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BIOMARKER
Biomarkers

Biomarkers for diagnosis and prognostication of acute aortic syndromes

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Acute aortic syndromes (AAS) are life-threatening cardiovascular diseases affecting the thoracic aorta, variably involving the abdominal aorta and the main aortic branches. AAS include the subtypes of 'classic' aortic dissection (70–90% of cases), intramural haematoma (IMH, more common in elderly and Asian patients), and atherosclerotic penetrating aortic ulcer (PAU). Rapid diagnosis is necessary to prevent negative outcomes, but accurate and efficient recognition of AAS is challenging. AAS lead to a wide range of unspecific clinical signs and symptoms, most commonly caused by other more prevalent diseases such as acute coronary syndromes, pulmonary embolism, stroke, and gastrointestinal diseases.[1] Hence, the diagnostic approach to AAS faces the challenges of a low signal to high noise scenario, hampered by both frequent misdiagnoses (5–25%) and low diagnostic yield.

The current gold-standard diagnostic test for AAS in the acute setting is contrast-enhanced computed tomography angiography (CTA). This tool is largely but not universally available in emergency departments and has limits related to risks of anaphylaxis, radiation, and kidney failure. Clinical gestalt, standardized clinical scores (e.g. aortic dissection detection, ADD, and aorta simplified, AORTAs), and echocardiography can rapidly and accurately identify patients at high pre-test probability of AAS, for whom a CTA is urgently indicated. However, for most non-critical patients with compatible symptoms and for patients with atypical and confounding clinical findings, biomarkers can help, particularly in the early rule-out of AAS to reduce overuse of CTA exams. Biomarkers can also identify AAS-related organ damage, thrombosis, inflammation and tissue remodeling, thus contributing to outcome prognostication (*Figure 1*).

Currently, the aortic biomarker supported by the most compelling data is D-dimer, a plasma fibrin degeneration product largely applied in acute cardiovascular medicine for suspected venous thromboembolism. D-dimer is highly sensitive but only moderately specific for AAS. In a recent meta-analysis, the pooled sensitivity and specificity of D-dimer for AAS were 96% and 70%, using a cut-off value of 500 ng/mL fibrinogen equivalent units.[2] However, specificity can be significantly lower, especially in patients with a history of aortic aneurysm and in elderly patients. Accordingly, recent evidence suggests that the application of an age-adjusted D-dimer cut-off (calculated as patient's age × 100), already in use for pulmonary embolism, could slightly improve specificity without compromising sensitivity. In patients classified at low pre-test probability using the ADD or AORTAs score, a negative D-dimer allows to rule out AAS with a pooled sensitivity of 99% and a failure rate of 0.1%.[3] So far, only one prospective multi-centre study has validated these findings, but the results of two other large studies are awaited in the near future (*clinicaltrials.org* NCT04430400 and NCT05582967).[4] In compliance with American and European guidelines, pre-test probability assessment should be applied in all non-critical patients with AAS-compatible symptoms, proceeding with D-dimer measurement in patients with an ADD or AORTAs score of 0 or 1. In these low-probability patients, if D-dimer is negative, an AAS can be confidently ruled out. However, a note of caution must be added, remembering that D-dimer negative cases can be found especially in very early or late presenters and in patients with small aortic lesions (e.g. limited IMH or PAU and focal dissections). Another potential caveat for D-dimer might be Asian ethnicity, since the lowest sensitivity estimates for D-dimer have been reported especially in Chinese studies. Apart from D-dimer, other aortic biomarkers represent work in progress, including soluble ST2 and miRNAs.[5,6]

