EDITORIAL

European Society of Cardiology practice guidelines on acute pulmonary embolism

An American's commentary and personal perspectives

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The European Society of Cardiology (ESC) has published an outstanding set of 2008 guidelines on the diagnosis and management of acute pulmonary embolism (PE).[1] Indeed, European investigators have been in the forefront of clinical research and practice related to PE. Therefore, it is natural that these leaders have collaborated across country lines in what was certainly a time-consuming and painstaking labor of love. These guidelines display the command of the European community for clear communication and explicit recommendations. The document contains a treasure of information. It cites 400 important references, most of which have been published within the past several years. I believe it is currently the best source of references for contemporary citations related to acute PE. One also finds 2 Figures, 18 Tables, and multiple un-numbered charts, in addition to supplementary information available at the following ESC website: www.escardio.org/guidelines.

The other well-known set of PE guidelines is published by the American College of Chest Physicians (ACCP), most recently the Eighth Addition in 2008.[2] It is natural to muse about the similarities and differences between the "American" guidelines and the "European" guidelines. The more subtle question, usually not asked in polite company, is to query which set of guidelines is better written, more worthwhile, and based upon more rigorous scientific methodology and analysis. It is a question posed as if one were comparing the value of the U.S. dollar with the Euro on the fluctuating currency markets. Some critics enjoy comparing the 2 documents as if they represent different philosophies of automobile manufacture: the small-font, literally heavy 900-page "American" document which is of necessity unwieldy and which guzzles timber supplies in its paper rather than electronic version versus the sleek, fashionable "European" model, which has attractive-looking color Figures, more user-friendly font, and which compresses valued information into a 40-page document.

I contend that acute PE as a discipline is now so globalized that it is artificial – indeed, it is virtually impossible – to compare American versus European philosophies of PE management for at least three reasons. First, U.S. thought leaders represent a minority of members of the various committees that wrote the Eighth Edition of the ACCP guidelines (in contrast, U.S. representation on the ESC Task Force is minimal). For the ACCP undertaking, there were prominent contributors holding leadership positions from Canada, the United Kingdom, and continental Europe – especially France, Italy, and the Netherlands – plus representation from all of the Americas (North, Central, and South), Asia, and Australia-New Zealand. Second, the 2 sets of guidelines utilized the same source data to construct evidence-based recommendations. Third, the recommendations from both sets of guidelines used virtually identical rules of evidence, recognizing that consensus recommendations were based upon a spectrum of rigor ranging from multiple randomized clinical trials on a single topic to expert opinion formulated in the absence of a firm database.

I feel flattered by the invitation to comment upon the ESC guidelines for acute PE diagnosis and management. But many of my comments can be applied equally to the ACCP guidelines.

Diagnosis of PE consumes 10 pages of the 40-page ESC guidelines. The central tenet of diagnosis section of the ESC guidelines is to undertake a clinical assessment of the likelihood of PE, using clinical prediction rules from either the revised

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Geneva score[3] or the Wells score.[4] The ESC guidelines rightly point out that "the main limitations of implicit judgment are lack of standardization and the impossibility of teaching it. Clinical evaluation makes it possible to classify patients into probability categories corresponding to an increasing prevalence of PE, whether assessed by implicit clinical judgment or by a validated prediction rule". When rounding in European hospitals, I have not found routine use of any standardized clinical prediction rule for PE. I wish the ESC guidelines had advocated more forcefully for use of the Geneva or Wells scores to be integrated with daily clinical practice.

The ESC guidelines do an excellent job emphasizing the importance of risk stratification and prognostic assessment. The mainstays are evaluating right ventricular function, primarily by echocardiogram, as well as biomarkers of myocardial injury such as cardiac troponins. The guidelines make the important point that assessment of the anatomical burden and distribution of the pulmonary artery thrombus are less relevant for risk stratification than functional consequences of PE determined by the right ventricular dysfunction or enlargement and elevation of biomarkers.

The discussion of thrombolysis lists 12–24 hour infusions of streptokinase or urokinase as approved thrombolytic regimens for PE. This is technically true, but these regimens are no longer used. Streptokinase and urokinase (no longer available in the USA) are administered in 1–2 hour infusions to improve efficacy and safety. The most commonly administered thrombolytic agent is tissue plasminogen activator in a dose of 100 mg infused through a peripheral vein >2 hours. Like the ACCP guidelines, the ESC guidelines endorse thrombolysis for treatment of PE with shock or persistent arterial hypotension. In patients with normal blood pressure and right ventricular dysfunction and/or troponin elevation, thrombolysis "may be considered…after thorough consideration of conditions increasing the risk of bleeding". Wisely, the guidelines also approve pulmonary embolectomy "in patients with high-risk PE in whom thrombolysis is absolutely contraindicated or has failed". The guidelines also remind the reader that "catheter embolectomy or fragmentation of proximal pulmonary arterial clots may be considered as an alternative to surgical treatment in high-risk PE patients when thrombolysis is absolutely contraindicated or has failed".

The ESC guidelines recommend only 3 months of anticoagulation for PE provoked by a reversible factor such as surgery or trauma. Perhaps this recommendation is the single biggest difference from usual care in the USA, where such patients receive a minimum of 6 months of anticoagulation. The ESC guidelines make the important point that, counterintuitively, markers of hypercoagulability such as heterozygous factor V Leiden or heterozygous prothrombin gene mutation do not predict an increased likelihood of recurrent PE after anticoagulation is discontinued. There is general agreement with this statement in the USA, but nevertheless these patients in the USA often receive indefinite duration anticoagulation.

While the ESC guidelines state that "patients with lupus anticoagulant, those with confirmed deficit of protein C or protein S, and patients homozygous for factor V Leiden or prothrombin gene mutation may be candidates for indefinite anticoagulant treatment after a first unprovoked venous thromboembolism", this statement is not particularly helpful. After all, according to ESC guidelines, these patients ordinarily receive indefinite duration anticoagulation, regardless of the presence or absence of thrombophilia, "when this is consistent with the patient's preference".

The ESC guidelines for treating cancer patients with PE are virtually identical when compared with the ACCP. At least 3–6 months of treatment with low molecular weight heparin as monotherapy without warfarin is recommended, followed by treatment with low molecular weight heparin or warfarin as long as the cancer is considered active.

In summary, members of the ESC Task for the diagnosis and management of acute PE are to be congratulated for their excellent set of guidelines. I hope they will now undertake writing consensus guidelines for the prevention of venous thromboembolism.

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