

Low and intermediate risk aortic dissection detection risk score and negative D-dimer: a word of caution

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ABSTRACT

A low or intermediate aortic dissection detection risk score coupled with a negative D-dimer has been proposed as a reliable rule-out strategy for acute aortic syndrome (AAS) in the emergency department. Locally, its use has crept into the work-up of patients with suspected AAS. This opinion piece offers a word of caution—the stakes are high for missing AAS. Although the rule-out strategy does show exciting potential, it remains to be validated, especially for Australasian patients. Patients with suspected AAS should continue to be investigated with timely advanced imaging such as contrast-enhanced computed tomographic aortography.

Acute aortic syndrome (AAS) comprises acute aortic dissection, intramural haematoma and penetrating aortic ulcer. Together with aortic rupture and aortic embolus, AAS remains a life-threatening vascular emergency for emergency department (ED) patients presenting with chest, back or abdominal pain.

AAS is often difficult to diagnose in the ED because of its non-specific clinical presentations and relatively low incidence. There are also no validated rule-out strategies. Thus, for patients in whom AAS is being considered, diagnostic imaging must be undertaken, which is usually with contrast-enhanced computed tomographic aortography (CTA). However, CTA remains limited by access issues and concerns around contrast nephropathy and contrast anaphylaxis. EDs are also becoming increasingly busy, leading to delays in obtaining timely scans. Such delays can have important clinical consequences for patients waiting in the ED with undiagnosed AAS.

Local experiences of catastrophic outcomes contributed to by delayed imaging led to a recent retrospective cohort study of all CTAs performed in the ED at Auckland City Hospital, between 2009–2019, for the work-up of AAS.¹ Waqanivalagi et al. observed that, during the 11-year study period, there were 135 (8.2%) cases of at least one AAS diagnosis and 220 (13.4%) cases where an alternative diagnosis was made. During the study period, thoracic CTA use for investigating suspected AAS increased. Although the annual incidence of AAS did not increase, it remained higher than reported in overseas institutions.

In 2010, the American Heart Association and American College of Cardiology released guidelines for the diagnosis and management of patients with thoracic aortic disease, including 12 high-risk clinical features to assist in the early detection of AAS. Rogers et al. examined patients enrolled in the International Registry of Acute Aortic Dissection between 1996–2009 and evaluated the number of patients with confirmed AAS who presented with at least one of the 12 clinical parameters.² An aortic dissection detection risk score (ADD-RS) from zero–three was then calculated based on the presence of any high-risk clinical feature from any of the three high-risk categories (**Table 1**). It was observed that, of 2,538 patients with AAS, 2,430 (95.7%) had at least one high-risk clinical feature. Increasing ADD-RS scores were also found to correlate with an increasing incidence of AAS. Thus, it was suggested that the ADD-RS may play a useful role in risk-stratifying AAS.

Suzuki et al. investigated the role of D-dimer, a biomarker used to exclude deep vein thrombosis and pulmonary embolism, in the exclusion of AAS.³ They conducted a prospective multicentre study of 220 patients suspected of having AAS, of whom 87 were diagnosed with AAS and 133 with other diagnoses. D-dimer was markedly elevated in patients with AAS using a cut-off value of 500 ng/mL, with a negative likelihood value of 0.07 throughout the first 24 hours. Suzuki et al. thus concluded that D-dimer may be useful in risk-stratifying patients with AAS in the first 24 hours of symptom onset.

Nazerian et al. combined a low or intermediate risk ADD-RS (<1) with a negative D-dimer in their multicentre prospective observational study of patients presenting with any of: chest/abdominal/back pain, syncope, or perfusion deficit, and suspected AAS.⁴ Of 1,850 patients included in the study, 924 patients had an ADD-RS <1 and negative D-dimer, of whom three were positive for AAS. This yielded a failure rate of 0.3%.

