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Improved rule-out diagnostic gain with a combined aortic dissection detection risk score and D-dimer Bayesian decision support scheme

Amado Alejandro Baez, MD, MSc, MPH [a,*], Laila Cochon, MD [b]

[a] Department of Emergency Medicine, Jackson Memorial Hospital, Miami, FL
[b] Center for Evidence Based Radiology, Brigham and Women's Hospital, Boston, MA

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ABSTRACT

The objective of this study was to develop a Bayesian clinical decision support mathematical model that can assist in assessing a diagnostic utility integrating the aortic dissection detection risk score (ADD-RS) combined with the diagnostic quality of D-dimer testing.

Methods: Our method uses the Bayes nomogram. Pretest probability scoring for the ADD-RS was obtained using their derived precalculated effects models. Sensitivity, specificity, and positive and negative likelihood ratios (LRs) for D-dimer testing were obtained by meta-analysis. Posttest probability was obtained from Bayesian statistical modeling integrating low, intermediate, and high pretest for the ADD-RS and LRs for D-dimer testing. Relative (RDG) and absolute (AADG) diagnostic gains were calculated.

Results: Pool meta-analysis of D-dimer data demonstrated a sensitivity of 0.97 (95% confidence interval [CI], 0.94-0.99), specificity of 0.56 (95% CI, 0.51-0.60), negative LR of 0.06 (95% CI, 0.03-0.12), and positive LR of 2.43 (95% CI, 1.89-3.12). Bayesian modeling for negative LRs demonstrated posttest probabilities scores of 0.24% for low risk (AADG = 4.06% and RDG = 94.42%), 3.4% for intermediate risk (AADG = 33.1% and RDG = 90.68%), and 7.9% for high risk (AADG = 51.3% and RDG = 86.65%).

Conclusion: The integration of the ADD-RS and D-dimer testing in a decision support scheme suggested rule-out diagnostic value and gains, mostly evidenced in the AADD-RS low and intermediate pretest probability categories. We propose further evaluating the use of this decision support scheme in a prospective model and as a potential triage tool for aortic dissection.

1. Introduction

Acute aortic dissection (AAD) is the most lethal among cardiovascular conditions. With an often imprecise and equivocal clinical presentation, it is of fundamental importance to diagnose and manage effectively and swiftly, making it a true emergency medicine challenge. The incidence of acute AAD in the United States is estimated at 10 000 cases annually, whereas emergency department visits are approximately 100, 000, 000 during the same period [1], further supporting the importance of protocolized cost-effective methods of screening and ultimately diagnosing AAD in an emergency department setting.

The aortic dissection detection risk score (ADD-RS) is a tool developed by the IRAD database [2], with the aim of providing clinicians with a simple, systematic method for screening large volumes of patients at the bedside. By focusing on specific high-risk predisposing conditions, pain features, and physical examination findings, patients are grouped into 1 of 3 categories on the basis of their pretest risk of acute AAD. The goals are to rapidly identify patients at high risk and to provide a framework for additional diagnostic testing based on a pretest probability of disease [2].

The Acute Care Diagnostic Collaboration is a multicenter, multinational research effort that introduces a Bayesian method and statistical modeling on pretest probability with emergency medicine clinical decision rules, combining it with assessments on diagnostic quality and cost-effectiveness of clinical analytic tools in various patient populations. Using the Bayes theorem, the initial clinical assessment is graded by means of probability and, when subsequently merged with clinical suspicion and diagnostic test results, either rules out or rules in the diagnosis [3].

For acute aortic dissection imaging, studies in the shape of computed tomography (CT) and echocardiography are used for early detection.

In 2010 the American Heart Association implemented a decision algorithm to aid in the evaluation of AAD [2]. The ADD-RS is a clinical tool used to gauge risk of disease [4]. D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. D-dimer has been investigated for its use as a rule-out biochemical marker for AAD [5-11]. Ultimately, this particular combined diagnostic method may limit unnecessary exposure to radiation while proving to be time- and cost-effective in ruling out AAD [12].

* Corresponding author at: Jackson Memorial Hospital, Department of Emergency Medicine, 1611 NW 12th Ave, Miami, FL 33136.
E-mail address: aabaezmd@gmail.com (A.A. Baez).

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In probability theory and statistics, Bayes theorem describes the probability of an event, based on conditions that might be related to the event Bayes theorem then links the degree of belief in a proposition before (pretest probability) and after (posttest probability) accounting for evidence. With the Bayesian probability interpretation, the theorem expresses how a subjective degree of belief should rationally change to account for evidence: this is Bayesian inference, which is fundamental to Bayesian statistics. The Bayesian nomogram is a graphical calculator that is a useful and convenient way to perform calculations without the need to remember the formula integrating pretest probability with diagnostic tests of likelihood ratios (LRs; Fig. 1). The use of the Bayes nomogram has simplified the use of diagnostic test information and is now frequently used by numerous physicians.

The objective of this study was to develop a Bayesian clinical decision support mathematical model that can assist in assessing the diagnostic utility integrating the ADD-RS combined with the diagnostic quality of D-dimer testing.

2. Methods

One reviewer (LRC) independently conducted a literature review through a search of MEDLINE, EMBASE, the Cochrane Controlled Trials Register, and the Cochrane Database to identify articles on studies that used D-dimer as a diagnostic test for adults with acute aortic dissection. Keywords such as ("D-Dimer and Aortic Dissection") were used.

