Pulmonary Embolism Prevalence in Admitted Syncope Patients: 1 in 6 Really?

Answers to the March 2017 Journal Club Questions

Guest Contributors
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Editor's Note: *You are reading the 56th installment of* Annals of Emergency Medicine *Journal Club. This Journal Club refers to the article by Prandoni et al*[1] *published in the October 20, 2016, edition of the* New England Journal of Medicine. *Information about Journal Club can be found at http://www.annemergmed.com/content/journalclub. Readers should recognize that these are suggested answers. We hope they are accurate; we know that they are not comprehensive. There are many other points that could be made about these questions or about the article in general. Questions are rated "novice" (NOV), "intermediate" (INT), and "advanced" (ADV) so that individuals planning a journal club can assign the right question to the right student. The "novice" rating does not imply that a novice should be able to spontaneously answer the question. "Novice" means we expect that someone with little background should be able to do a bit of reading, formulate an answer, and teach the material to others. Intermediate and advanced questions also will likely require some reading and research, and that reading will be sufficiently difficult that some background in clinical epidemiology will be helpful in understanding the reading and concepts. We are interested in receiving feedback about this feature. Please e-mail journalclub@acep.org with your comments.*

DISCUSSION POINTS

1. Prandoni et al[1] performed a systematic evaluation for pulmonary embolism (PE) among admitted patients with syncope at 11 Italian hospitals.

NOV A. What was the study's primary result? Does the study result reflect your clinical experience?

NOV B. Describe the admission criteria for syncope in these hospitals. Are these admission practices similar to those in your practice setting?

INT C. Discuss the apparent morbidity level of the patients included in the study cohort. How does the baseline disease burden of the patients in this study compare with that of syncope patients in your emergency department (ED)?

INT D. How might study results differ from those of a study conducted in hospitals like yours?

2. NOV A. The authors used the Evaluation of Guidelines in Syncope Study Score to determine a high probably of cardiac syncope. What elements does that score use?

NOV B. What objective tests did all patients undergo? Is this different from the evaluation you typically order for a patient with syncope?

3. NOV A. What risk-stratification scores exist for PE? Which scores were used in Prandoni et al?[1] Which ones do you use clinically?

INT B. What percentage of patients in this study followed the suggested diagnostic algorithm? Did the diagnostic algorithm follow accepted guidelines for PE evaluation?

INT C. Were the PEs diagnosed in this study clinically relevant? Do you think the PEs diagnosed in the study explain the presentation of syncope?

4. The study concludes that 17.3% of patients hospitalized for syncope have a PE.

INT A. Of all patients who visited the ED for syncope, what percentage of them received a definitive diagnosis of PE?

NOV B. How did the study authors account for patients who died or were lost to follow-up?

NOV C. What was the mean age of patients in the study population? How does this change the way you interpret the data?

INT D. How does this study affect your decision to aggressively evaluate syncope patients for PE in the ED who do not otherwise appear to have a PE? What would be the downstream effects if more of these patients were to undergo evaluation for PE?

5. One's interpretation of this study is highly dependent on understanding exactly who was in the study.

INT A. What exactly do you know about these patients (and the patients who were excluded)? What do you not know that you would like to know?

ADV B. This study design falls under the Strengthening the Reporting of Observational Studies in

Epidemiology (STROBE) reporting guideline.[2] What does STROBE say about how the study cohort should be described? Did the authors meet the STROBE requirement? If not, how so? If yes, is STROBE adequate to ensure reporting that is sufficient to allow us to determine the external validity of the study?

ANSWER 1

Q1. Prandoni et al[1] performed a systematic evaluation for pulmonary embolism (PE) among admitted patients with syncope at 11 Italian hospitals.

Q1.a What was the study's primary result? Does the study result reflect your clinical experience?

