2007;22:317–324.
10. **Novicoff WM, Brown TE, Cui Q, et al.** Mandated venous thromboembolism prophylaxis: possible adverse outcomes. *J Arthroplasty* 2008;23:15–19.
11. **Bozic KJ, Vail TP, Pekow PS, et al.** Does aspirin have a role in venous thromboembolism prophylaxis in total knee arthroplasty patients? *J Arthroplasty* 2010;25:1053–1060.
12. **Callaghan JJ, Warth LC, Hoballah JJ, Liu SS, Wells CW.** Evaluation of deep venous thrombosis prophylaxis in low-risk patients undergoing total knee arthroplasty. *J Arthroplasty* 2008;23:20–24.
13. **Lotke PA, Lonner JH.** The benefit of aspirin chemoprophylaxis for thromboembolism after total knee arthroplasty. *Clin Orthop Relat Res* 2006;452:175–180.
14. **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-A:527–535.
15. **Norris SL, Holmer HK, Burda BU, Ogden LA, Fu R.** Conflict of interest policies for organizations producing a large number of clinical practice guidelines. *PloS One* 2012;7:37413.
16. **Jacobs JJ, Mont MA, Bozic KJ, et al.** American Academy of Orthopaedic Surgeons clinical practice guideline on: preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty. *J Bone Joint Surg [Am]* 2012;94-A:746–747.
17. **Falck-Ytter Y, Francis CW, Johanson NA, et al.** Prevention of VTE in Orthopedic Surgery Patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141:278S–325S.