Editorial

International Consensus Meeting on Venous Thromboembolism

"Patients undergoing orthopedic procedures are at higher risk of mortality from venous thromboembolism (VTE)". Although there is little evidence for this statement in modern orthopaedic practice, it is still frequently seen in publications exploring the issue of VTE in orthopedics (Fig. 1). This has perpetuated a long-standing fear of VTE-related morbidity and mortality among both the medical community and patients alike[1]. Hence, numerous organizations such as the American Academy of Orthopaedic Surgeons (AAOS)[2] and the American College of Chest Physicians (ACCP)[3] in the U.S., and numerous other organizations across the globe, have created guidelines related to the issue of VTE in orthopedics.

In view of the imperfect data available on the subject of VTE, it is no surprise that these guidelines have been criticized on some grounds. Many guidelines have limited their scope to a specific surgical procedure (e.g., total hip or knee replacement), some have failed to recognize the importance of variations in geographic and racial predisposition to VTE, and almost all have attempted to create recommendations by either preferentially or exclusively relying on high level studies only. While understandable from the methodological perspective and commendable, the latter strategy has resulted in the inclusion of studies conducted by the pharmaceutical industry, as part of regulatory requirements, to have a new chemoprophylaxis agents approved for clinical use. Such studies often have been powered to evaluate the difference in the incidence of distal deep venous thrombosis as detected with venography, but not clinically important symptomatic VTE or the rare fatal pulmonary embolus, which is the real concern for both the medical community and their patients[4,5]. Some guidelines have been criticized for overlooking the complications that can arise as a result of administration of some of these agents (e.g., bleeding, wound-related complications, and infection), which result in immense expense to the health-care system and can also lead to fatality[6].

The International Consensus Meeting (ICM), having recognized the limitations of the current guidelines and the need for unbiased randomized trials with clinically important end points, convened a group of experts from around the globe to generate guidelines or recommendations that address the real-world issues. Delegates from 135 international societies, 68 countries, and various specialties, including anesthesia, cardiology, hematology, internal medicine, and orthopedics, were invited to comb through the literature in a systematic review format and to create practical recommendations related to all subspecialities in orthopedics that would also have global applications. This immense initiative engaged nearly 600 experts who followed the strict Delphi process[7], as in prior ICM activities[8,9], to generate the monumental document that stands in front of you. Over a period of 1 year, and with the critical guidance of the steering committee and engagement of the organizing committee, librarians, biostatisticians, epidemiologists, and experts from the Cochrane group, ALL published work related to VTE and orthopaedics was reviewed to generate a response/recommendation to the nearly 200 issues (questions) that had been collated from the field.

The delegates were nominated by societies or recruited on the basis of their interest in the subject matter and were selected on the basis of their published expertise (with a minimum of 3 publications related to VTE). Each question was assigned to 2 delegates who were provided the MESH terms, and at times the list of publications, by the librarians. The delegates were free to work together or independently. After 6 months of literature review and extraction of data, the delegates created the initial draft of the recommendations. The first draft of the document was then sent for review by 1 or 2 other delegates with expertise in that subject matter. The critique or suggestions arising from this initial review were sent to the authors to address. The revised document underwent a second review by an additional group of delegates. At all times, the living documents were posted on the ICM website for all to view and provide comments. All generated comments through the website were also shared with the authors of each document.

The document underwent 2 additional reviews prior to submission to *The Journal of Bone and Joint Surgery*. One review was done by a member of the organizing committee to ensure completeness of the document, and another review was provided by the corresponding editor for each subspeciality. The submitted work was then subjected to the usual editorial scrutiny of JBJS prior to going into "print."

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJS/G906).

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Dear Javad

Reference: ICM VTE work and subsequent publication

As we have discussed I commend you for the organisation of this work and for cracking the whip to get it done so relatively quickly – it took us over two years to get to almost the same point when I was involved doing the same work in the UK for NICE!

The outcome from the ICM VTE consensus group has essentially concluded that the scientific evidence to guide the medical community globally on VTE prevention in Trauma & Orthopaedic surgery is generally of poor quality / low GRADE.

The current research has shown that there is presently no good evidence that any thromboprophylaxis strategy will protect against fatal pulmonary embolus. That does not mean however that we should not attempt to limit the chances with a common sense and risk stratification approach.

There is no current good evidence for a validated risk analysis and assessment stratification tool in Trauma & Orthopaedic surgery. This should be an item of priority research. Patients should undergo some form of risk analysis, be advised accordingly and get good impartial advice informing them of all the risks and benefits. Everything we do, prescribe or give to a patient has a risk:benefit ratio. We all get a skewed view of life in our own speciality and sub-speciality silos. Chemical thromboprophylaxis is not without it's risks. In our own small unit not infrequently we have a patient on our acute Trauma lists who requires urgent surgery as a direct result of the complications of chemical thromboprophylaxis. Our views have been coloured by the results of studies that use "surrogate end points" – non clinically apparent VTEs that we would be unaware of and would also often not treat if the patient is asymptomatic. We are aware that these surrogate end points may occur at least a factor of ten, and sometimes a factor of 100, greater than the clinical events. Post-phlebitic syndrome does not occur as often as has been suggested in some of the medical literature. Asymptomatic VTEs in a patient population over the age of 60 in high income countries, particularly lower limb DVT, is rarely reported and may approach 16% (Gabriele Ciuti et al: Thromb Res 2012). We need to "live in the real world" and factor in the risks: "First do no harm".

We should also recognise that we are most unlikely to ever to be able to get good level 1 evidence in this clinical area. If we are dealing with a clinical event that may occur 1%, or less, of the time: to be able to conduct a properly designed and powered two arm clinical trial, that uses clinical and not surrogate end points, depending on the outcome being evaluated, will require a study patient population of 20,000 to 90,000. This is most unlikely to ever be achieved and particularly as we will need multiple studies like this and trials that will involve more than two arms – making them even less achievable. This being the case a global agreement must be reached that all studies, databases and large audits (eg national audit databases, like the British National Joint Registry) must be included to be able to attempt to come to a global consensus on the best possible advice to the medical community, and public, on the best VTE prevention strategies.

What are my credentials for making these comments?: I have been a member of a UK National Institute of Health & Care Excellence (NICE) committee on VTE. I am a clinical trials review panel member for the UK National Institute of Health Research (NIHR). I am a Past (& Founding) President of the Orthopaedic Trauma Society and am an Emeritus International member of the Orthopaedic Trauma Association. I also: Chair Incision Medical Indemnity: insuring ~1000 surgeons, Chair the Primary Trauma Care Foundation and sit on the G4 Alliance strategic board advocating for Trauma care globally.

Kindest regards

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JP ICM VTE 070921

Fig. 1

Letter from Dr. Nigel Rossiter.

This enormous task could not have been completed in short order without the sacrifice and dedications of many. Above all, a deep gratitude goes to the delegates from around the world who selflessly dedicated hours of their scarce time to complete the task in such an expeditious and thorough manner. An initiative of this magnitude could not be completed without the critical contribution of many others (see Acknowledgements).

We are hopeful that the generated work will serve the patients and our community for years to come. ■

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