Correspondence to: John P. V. Rigby, BM, Huntsmoor Weir, Old Mill Lane, Cowley, Uxbridge, United Kingdom UB8 2JH

Prevention of Fatal Pulmonary Embolism in the Hospital

To the Editor:

A recent discussion with resident physicians regarding the relative benefits of various VTE prophylaxis regimens prompted a review of the article in *CHEST* by Goldhaber et al[1] entitled, "New Onset of Venous Thromboembolism Among Hospitalized Patients at Brigham and Women's Hospital Is Caused More Often by Prophylaxis Failure Than by Withholding Treatment" (December 2000). To my knowledge, there has been no specific correspondence regarding this study, which concluded with the statement that "most deaths from pulmonary embolism (PE) among patients hospitalized for other conditions occurred in the setting of failed prophylaxis rather than omitted prophylaxis." Several explorations would seem warranted regarding this conclusion.

Goldhaber et al[1] described 384 patients who developed venous thromboembolism (VTE) either in the hospital (211 patients) or within 30 days of prior hospital discharge (173 patients). Among this pooled set of patients, 201 had received some form of VTE prophylaxis. Details other than the type of modality employed (*eg*, the dose of unfractionated heparin or the duration of prophylaxis prior to diagnosis) are not provided.

By the definitions used for *failure*, an assumption is made that the patients who presented within 30 days of hospital discharge (173 of the total of 384 patients) would have developed their deep vein thrombosis (DVT)/VTE while they were hospitalized and receiving some sort of prophylaxis. If this assumption is rejected, then fully 45% of the patients described cannot be considered as having failed. It is more conceivable that the 173 patients who developed VTE after hospital discharge simply presented with a manifestation of their underlying disease processes while no longer receiving VTE prophylaxis.[2]

The main conclusion itself, that "most deaths from pulmonary embolism among patients hospitalized for other conditions occurred in the setting of failed prophylaxis rather than omitted prophylaxis" is intriguing but bears closer scrutiny. The authors themselves state that, because the patients they described represented < 0.5% of all hospital admissions, VTE prophylaxis was "quite possibly almost always successful." Since the most important failure of VTE prophylaxis should be considered fatal PE, an attempt to critically understand the conditions surrounding such failures would be useful. However, some of the data that could contribute to such an understanding are confusing:

1. Among the patients whose death was attributed to PE and "failure of prophylaxis," it is not clear that these patients were receiving adequate prophylaxis. Inadequate application of an accepted regimen should not be interpreted as that regimen having failed.
2. It is not clear exactly how the course to diagnosis of VTE proceeded in the patients who died, as follows:
   - ". . . 112 patients are described as having PE (62 alone and 50 in association with DVT). . . " (in "Results" section of article).
   - "PE was diagnosed primarily by high-probability lung scan (38 patients), intermediate lung scan with high clinical suspicion (50 patients) using revised criteria of the Prospective Investigation of Pulmonary Embolism Diagnosis, or positive pulmonary angiography (33 patients)" (total, 121 patients [in "Materials and Methods" section]).
   - In the 13 patients whose deaths were attributed to PE, that diagnosis was made at autopsy in 8 patients, clinically alone in 2 patients, and by a combination of clinical findings and ultrasound in 3 patients (in Table 6 of the article by Goldhaber et al[1]). These data would seem to imply that in none of the fatalities was the diagnosis suspected sufficiently to employ one of the three primary diagnostic modalities.
3. Seven percent of the patients in whom VTE was diagnosed (26 of 384 patients) in this study did not receive any treatment for the disorder. It is not clear that the patients who died were not overly represented within this group that did not receive treatment.
4. It is not possible to discern from the data presented whether, in the cases of fatal PE, any of the patients who failed VTE prophylaxis received diagnoses tardily and/or were treated inappropriately once the suspicion of PE was raised. Because hospitalized patients are likely to be diagnosed and treated promptly for any acute clinical deterioration, this was probably not the case. However, such reassurance is not provided.

It is generally accepted that, once diagnosed, acute nonfatal VTE is at best an uncommon cause of death, recurring in only a small minority of patients, with most deaths actually attributable to underlying diseases.[3,4] Therefore, absent the data mentioned, I wonder whether standard VTE prophylaxis, while not 100% successful in preventing all cases of VTE, might actually come quite close to that percentage in preventing fatal PE. Indeed, a more recent article by Arnold et al[5] suggests this may well be the case. In that article, the majority of nonpreventable thromboses (*ie*, thromboses that occurred despite adequate prophylactic regimens) were lone distal DVT.

