Duration of Warfarin in Pulmonary Embolism

To the Editor:

Like numerous physicians, we always look forward to seeing the latest American College of Chest Physicians guidelines on antithrombotic therapy, and the latest (Seventh) edition is of the same superb quality as its predecessors. For several years,1 the British Thoracic Society has advised that 3 months of therapy is sufficient for the first episode of pulmonary embolism, including idiopathic cases, whereas our North American colleagues have interpreted the same available data to conclude that the traditional 6-month approach is preferable. This difference of opinion partly arose because, until recently, the only relevant studies included a high proportion of patients with deep vein thrombosis alone.

As members of the British Thoracic Society working party who recently updated our guidelines,2 we understood that the issue had been resolved by an excellent large multicenter study3 that only recruited patients with a first episode of proven clinical pulmonary embolism, and showed that continuing warfarin beyond 3 months merely deferred proven recurrence, both in idiopathic cases and in patients with a temporary risk factor (interestingly, the same group4 had previously reached similar conclusions in deep vein thrombosis). The interpretation of this is that in such cases there are only two logical alternatives: (1) stop at 3 months, but review in the event of a proven recurrence; or (2) use lifelong treatment, but review in the event of a significant iatrogenic bleed.

This important study was analyzed by the six international experts, one of whom was Professor Agnelli himself. For first-episode idiopathic pulmonary embolism, an option that can be “considered” (Recommendation 5.1.3 - Grade 2A) is indefinite treatment, the same as (2) above. However, we were very surprised that, for such cases, their preference (“we recommend”) is “at least 6 to 12 months” (Recommendation 5.1.2). Can the latter really still be considered Grade 1A? Why is there no recommendation for 3 months, which should certainly justify the same grade as that proposed?

Leaving out such guidance means that patients will receive anticoagulation for much longer than the evidence suggests, which is inconvenient and expensive. More worryingly, there will be some (not many, but some) patients who will experience a catastrophic bleed due to treatment unnecessarily prolonged beyond 3 to “at least 6 to 12 months” as a result of this selective advice.

Could we please be enlightened?

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The authors have no conflicts of interest to disclose.

REFERENCES

To the Editor:

We appreciate the comments of Dr. Miller and colleagues, and also the efforts of the British Thoracic Society. Our recommendations were developed using the following key principles: a transparent link to the strength of the relevant evidence, evaluation of the balance between risks and benefits, and explicit identification of the underlying values and preferences.1 Our recommendation that patients with a first episode of idiopathic pulmonary embolism receive treatment for 6 to 12 months was supported by the aggregate evidence available at the time for patients with idiopathic venous thromboembolism.2,5 This evidence supported three conclusions: (1) stopping treatment at 3 months resulted in a high incidence of recurrent thromboembolism, (2) an extended duration of anticoagulant treatment was effective for preventing recurrent thromboembolism while patients continued therapy, and (3) the optimal duration of anticoagulant therapy remained uncertain. The study by Professor Agnelli and colleagues4 in patients with pulmonary embolism did not include sufficient patients with idiopathic pulmonary embolism to definitively conclude that 1 year of treatment was not more effective than 3 months, since the 95% confidence interval for the relative risk of recurrent thromboembolism in this subgroup ranged from 0.45 to 2.16. A similar conclusion applied to the study by Pinede and colleagues,5 in which the 95% confidence interval for the relative risk of recurrent venous thromboembolism for 6 months vs 3 months of treatment ranged from 0.47 to 1.57 in the subgroup with idiopathic venous thromboembolism. The aggregate evidence available at the time, and particularly the study by Kearon et al,5 suggested strongly that 3 months was an insufficient duration of treatment for idiopathic venous thromboembolism. We therefore recommended treatment for at least 6 to 12 months (grade 1A),
providing the clinician some flexibility to tailor the duration of treatment to the patient’s specific clinical situation. We also made a separate recommendation to consider patients with idiopathic venous thromboembolism for indefinite anticoagulant treatment (grade 2A). Finally, we also included an explicit statement of the values and preferences underlying our recommendation, namely, “This recommendation ascribes a relatively high value to preventing recurrent thromboembolic events and a relatively low value on bleeding and cost.” Therefore, by including this explicit statement, we acknowledged that our recommendation was weighted toward preventing recurrent thromboembolism, and that clinicians may select a shorter duration of treatment, such as 3 months, for those patients who place a relatively higher value on avoiding bleeding than on preventing recurrent thromboembolism.

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The Coanda Effect and Preferential Right Atrial Streaming

To the Editor:

I read with interest the piece by Zanchetta et al (August 2005) regarding right-to-left shunting through a patent foramen ovale (PFO). Although the authors proposed a hypothesis for inferior caval-to-PFO streaming, they did not propose or address the mechanism for the well-described preferential superior vena caval (SVC) to right atrioventricular valve blood flow.

This dual preferential streaming within the right atrium was initially observed in the 1930s and is not only significant in right-to-left shunting but also performs a fundamental role in fetal circulation and development. Both streams are mutually important as disordered blood flow from one stream could interfere with the blood route of the other; for example, misdirected blood from the SVC arriving at the inferior vena cava (IVC) or the IVC-PFO tract would interfere and hinder the blood flow of the right-to-left shunt.

The blood stream from the SVC has been imaged by magnetic resonance velocity mapping and demonstrates that the stream flows anteriorly over the convex muscular inferior surface of the anterior right atrial wall directed to the right atrioventricular valve. Such a stream of flow was first noted in 1910 by Romanian aerodynamics visionary Henri Marie Coanda (1886 to 1972), for whom the effect is eponymously named, stating that a fluid stream has a natural tendency to follow the shape of a body as it flows past it. Without the characteristic morphology of the right atrial muscular anterior wall therefore, SVC-to-PFO flow could be interrupted by an SVC blood stream, opposing the right-to-left shunt and resulting in disordered and suboptimal fetal oxygenation. The Coanda effect therefore contributes to the unique mechanism by which the right atrium keeps these two streams separate.

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The author has no conflict of interest to disclose.

Impact of Positron Emission Tomography on Clinical Decision Making

To the Editor:

We read with interest the article by Sachs and Bilfinger (August 2005) on the impact of positron emission tomography (PET) on clinical decision making in an academic lung cancer center and wish to comment regarding the consistency of the data and also on the generalizability of the findings. In calculating the false-positive rate of PET for the primary site, the authors

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