In 2020, Bima et al. systematically reviewed studies integrating the ADD-RS with D-dimer.⁵ Four articles met their inclusion criteria, including the prospective study by Nazerian et al. and three retrospective studies with methodological limitations.^{4,6-8} Despite the study limitations, Bima et al. observed negligible heterogeneity and consistently high sensitivity of an ADD-RS <1 with negative D-dimer, thus concluding that the rule-out test may be reliably used.⁵

Bhat et al. evaluated the efficacy of D-dimer in ruling out AAS in low and intermediate risk patients undergoing CTA for the Auckland cohort.⁹ They observed that, during the 11-year study period, 14.3% (236/1,646) of CTAs were preceded by a serum D-dimer. A subsequent negative D-dimer result had a sensitivity of 100% (95% CI: 66–100%) and negative predictive value of 100% (95% CI: 97–100%) for ruling out AAS in low and intermediate risk patients. It was also shown that the annual number of D-dimer requests increased significantly during the study period ($p=0.0059$ using the Mann–Kendall trend test), which likely resulted from a significant rise in the number of negative ($p=0.0036$), rather than positive ($p=0.15$), D-dimer results. It was highlighted that there were no missed cases of AAS in patients with a negative D-dimer who were at low or intermediate risk for AAS. The authors concluded that a D-dimer <500 ng/mL might be useful in reducing CTA-use in patients at low or intermediate risk presenting with suspected AAS.

In saying this, an ADD-RS <1 coupled with a negative D-dimer as a rule-out strategy for AAS remains to be validated.^{1,10} It is also plausible that the 12 high-risk clinical features comprising the ADD-RS are not sufficiently sensitive for AAS in the New Zealand population. Bhat et al. analysed the Auckland cohort of patients through an ethnic lens and observed that the age-standardised AAS incidence per 100,000 ED presentations was significantly higher in Māori (6.9) and Pacific

Islanders (5.3) than patients of other ethnicities (2.3).¹⁰ Despite the higher incidence, disproportionately fewer CTAs were requested in the ED for Māori (9.2 CTAs per AAS diagnosis) and Pacific Islanders (9.2 CTAs per AAS diagnosis) than for patients of other ethnic groups (13.8 CTAs per AAS diagnosis). Thus, it was recommended that the increased risk of AAS in Pacific Islander and Māori patients be considered by clinicians when investigating AAS. Similar inequities were observed by Xu et al. in Waikato.¹¹

It has previously been observed that the three- to four-fold higher incidence of AAS among Māori, when compared with non-Māori, is associated with higher incidences of thoracic aortic aneurysms, use of cigarettes and vascular risk factors.¹² This higher incidence of AAS makes it especially notable both that an AAS registry does not presently exist within New Zealand and that there are few, if any, prospective studies that include New Zealand patients.

Despite all the benefits of a rule-out strategy for AAS, it appears that the ADD-RS and negative D-dimer pathway is not yet appropriate for local emergency physicians to rely upon in the ED. Indeed, the stakes are high, and missing even one case of AAS will likely have serious consequences for the patient, the patient's next of kin and for the treating doctor. It may be prudent for governing bodies to monitor the progress of high-risk rule-out strategies such as the ADD-RS and D-dimer pathway and then endorse its use once a satisfactory evidence base is available to justify it.

Locally, the ADD-RS and D-dimer pathway has crept into the work-up of suspected AAS on an *ad hoc* basis. Indeed, there is increasing evidence that suggests the pathway may soon play an important role in risk-stratifying patients with suspected AAS. However, given that the pathway remains to be validated, its utility in New Zealand patients remains to be explored, and the potential for patient harm in missed cases is extremely high. It is suggested that, for patients in whom AAS is being considered, ADD-RS and D-dimer rule-out is not undertaken, but advanced imaging is instead performed in a timely fashion. Establishment of an AAS registry and a well-designed, prospective study of the ADD-RS and D-dimer pathway are two important next steps to validating the pathway for patients with suspected AAS in New Zealand.

Table 1: The high-risk clinical features of the aortic dissection detection risk score spread across three high-risk categories: high-risk pain conditions, high-risk pain features and high-risk exam features.

Finding		Points
Any high-risk condition	Marfan syndrome	1 point
	Family history of aortic disease	
	Known aortic valve disease	
	Recent aortic manipulation	
	Known thoracic aortic aneurysm	
Any high-risk pain feature	Chest, back or abdominal pain described as any of the following:	1 point
	Abrupt onset	
	Severe intensity	
	Ripping or tearing	
Any high-risk exam feature	Evidence of perfusion deficit (pulse deficit, systolic BP differential or focal neurological deficit in conjunction with pain)	1 point
	New murmur of aortic regurgitation (with pain)	
	Hypotension or shock state	

COMPETING INTERESTS

Nil.

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