Accuracy of the Alveolar-Arterial Gradient for the Diagnosis of Pulmonary Embolism: A Systematic Review and Meta-analysis.

Jason R. West1, Zachary Levine2, and Nicholas Caputo3

1Lincoln Medical and Mental Health Center - Weill Cornell Medicine, 2LINCOLN MEDICAL AND MENTAL HEALTH CENTER, 3Lincoln Medical Center

Background: The relationship between the Alveolar-arterial (A-a) gradient and pulmonary embolism (PE) has been studied for decades, but no systematic review or meta-analysis has been performed on the accuracy of the A-a gradient, a rapid and non-invasive test, to exclude the diagnosis of PE. This analysis is the first systematic review and meta-analysis to determine the diagnostic utility of an elevated A-a gradient to identify PE.

Methods: We conducted a search of MEDLINE, EMBASE, and Scopus databases using search terms aided by a librarian to identify articles from database inception to present using Medical Subject Headings (Mesh) and keywords for synonyms of blood gas analysis and PE. All articles were screened for inclusion by two independent reviewers using the Quality of Assessment of Diagnostic Studies Statement (QUADAS-2) to assess bias. In the case of disagreement between the 2 reviewers, a third reviewer was added to determine study inclusion. The diagnosis of PE was determined by advanced imaging in all the included studies. GRADE methodology was used to determine the quality of the included studies.

Results: Of the 367 articles excluding duplicates from the database screening, 32 underwent full review. 12 studies were included in the analysis. All included studies were classified by GRADE methodology to be of low or very low quality of evidence, and none of the studies used either physician gestalt or formal risk stratification, via widely-available clinical decision rules, for risk stratification. Of the 12 included studies including 3,356 patients (pooled prevalence of PE was 34.0%), the sensitivity was 90.2% (95%CI 88.3-91.9) and specificity was 18.4% (95%CI 16.8-20.1). In the subgroup analysis of the 5 studies utilizing an age-adjusted A-a gradient including 2,367 patients, the sensitivity was 92.8% (95%CI 90.7-94.4) and specificity was 13.6% (95%CI 11.9-15.4).

Conclusion: The A-a gradient has moderate sensitivity and low specificity to detect PE among ED patients tested for PE. The use of age-adjusted A-a gradient increases the accuracy of the A-a gradient to exclude the diagnosis of PE. Further studies including risk stratification for PE are needed to determine whether the A-a gradient can be a useful diagnostic test to exclude PE in patients who are evaluated at low risk of PE, whether by gestalt or available clinical decision rules.

Presyncope Carries Similar Risk as Syncope in Emergency Department Patients with Acute Pulmonary Embolism

Darcy C. Engelhardt1, Disha Bahl1, Ashley S. Abraham1, William P. Swanson2, Dale M. Cotton3, William C. Krauss4, Jie Huang5, Mary E. Reed5, Dustin G. Mark3, and David R. Vinson3

1The CREST Network, 2University of California, Davis, 3The Permanente Medical Group, 4Department of Emergency Medicine Kaiser Permanente San Diego Medical Center, 5Kaiser Permanente Division of Research

Background: Syncope indicates a more severe case and prognosticates a worse outcome in Emergency Department patients with acute pulmonary embolism (PE). Whether this is true of presyncope is unknown. We compare these groups on markers of severity: proximal clot location, PE Severity Index (PESI) Class, subjective and objective PE type, Emergency Department ventilatory support, intensive care unit (ICU) admission, and 30d all-cause mortality.

Methods: This retrospective cohort study included all adults with acute PE in 21 community Emergency Departments from 01/2013 through 04/2015. We combined electronic health record extraction with manual chart abstraction. We defined syncope as an abrupt, transient, complete loss of consciousness with loss of postural tone, with rapid, spontaneous recovery and presyncope as an abrupt, transient feeling of nearly fainting or losing consciousness with rapid, spontaneous recovery as documented by the EM or consultant physician. Non-specific dizziness and light-headedness were not included. Categorization was confirmed by two abstractors and arbitrated, if needed, by a third. Proximal clots involved lobar or main pulmonary arteries. Higher-risk PESI included Classes IV-V. Massive PE had sustained SBP.

Results: Among 2,996 patients with objectively-confirmed PE, 82 (2.7%) had presyncope and 109 (3.6%) had syncope. Comparing presyncope with syncope, we found no statistically significant differences in any marker of severity (p>0.10 for all): proximal clot location (61.0% vs 62.4%), higher-risk PESI Class (48.8% vs 54.1%), submassive or massive PE (62.2% vs 52.3%), Emergency Department ventilatory support (12.2% vs 13.6%), ICU admission (19.5% vs 26.7%), or 30d all-cause mortality (4.9% [n=4] vs 9.2% [n=10]).

Conclusion: Multiple markers of severity were as prevalent among PE patients presenting to the Emergency Department with presyncope as with syncope in this multicenter study. Larger prospective studies are needed to investigate the apparent similarity in attributable risk between presyncope and syncope.

Bedside End Tidal Carbon Dioxide in Evaluation for Pulmonary Embolism

Marianne C. Wallis1, Matthew D. Wilson2, Lydia Koroshetz3, Rui Soares3, and Munish Goyal1

1MedStar Washington Hospital Center, Georgetown University, 2MedStar Washington Hospital Center, 3Georgetown University

Background: Pulmonary embolism (PE) presents a diagnostic challenge to the emergency physician. The D-dimer test can be difficult to use because it is non-specific; CT scan of the chest requires clinical stability, administration of contrast and radiation exposure. Studies suggest that it is possible to use end tidal carbon dioxide (ETCO2) as a screening modality for PE, however none have conclusively evaluated this prospectively in emergency department patients. We sought to determine if ETCO2 can rule out the presence of clinically significant PE. We hypothesized that no patients with significant PE would have an ETCO2 greater than 35 mm Hg. Our secondary hypothesis was that the mean ETCO2 would be significantly lower in patients with PE versus without PE.

Methods: A prospective observational study was performed on a convenience sample of adults presenting to a tertiary academic emergency department that receives 57,000 visits annually. Patients with suspected PE who were ordered for either D-dimer, CT for PE, or ventilation/perfusion scan were approached, consented and enrolled in the study to be trained research assistants. The mean ETCO2 level was measured via nasal cannula and recorded using a standardized data collection sheet, along with vitals and demographic data. After definitive testing, a play with vital signs chart reviewer extracted which patients had clinically significant PE, defined a priori as PE causing hypotension, tachycardia, hypoxemia, right heart strain, or newly elevated troponin or BNP. Comparison of ETCO2 in patients with and without PE was made using robust regression models with iterative re-weighted least squares method (IRLS), adjusting for COPD status, age and gender. A preplanned secondary analysis was performed excluding patients with COPD.

Results: A total of 69 patients with suspected PE were enrolled; eight had clinically significant PE. The primary hypothesis was rejected as three patients with significant PE had ETCO2 greater than 35 mm Hg. IRLS showed that the mean ETCO2 level was significantly lower by 6.6 mm Hg for those with PE (35.2 vs 41.8, p <0.01).

Conclusion: The use of bedside ETCO2 35 mmHg to rule out clinically significant PE is not supported by our data. However, ETCO2 levels are significantly lower in ED patients with PE than in those without. Further studies of ETCO2 measurement for risk stratification are warranted.