The primary outcome was prevalence of PE in patients admitted for syncope. The authors concluded that 1 in 6 admitted patients with syncope had PE as the cause. Although every hospital and practice setting is unique, our experience in urban private and public hospitals in the United States suggests that PE as the cause of syncope is substantially less common than suggested by this study.

Q1.b Describe the admission criteria for syncope in these hospitals. Are these admission practices similar to those in your practice setting?

Admission criteria in this study included syncope plus trauma related to falls, severe coexisting conditions, failure to identify an explanation, or high probability of cardiac cause. Although there is variation in admission criteria for syncope among different providers and practice settings, the stated criteria are not dissimilar to those in our own practice.

Q1.c Discuss the apparent morbidity level of the patients included in the study cohort. How does the baseline disease burden of the patients in this study compare with syncope patients in your ED?

To understand the external validity of this study, we need a clear picture of the baseline morbidity of the patients. Unfortunately, the article does not provide a great deal of detail in regard to baseline morbidity. We do know that the mean age of patients in the study was 76 years and obesity rate was low. The authors do disclose the rates of recent trauma, surgery, active cancer, and infectious disease. Patient age and cancer prevalence are substantially higher than in our syncope population. Comorbidities alone might contribute to the high rate of PE in the study population. Unfortunately, we are provided only with ecologic data and little sense of each patient's condition and how that related to PE risk.

Q1.d How might study results differ from those of a study conducted in hospitals like yours?

In emergency medicine, we are much less concerned with the prevalence of PE in admitted syncope patients. What is more relevant is determining the appropriate threshold to commence PE evaluations in unselected groups of patients presenting to the ED with syncope. Although there is a small amount of data on the undifferentiated patient presenting to the ED with syncope, they are sparse and largely outdated.[2-4] Inpatients, on the other hand, appear to have a high prevalence of PE in syncope.[5] We would be surprised if the PE rate were anywhere near as high as reported in this study among an undifferentiated group of syncope patients in a typical United States ED.

ANSWER 2

Q2.a The authors used the Evaluation of Guidelines in Syncope Study Score to determine the probability of cardiac syncope. What elements does that score use?

The Evaluation of Guidelines in Syncope Study Score uses the following elements: abnormal ECG result or heart disease, palpitations before syncope, syncope during effort or in supine position, absence of autonomic prodromes, and presence of classic syncope risk factors such as warm crowded places, prolonged standing, pain, fear, or emotion.[6] The higher the score, the higher the probability of cardiac syncope.

Q2.b What objective tests did all patients who presented with syncope undergo? Is this different from the evaluation you typically order for a patient with syncope?

All patients with syncope underwent chest radiography, ECG, arterial blood gas testing, and "routine blood testing" that included a D-dimer assay. If indicated, patients underwent carotid sinus massage, tilt testing, echocardiography, and 24-hour electrocardiography. In the ED, many of the tests described in this article are obviously not performed. In our experience, there is great variation in ED syncope evaluations. Many clinicians rely heavily on history and physical, whereas others adhere to the San Francisco Syncope Rule.[7,8] Some physicians perform a battery of investigations regardless of perceived risk.

ANSWER 3

Q3.a What risk-stratification scores exist for PE? Which scores were used in Prandoni et al? Which ones do you use clinically?

The Wells criteria,[9] pulmonary embolism rule-out criteria rule,[10] and Geneva score[11] are 3 commonly used

risk-stratification tools for PE in the ED. In general, they share many similar elements: clinical risk factors for PE or deep venous thrombosis, abnormalities of vital signs, and, notably, subjective assessment of PE risk. The original Geneva score adds testing elements such as PaO_2, $PaCO_2$, and chest radiography findings. Prandoni et al used the Wells score in their algorithm.

Q3.b What percentage of patients in this study followed the suggested diagnostic algorithm? Did the diagnostic algorithm follow accepted guidelines for PE evaluation?