The quality of methods was independently assessed by 2 researchers (LRC, AAB).

A meta-analysis that includes 11 studies and a total of 349 acute aortic dissection patients was selected [13].

Sensitivity was defined as the ability of a test to correctly identify those with the disease (true positive rate), whereas *test specificity* was defined as the ability of the test to correctly identify those without the disease (true negative rate). Likelihood ratios were used as epidemiologic instruments to show how much we should shift our suspicion for a particular test result. The positive LR was defined as probability of an individual with the condition having a positive test result; LR+ = probability of an individual without the condition having a positive test. Similarly, the negative LR was defined as probability of an individual with the condition having a negative test result; LR− = probability of an individual without the condition having a negative test result. We defined the LR+ and LR− in terms of sensitivity and specificity:

$$LR+ = \frac{\text{sensitivity}}{1-\text{specificity}} \quad LR- = \frac{1-\text{sensitivity}}{\text{Specificity}}$$

Bayes theorem was used to convert the results from D-dimer testing into the probability of the event. Bayes math describes the analysis as a relation of Pr(*A*|*X*), the chance that an event *A* happened given the indicator *X*, and Pr(*X*|*A*), the chance the indicator *X* happened given that event *A* occurred. Our mathematical method uses the Bayes

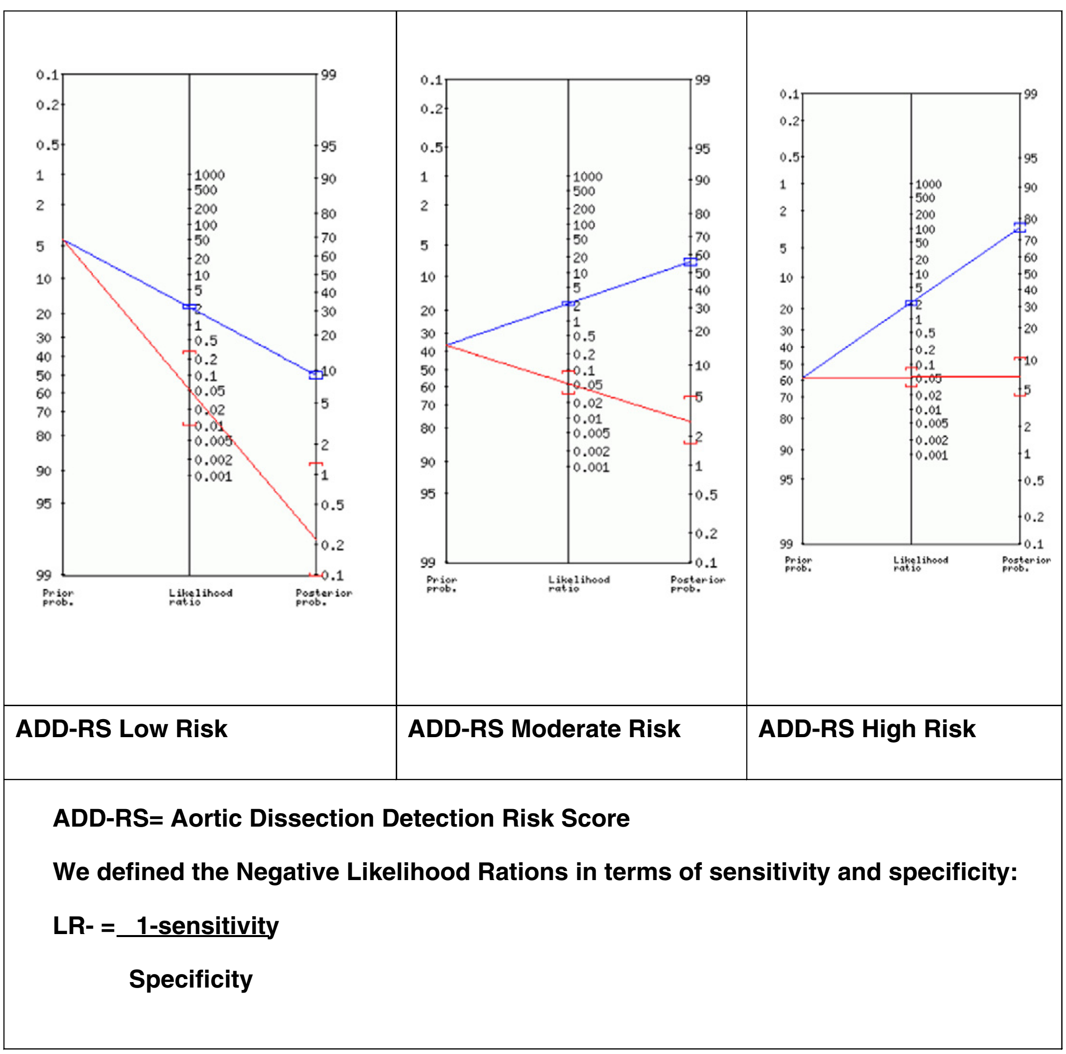

Fig. 1. Bayesian nomogram for ADD-RS and D-dimer. Positive LRs (blue); negative LRs (red).