In summary, the following three points deriving from a critical appraisal of the study by Goldhaber et al[1] are likely to be important when considering the concept of VTE prophylaxis failure:

1. It does not follow that patients who go without VTE prophylaxis for any time should be considered as having failed VTE prophylaxis. It is not clear that pooling patients, as was done in the study by Goldhaber et al,[1] is valid. Further illustrative of this point, as an example, is data showing that extended (*ie*, out-of-hospital) VTE prophylaxis is useful in hip surgery patients but not necessarily in those undergoing knee surgery.[6] Such a distinction further underscores the importance of unique patient characteristics or disease-associated alterations in coagulability.
2. Unique and possibly peculiar individual patient characteristics may be important factors with respect to our evolving understanding of VTE prophylaxis failure. Clinical signs and symptoms, exact methods of prophylaxis, and time to diagnosis and treatment would be useful information that should be available for hospitalized patients. Because hospitalized patients are likely to be diagnosed and treated promptly for any acute clinical deterioration, it is possible that routine standard VTE prophylaxis may be close to 100% effective in the prevention of fatal PE in the hospital.
3. I believe there is persistent contention regarding whether subcutaneous unfractionated heparin, administered two or three times daily in doses of either 5,000 or 7,500 U, is adequate prophylaxis in any population of hospitalized

patients. No conclusion from this study can be drawn regarding the utility of this inexpensive drug.

Dominick A. Rascona, MD, FCCP
United States Naval Medical Center
Portsmouth, VA

Correspondence to: Dominick A. Rascona, MD, FCCP, Pulmonary and Critical Care Medicine, US Naval Medical Center, Portsmouth, VA 23708; e-mail: darascona@mar.med.navy.mil

References

1 Goldhaber SZ, Dunn K, MacDougall RC. New onset of venous thromboembolism among hospitalized patients at Brigham and Women's Hospital is caused more often by prophylaxis failure than by withholding treatment. Chest 2000; 118:1680–1684
2 Schafer AI. Venous thrombosis as a chronic disease. N Engl J Med 1999; 340:955–956
3 Carson JL, Kelley MA, Duff A, et al. The clinical course of pulmonary embolism. N Engl J Med 1992; 326:1240–1245
4 Douketis JD, Kearon C, Bates S, et al. Risk of fatal pulmonary embolism in patients with treated venous thromboembolism. JAMA 1998; 279:458–462
5 Arnold DM, Kahn SR, Shrier I. Missed opportunities for prevention of venous thromboembolism: an evaluation of the use of thromboprophylaxis guidelines. Chest 2001; 120:1964–1971
6 Pineo GF. Prevention of venous thromboembolic disease. UpToDate Version 11.3. www.uptodate.com. Topic updated July 16, 2003. Accessed October 10, 2003

Sleep, Breathing, Oxygen, and Heart

To the Editor:

We read with interest the recent report by Hayashi et al (September 2003)[1] proposing a relationship between sleep-disordered breathing (SDB) and coronary artery disease (CAD).

There are several deficiencies in the study that negate the authors' conclusions that "repetitive NOD [nocturnal oxygen desaturation] due to SDB is an important and independent risk factor for the development of coronary atherosclerosis." First, a statistically significant correlation coefficient between NOD and CAD score does not necessarily reflect a causal relationship, as was assumed by the authors. Second, the degree of sleep hypoxemia experienced by these subjects appears to be relatively mild. There was no significant difference between the less and the more severe CAD groups in the time spent at < 90% oxygen saturation. While the lowest oxygen saturation readings were significantly lower in patients with more severe CAD, the total duration (and thus, the relevance) of such episodes is not stated. The authors' hypothesis about the role of hypoxemia in "triggering" the coronary vascular disease process is also inaccurate since the study did not reveal any significant hypoxemia in patients with angiographically proven CAD of lesser severity (group N in the study). Furthermore, the basic premise that NOD would reflect obstructive sleep apnea in a cohort with lean body habitus, and thus, a low pretest probability of having obstructive sleep apnea, is faulty, as was appropriately pointed out by Dr. Sin in his editorial.[2]

From a health-care perspective, the more significant finding in the study appears to be the gross underutilization (8.4% of all patients) of therapy with β-blockers in these patients with proven coronary vascular disease.[3]

In conclusion, we believe that the authors' assertion about the role of SDB in the genesis of coronary vascular pathology is an overstatement of the actual results of the study and has the risk of being taken at face value by readers of *CHEST*.

Rohit Budhiraja, MD
David Hudgel, MD, FCCP
Henry Ford Hospital
Detroit, MI

Correspondence to: David Hudgel, MD, FCCP, Professor of Medicine, Chief, Section Head, Sleep Disorders and Research Center, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202; e-mail: dhudgel1@hfhs.org

References

1 Hayashi M, Fujimoto K, Urushibata K, et al. Nocturnal oxygen desaturation correlates with the severity of coronary atherosclerosis in coronary artery disease. Chest 2003; 124:936–941
2 Sin DD. Sleep-disordered breathing: a heart-changing experience? Chest 2003; 124:778–780
3 Frishman WH. Cheng A. Secondary prevention of myocardial infarction: role of beta-adrenergic blockers and angiotensin-converting enzyme inhibitors. Am Heart J 1999; 137:S25–S34