This is not explicitly stated, but syncope patients who were admitted to the hospital and entered into the study (22% of all syncope patients) appeared to have a fairly standard evaluation of Wells stratification, D-dimer, and ventilation perfusion or computed tomography (CT) pulmonary angiogram imaging if indicated.

The authors' approach to the evaluation of PE is not broadly agreed on. The American College of Emergency Physicians' clinical policy on management of suspected PE states that either objective criteria or gestalt can be used to risk-stratify patients because there is insufficient evidence to support the preferential use of one over the other.[12]

Q3.c Were the PEs diagnosed in this study clinically relevant? Do you think the PEs diagnosed in the study explain the presentation of syncope?

The clinical importance of the diagnosed PEs in this study is unclear. Indeed, the clinical significance of many diagnosed PEs is unclear.[13] The implication of this study is that the PEs diagnosed in patients with syncope were actually the *cause* of their syncope. The study provides no direct evidence for this conclusion, and in sicker patients with other clot-promoting disease processes, these findings may well be incidental.

ANSWER 4

Q4. The study concludes that 17.3% of patients hospitalized for syncope have a PE.

Q4.a Of all patients who visited the ED for syncope, what percent of them received a definitive diagnosis of PE?

Of the 2,584 patients who visited the ED for syncope, 97 had a confirmed PE. That equates to approximately 4% of the patients presenting to the study hospitals for syncope.

Q4.b How did the study authors account for patients who died or were lost to follow-up?

They report only one death in the study group and confirmed PE on autopsy, but the accuracy of this practice has been questioned.[14] There were no patients lost to follow-up.

Q4.c What was the mean age of patients in the study population? How does this change the way you interpret the data?

The mean age of patients enrolled was 76 years. Increasing age is associated with elevated disease burden and PE risk. Clinicians working with generally younger patient populations can reasonably expect the PE rate to be substantially lower than in this study.

Q4.d How does this study affect your decision to aggressively evaluate syncope patients for PE in the ED who do not otherwise appear to have a PE? What would be the downstream effects if more of these patients were to undergo workup for PE?

After reading this article, some providers may consider additional, aggressive diagnostic tests to rule out PE in patients who present with syncope. Increased diagnostic testing for PE will inevitably result in increases in CT pulmonary angiogram use, cost, length of stay, and radiation exposure. Should additional PEs be detected, it remains wholly unclear whether these patients will benefit from their detection and treatment.[13]

ANSWER 5

Q5. One's interpretation of this study is highly dependent on understanding exactly who was included in the study.

Q5.a What exactly do you know about these patients (and the patients who were excluded)? What do you not know that you would like to know?

Patients included in the study were aged 18 years or older, with a first-ever episode of syncope. Patients were admitted if there was trauma related to the fall, severe coexisting conditions, failure to identify an explanation for syncope, or a high probability of cardiac syncope. Among the excluded patients were those who were pregnant, had previous episodes of syncope, or were receiving anticoagulation. One thousand eight hundred sixty-seven patients with syncope were discharged directly from the ED because the cause of their syncope was considered obvious or, in 81 cases, they refused admission. We do not know which of the discharged patients may have had a PE identified if further evaluation had been pursued.

A more detailed explanation of the differences between the patients entered in the study and those admitted for evaluation would be helpful in determining external validity.

Q5.b This study design falls under the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.[15] What does STROBE say about how the study cohort should be described? Did the authors meet the STROBE requirement? If not, how so? If yes,

is STROBE adequate to ensure reporting that is sufficient to allow us to determine the external validity of the study?

According to the STROBE guidelines, the study cohort participants should include a description of the eligibility criteria, include the sources and methods of selection of participants, and describe methods of follow-up. There should be an explanation of how loss to follow-up was addressed. This study does follow the STROBE guidelines, but there is a level of detail that is missing. In general, it is extremely helpful to provide a very clear description of the types of patients enrolled in the study so that one can compare the study cohort to one's own patient population and determine whether study findings are likely to be relevant.

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