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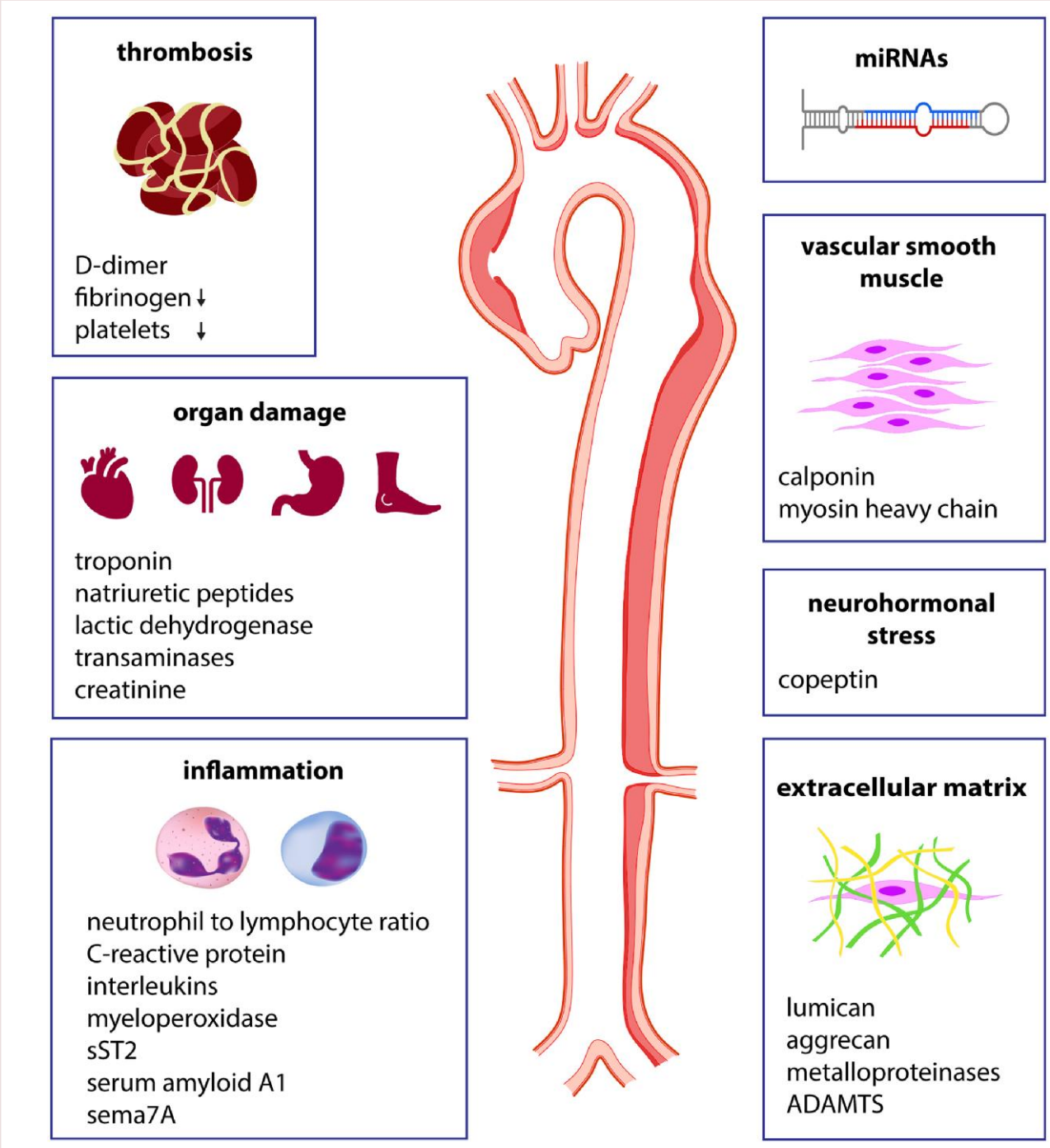

Figure 1 Potential aortic biomarkers for diagnosis and prognostication of acute aortic syndromes. ADAMTS, a disintegrin and metalloproteinase with thrombospondin motifs; miRNA, microRNA; sST2, soluble suppression of tumorigenesis-2.

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Data availability

No new data were generated or analysed in support of this research.

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