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EDITORIAL COMMENT

Toward an Easily Obtainable Novel Biomarker for Type A Dissection?*

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Acute aortic dissection (AAD) is a life-threatening emergency associated with high morbidity and mortality. The involvement of the ascending aorta (acute type A aortic dissection [ATAAD]) can lead to mortality complicated by rupture of the aorta, pericardial tamponade, aortic regurgitation, associated acute heart failure, and end-organ malperfusion unless prompt surgical repair can be performed.[1] In early data from the 1950s, the mortality rate for ATAAD during the initial 48 hours was reported to be 1% to 2%/h.[2] Recently published data from the IRAD (International Registry of Acute Aortic Dissection) revealed that the mortality rate for ATAAD in the contemporary era was 4.4% (0.09%/h) in the surgery group and 23.7% (0.5%/h) in medically treated patients at 48 hours. These recent lower estimates can be attributed to the improvements in diagnostic imaging modalities, medical management, and surgical techniques since the 1950s, but they are still substantial.[3]

Inflammation is definitely associated with the pathogenesis of AAD. Macrophage mobilization and activation are important in initiating the inflammatory and matrix degradation processes. The leading players in these processes are proinflammatory cytokines and the balance between matrix metalloproteinases and their tissue inhibitors. Therefore, biomarkers of inflammation, such as C-reactive protein and white blood cell count, are independently associated with outcomes in patients with AAD.[4]

Thrombosis is also involved in the pathogenesis of AAD. Consumption coagulopathy caused by extensive or partial thrombus formation in the false lumen is independently associated with mortality in patients with AAD. Activated and dysfunctional platelets participate in the formation of thromboses in the acute phase of AAD. Therefore, it is natural that thrombotic biomarkers, such as the platelet count (PC) and D-dimer level, have been tested as prognostic factors. Because the measurement of platelet function is a costly and complicated procedure, platelet indexes, such as PC, mean platelet volume, and the mean platelet volume/PC ratio, have been used as alternative markers that reflect platelet function and predict short- and long-term outcomes.[5]

In this issue of *JACC: Asia*, Liu et al[6] reported the usefulness of a novel hematological parameter, the systemic coagulation-inflammation index (SCI), for risk stratification in patients with ATAAD. Patients with ATAAD who underwent open surgical repair between January 2016 and December 2020 at 12 Chinese cardiovascular centers were retrospectively analyzed. The SCI ([platelet count × fibrinogen level]/white blood cell count), which simultaneously reflects inflammation and coagulation pathways, is easily obtainable with parameters available in routine clinical practice. In that regard, the SCI can always be obtained, even in emergencies. The outcome parameters used to measure the performance of the SCI were 90-day mortality, defined as any death, regardless of cause, occurring within 90 days after surgery in or out of the hospital (the primary endpoint); and composite outcomes, including 30-day, hospital, and intensive care unit mortality, as well as mechanical ventilation duration, intensive care unit length of stay, bleeding, and stroke (secondary endpoints). Patients were stratified by SCI tertile: low SCI (<40); middle SCI (40-100); or high SCI (>100). The 90-day survival increased with SCI (low: 86.9%; middle: 92.7%; high 96.4%). SCI was also independently associated with 90-day mortality (adjusted HR: 0.549; 95% CI: 0.424-0.710). The prediction performance (the AUC value) of SCI was 0.662, better than that of other well-known prognostic

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markers, including C-reactive protein, platelet count, and fibrinogen levels. The SCI showed superior performance in predicting 90-day mortality compared with other combined laboratory signatures, including the systemic immune-inflammation index ([platelet count × neutrophil count]/lymphocyte count), the platelet to lymphocyte ratio (platelet count/lymphocyte count), and the neutrophil to lymphocyte ratio (neutrophil count/lymphocyte count). Moreover, the investigators found that the SCI had an incremental prognostic value over the prognostic model built with conventional risk factors (age, serum creatinine, DeBakey class, and location of intimal entry site).

The study presents a valid evaluation of the prediction performance of a novel SCI index that is readily obtainable, even in an emergency. However, care should be taken regarding the general use of this biomarker in all ATAAD patients. Recently published data from IRAD reported early mortality rates of 5,611 ATAAD patients enrolled in the United States between 1996 and 2018. IRAD developed a multivariate model for predicting in-hospital mortality (C-index: 0.787), including time from the initial hospital admission to surgery, age, presenting with hypotension (shock), prior cardiac surgery, preoperative malperfusion, and body mass index.[3] The patients included in the study by Liu et al[6] were younger, had lower body mass indexes, had lower rates of hypotension (shock) or cardiac tamponade, and had no mesenteric malperfusion, resulting in better short-term outcomes than those from IRAD. Moreover, a watchful waiting strategy with medical management and timely surgical intervention may be a reasonable option for stable patients with retrograde ATAAD.[7,8] Although the investigators included those retrograde ATAAD patients (2.3% of total study subjects) for whom medical management failed, the overall prognosis of this group is better than that of ATAAD patients whose intimal tear site is located in the ascending aorta. Finally, the proportion of patients with invisible intimal tear sites is higher than expected. The primary goal of surgical repair for ATAAD is to eliminate the primary entry (intimal) tear site to restore true lumen flow. The aortic arch should be totally or partially replaced when the intimal tear site is located in the aortic arch. Therefore, preoperative detection of the intimal tear by computed tomography (CT) is crucial for preprocedural planning. Significantly, detection of the intimal tear site in the ascending aorta is dependent on the CT scanner; electrocardiography-gated multidetector CT angiography is more accurate than non-electrocardiography-gated CT angiography.[9] Moreover, the role of experienced and well-trained radiologists and cardiac surgeons is influential in detecting intimal tear sites.[10] However, intramural hematoma is sometimes referred to as "AAD without an intimal tear" or as "thrombosed type AAD," and a significant proportion of patients without visible intimal tears on imaging modalities were found to have entry tears in the ascending aorta/arch after intraoperative confirmation.[11] Therefore, ATAAD without a visible intimal tear on imaging may have a different prognosis than a typical ATAAD with an intimal tear site located in the ascending aorta.[8]

In summary, the investigators are to be congratulated for developing a novel index that is easily obtainable in the emergency setting and that performs moderately well as a predictor of short-term mortality and as a valuable tool for risk stratification in ATAAD patients.

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