

Are Asymptomatic DVTs Relevant?
One Measure for All

To the Editor:

Congratulations on publishing the ninth edition of the American College of Chest Physicians Antithrombotic Guidelines (February 2012), which are of paramount importance. Orthopedic recommendations for VTE prophylaxis in prior versions of the CHEST guidelines were based on experimental outcomes that combined asymptomatic and symptomatic DVTs. However, the current guidelines exclude from consideration asymptomatic DVTs. The designation of asymptomatic DVTs as clinically irrelevant outcomes has changed the calibration of clinical trials, rendering many of the results as not significant. Given the former position, we are puzzled by the observation that asymptomatic DVTs, which are incidentally found, are treated with anticoagulation for a period of 3 to 12 months. We would like to ask why the asymptomatic DVTs, if otherwise considered irrelevant in the orthopedic clinical trials, are treated formally with anticoagulation if found incidentally.

Adolfo Llinas, MD
Laura Cardenas, MD
Bogotá, Colombia

Conflicts of interest: None

References


Response

To the Editor:

We thank Drs Llinas and Cardenas for the opportunity to clarify the distinction between the methodologic issue of using asymptomatic VTE to estimate relative effects and the clinical issue of considering asymptomatic VTE as a patient condition requiring management. From the methodologic perspective, the three prevention chapters of the ninth edition of the American College of Chest Physicians Antithrombotic Guidelines (AT9) did not “exclude from consideration asymptomatic DVT.” We considered both symptomatic and asymptomatic venous thrombotic events reported in trials to estimate relative effects of interventions. However, asymptomatic VTE was viewed as a surrogate for symptomatic VTE and we extensively evaluated different strategies on how to conceptually link such surrogate measures to clinically relevant outcomes.

In short, when a meaningful number of symptomatic VTEs were available, we based our estimate of effect of an intervention on those patient-important outcomes. When only asymptomatic events from venography were reported, we used the relative effect estimates from those asymptomatic events, but applied this relative effect measure to our best estimate of baseline risk for symptomatic thrombotic events postoperatively. We rated down the quality of the evidence for those outcomes due to indirectness (surrogate outcome).

From the clinical perspective, we recommended strongly against screening asymptomatic patients for VTE with Doppler ultrasound after any orthopedic surgery to avoid detecting incidental DVTs, as moderate-quality evidence showed that harm of subsequent treatment outweighed any potential benefit. Consistent with this recommendation, the chapter by Kearon and colleagues on treatment of VTE does not comment on treatment of asymptomatic DVT detected by screening venography after surgery. That chapter does, however, provide recommendations for treatment of asymptomatic DVT and pulmonary embolism incidentally detected by imaging studies performed for other reasons (eg, CT scanning for staging of cancer). When these are DVTs, they are usually large intraabdominal thrombi, and not small thrombi that are confined to the distal deep veins of the leg.

Yngve Falck-Ytter, MD
Cleveland, OH
Cllete Kearon, MD
Hamilton, ON, Canada
Elie Akl, MD
Buffalo, NY
Charles Francis, MD
Rochester, NY

Conflicts of interest: None

Affiliations: From the Case Western Reserve University (Dr Falck-Ytter), School of Medicine, Department of Medicine, Case and VA Medical Center; Departments of Medicine and Clinical Epidemiology and Biostatistics (Dr Kearon), Michael De Groote School of Medicine, McMaster University; State University of New York at Buffalo (Dr Akl); Department of Internal Medicine, (Dr Akl), American University of Beirut; and University of Rochester Medical Center (Dr Francis), Hematology/Oncology Unit.

