Should the ‘adenosine-challenge test’ be part of the routine work-up for syncope?

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The adenosine compounds [adenosine and adenosine triphosphate (ATP)] exert negative chronotropic and dromotropic effects at the level of the sinus node and atrio-ventricular (AV) node.1 These effects are both potent and short lasting. Therefore, the adenosine compounds replaced verapamil as the first-line drug for terminating re-entrant supraventricular tachycardias involving the AV node (AV node re-entry tachycardia or AV reciprocating tachycardia).1 Cardiologists also take advantage of these effects for diagnostic purposes.2 For example, the transient AV block caused by iv injection of adenosine during sinus rhythm allows the identification of antegrade accessory pathways in patients with Wolff–Parkinson–White syndrome when only minor pre-excitation is present.3 Similarly, we have used the ‘adenosine challenge test’ for the identification of the presence of dual AV-node physiology and concealed (retrograde) accessory pathways in patients palpitations of unclear aetiology.4 Finally, since sudden bradycardia has strong effects on ventricular repolarization, we have proposed the ‘adenosine challenge test’ for diagnosing congenitally long QT syndrome.5

In this issue of Europace, Fragakis et al.6’s data suggest that the ‘adenosine challenge test’ may be as effective as invasive electrophysiological studies for diagnosing sinus node dysfunction.6 Since the adenosine challenge is a quick and safe bedside test, one could argue that such a test should become part of the routine evaluation of patients with unexplained syncope. We would argue, however, that such a conclusion would be premature, considering that the literature on ‘the adenosine challenge’ in patients with syncope is rather complex, if not confusing.7

As beautifully summarized by Parry et al. in a recent review,7 adenosine was originally given during the head-up phase of the tilt-table testing to improve the diagnosis of vasovagal syncope.8 Adenosine was indeed comparable with isoproterenol for provoking vasovagal syncope during tilting in susceptible patients.7,8 Subsequently, the adenosine test was performed instead of (and in addition to) the head-up tilt-table (HUT) test to diagnose vasovagal syncope.9 Adenosine-induced sino-atrial block or AV block, leading to ventricular asystole of ≥10 s, was induced more commonly among patients with syncope than among controls. However, when comparing adenosine with HUT testing, only very few patients had positive results in both tests.10 Rather than concluding that the supine adenosine test has limited value for diagnosing vasovagal syncope, a new concept of ‘adenosine sensitive AV block’ was proposed.11 In addition, provocation of sinus pauses lasting ≥6 s by adenosine or ATP in patients with a history of syncope was considered diagnostic of sinus node dysfunction in some small studies.12 Thus, the adenosine challenge test has been credited, at different times and by different investigators, as a useful test for the identification of patients with vasovagal syncope, AV block ‘not related to vasovagal syncope’, and/or sinus node dysfunction.12 Complicating matters further, some studies show that there is a poor correlation between the bradyarrhythmias provoked during the adenosine test (or for that matter, during the HUT test) and the spontaneous arrhythmias recorded by implantable Holters during real-life syncope.13,14 It is with this complex background in mind that the study of Fragakis et al.6 should be evaluated.

Fragakis et al.6 first performed an adenosine challenge test in 19 patients with sinus node dysfunction, seven patients with syncope of unknown origin, and 12 controls. All these patients then underwent evaluation of the corrected sinus recovery time (CSNRT) following rapid atrial pacing, either during invasive electrophysiological studies or by implanted permanent pacemakers. Evaluation of the CSNRT involves rapid atrial pacing for at least 1 min; sudden termination of this rapid pacing is invariably followed by transient suppression of sinus node activity with gradual resumption of baseline sinus rhythm. The CSNRT, which is considered by many as ‘the golden standard’ for diagnosing sinus node dysfunction, measures the time necessary for the sinus node to recover from the overdrive-suppression with a ‘correction’ that takes into account the sinus rate at baseline. The authors found that the sinus pauses provoked by adenosine were much longer in patients...
with sinus node dysfunction than in patients with syncope of unknown origin and in control patients. In fact, the sinus pauses provoked by adenosine were longer than those induced by rapid atrial pacing. Using predefined definitions of ‘positive’ and ‘negative’ results, the predictive accuracy of the adenosine challenge test was better than that of the invasive studies for ‘diagnosing’ sinus node dysfunction. These results are in agreement with two studies that have also shown that adenosine is as effective as rapid atrial pacing for suppressing the sinus node to unravel sinus node dysfunction.12,15

The study by Fragakis et al. is interesting, but has important limitations. The clinical diagnosis of sinus node dysfunction is not straightforward. Some would argue that documentation of sinus bradycardia or sinus pauses is not sufficient when the latter are not timely related to the symptomatology. Second, the patient groups were small and were not well matched for age (patients in the ‘sinus node dysfunction’ group were older than patients with syncope of unknown origin and much older than the controls).6 This limitation must be emphasized in the light of data indicating that, with increasing age, the response to adenosine is accentuated.10 Thus, larger studies including elderly patients as controls are necessary before routine use of the adenosine challenge test can be recommended for the evaluation of syncope.

References
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