DEM Journal Club

Article Appraisal

Article: Treatment of Pulmonary Embolism with Rivaroxaban: Outcomes by Simplified Pulmonary Embolism Severity Index Score from a Post Hoc Analysis of the EINSTEIN PE Study.

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Background and Study Objective(s):

In the US, most patients with pulmonary embolism (PE), regardless of their clinical stability, are admitted to hospital. The role of PE severity and prognostic indexes remains poorly defined, and some suggest such tools could be used to idenfity a group of patients at low risk for adverse outcomes and suitable for direct discharge from the ED. The purpose of this study was to assess adverse outcomes in PE patients enrolled in the EINSTEIN PE study using the previously validated simplified pulmonary embolism severity index (sPESI). The EINSTEIN PE Study was an open-label randomized control trial on treatment of stable PE with Rivaroxaban vs. Standard Treatment (Heparin & VKA) published in the NEJM in 2012. This established a large cohort of PE patients that the authors performed a post hoc analysis for adverse events on, categorized by the sPESI score.

Study Design:

The EINSTEIN PE study was an industry-sponsored multi-center RCT done in 38 countries that enrolled 4832 patients. Inclusion critera were any of: PE on CT, filling defect or suddent cutoff on pulmonary angiogram, perfusion defect on V/Q scan, or inconclusive resuts with demonstration of DVT by ultrasound or venogram. The sPESI score is calculated based on 6 patient factors available in the EINSTEIN PE database: age > 80, history of cancer, chronic cardiopulmonary disease, HR >= 110, Systolic BP < 100, and arterial O2 Sats < 90%. The authors examined the relationship between sPESI scores at 0, 1, and >= 2 and four outcomes: recurrent VTE, fatal PE, all cause mortality, and major bleeding at various time points.

Results:

The majority of patients had low sPESI scores (53.6% were 0, 36.7% were 1, and 9.7% were >=2). No patient had a score higher than 3. The risk of all 4 outcomes increased with increasing sPESI scores. The adverse events in patients with an sPESI of 0 and 1 were low during first 30 days, a trend that appeared to continue beyond that. Of note, risk of fatal PE at day 7 was <0.1% for both sPESI 0 and 1. Recurrent VTE was =< 1% at 30 days for both risk scores. All cause mortality was =< 0.8% at 30 days for both sPESI 0 and 1, but there appeared to be a little more variability between those two levels. Major bleeding was =< 1.1% at 30 days for both levels. Higher sPESI scores, particulary socres >=2, were associated with higher rates of major bleeding and all cause mortality. Only 10% of the enrolled popuation were treated in an outpatient manner, and they had various sPESI scores. The authors also included relative rates of each adverse events at various sPESI level between the Rivaroxaban and Standard Therapy groups in

supplementary tables online but this as not a primary focus of this study and was not discussed in detail at Journal Club.

Validity of Results:

The general sense of Journal Club attendees was that the results were valid, as the EINSTEIN PE study was well-designed prospective trail. It was noted that the enrolled group had a very low risk of adverse outcomes compared to other published studies, registries, and the sense of Journal Club attendees. This may in part be due to the inclusion criteria, which including patients who may not have had a clear PE but were proven to have a DVT. Despite this, it was felt that the association between sPESI levels with various risk events likely still holds, though the absolute risk could be lower than we might find in our location.

Generalizability of Results:

The overall sentiment of Journal Club attendees was that the results are generalizable to our setting, and show modest correlation of adverse outcomes in PE with sPESI score. The patient population appeared to reflect the population presenting with PE that we would likely see in local EDs. How, if at all, to actually apply this information generated significant discussion.

The Bottom Line:

This study provides good evidence that both sPESI 0 and 1 scores are associated with very low adverse events in the first 30 days and likely beyond (note the original sPESI score classified only those with sPESI 0 as low risk). This paper did not directly address which patients can or should be treated as outpatient, and in truth this decision could be argued to be best made on a site specific basis based on resources and whether the possibility of an adverse event at home is of concern to the patient and/or staff (irrespective of the likelihood that the ultimate outcome would be similar regardless of where an adverse effect occurred). This study was not designed or powered in a manner appropriate to reach clear conclusions regarding Rivaroxaban vs. Standard Treatment at various sPESI scores. When dealing with the key question of which stable PE patients can be sent home on treatment, the general sentiment amongst Journal Club attendees was that the decision should be made based on a combination of: 1) accepted and “usual” approach in that particular institution; 2) the full clinical picture , possibly with the use of scores like sPESI to support or justify a clinical inclination, but not at the expense of clinical gestalt. Finally, it was felt to be important to keep in mind that if local EPs chose to incorporate the results of this study in their decision, they should we aware that their event rates might be lower than other published results. Finally, it was felt that EPs we should never hesitate to ask consultants an opinion on cases where the admit/discharge decision is unclear.