Financial/nonfinancial disclosures: The authors of this guideline provided detailed conflict of interest information related to each individual recommendation made in this article. A grid of these disclosures is available online at http://chestjournal.chestpubs.org/content/141/2_suppl/e278S/suppl/DC1. Dr Kearon is a consultant to Boehringer Ingelheim and has received peer-reviewed funding for studies in the treatment of VTE. Dr Akl is a member of and prominent contributor to the GRADE Working Group. Dr Francis received research grant support from the National Heart, Lung, and Blood Institute and Eisai Co, Ltd, and served as a steering committee member for a clinical trial sponsored by Eisai Co, Ltd. Dr Falck-Ytter has reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
Resuscitation Status May Predict Mortality in Patients Admitted to the ICU

To the Editor:

In the October 2012 issue of CHEST, Keegan et al1 compare three severity of illness scoring systems for critically ill patients (Acute Physiology and Chronic Health Evaluation [APACHE], Simplified Acute Physiology Score [SAPS], and Mortality Probability Model [MPM]) with and without a variable indicating the existence of a do not resuscitate (DNR) order. They conclude that the model with the most variables (APACHE) had the best discriminatory ability, that adjusting for early DNR status did not improve model performance, and that all models were calibrated poorly. Although we agree with the authors’ first conclusion that more variables improve discrimination, we question the latter two.

This study implies that DNR status is not an important predictor of mortality in the ICU, even though it is significant in the MPM-III model. The authors saliently note that the SAPS 3 and APACHE IV models, which use more variables (20 and 142, respectively), may simply “capture” what predictive information DNR status conveys, making DNR status unnecessary. Unfortunately, the authors do not state if DNR status was statistically significant when added to the SAPS 3 or APACHE IV models.

Discrimination as measured by the C statistic (area under the receiver operating characteristic curve) indicates how well the model can separate survivors and nonsurvivors. If all nonsurvivors had higher predicted probabilities of dying than all survivors (regardless of the degree of predicted differences), then the C statistic would be 1, indicating perfect discrimination. Calibration as measured by the Hosmer-Lemeshow statistic measures how well predicted probabilities of mortality agree with observed numbers of deaths across deciles of risk.

Cook2 has shown that because the C statistic is based on ranks, it is less sensitive than likelihood measures of model fit. Consequently, a strong predictor often causes minimal change to the C statistic in an existing model but can substantially change the predicted probabilities of those with the predictor. Instead, a Bayesian Information Criterion analysis or a related technique would be better suited to determine if a DNR status should be included in a model.

The Hosmer-Lemeshow statistic, like any inference test, is more likely to be statistically significant when the sample size is large. A significant Hosmer-Lemeshow test does not necessarily mean that a predictive model is suspect. Adjunct measures of model calibration, such as a calibration plot for each model, can be helpful when sample size is large.

Finally, Cook2 has shown that there is a mathematical trade-off between good calibration and good discrimination, with well-calibrated models unable to achieve very high C statistics. Keegan et al’s1 study found that the MPM-III model had better calibration but worse discrimination than the APACHE or SAPS models. This does not suggest that one model is “better” than the others, but that each model has strengths and weaknesses and a more nuanced interpretation is required. Head-to-head comparisons of the three models are rare, and this article does fill a gap in the literature. However, more statistical analyses need to be done before one can definitively say that DNR status is not an important predictor of mortality or that these models are poorly calibrated.

Brian H. Nathanson, PhD
Longmeadow, MA

Thomas L. Higgins, MD, MBA
Springfield, MA

Affiliations: From OptiStatim, LLC (Dr Nathanson); and the Department of Medicine (Dr Higgins), Baystate Medical Center.

Financial/nonfinancial disclosures: The authors have reported to CHEST the following conflicts of interest: Dr Nathanson’s company, OptiStatim, LLC, has an ongoing consulting agreement with the Cerner Corporation and participated in the development of the MPM-III model, Dr Higgins served previously as a consultant to Cerner and participated in the development of the MPM-III model. Dr Higgins also owns stock in Cerner.

Correspondence to: Brian H. Nathanson, PhD, OptiStatim, LLC, PO Box 60944, Longmeadow, MA 01106; e-mail: brian.h.nathanson@att.net

© 2013 American College of Chest Physicians. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians. See online for more details.

DOI: 10.1378/chest.12-2558

REFERENCES


