LETTERS TO THE EDITOR

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The ajmaline challenge and a strange ECG

In the early years of invasive electrophysiology, the ajmaline test was introduced to induce or enhance intra-ventricular conduction delays in patients with fascicular block, because of its intrinsic pharmacological properties on the HV interval and QRS duration. Nowadays, a new ajmaline challenge has become a very popular test (both in tertiary and primary centres), because of the induction of a coved ST-segment elevation in the precordial leads, erroneously ascribed to a repolarization abnormality. Much evidence (simply recording late potentials during the infusion) has documented that a depolarization abnormality is what is obtained after the infusion. The induced ECG is similar to the one found in patients with the syndrome of right bundle branch block and sudden death. Unfortunately, the suspected diagnosis is so often told to the healthy subject, forgetting that for evidence-based data and ethical reasons nobody has the authority to drive the conclusions that an induced strange ECG is indicative of a lethal diagnosis. The large series of Veltmann et al.1 is exhaustive but confusing. One hundred and ten asymptomatic subjects of a mean age of 49.3 ± 14 years have been submitted to the test only because of a basal non-diagnostic saddle back ECG, with 85% positive test, but without any detail regarding the predictive value. The authors report that this saddle back ST-segment elevation is rare in the European population. This might be true in the old population, as the one investigated, but is not the real world in the young. Type 2 and 3 morphologies and first-degree right bundle branch block are not so rare in the young population that we usually see either for sport eligibility or in sedentary students, accounting for a 2–4% prevalence of this ECG pattern in healthy population (personal observations). If we perform ajmaline challenge in this population, how many positive results will be obtained and how many families will be frightened?

I saw yesterday the trace of a 23-year-old asymptomatic man with an ECG showing a first-degree right bundle branch block with minor ST abnormality, in which a previous written diagnosis of ‘suspected Brugada Syndrome’ was done. After this assumption, not based on other evidence, his family, who firstly consulted ‘Google’, became struck with terror.

Five cardiologists have later been consulted giving five different diagnoses and prognoses. When I was also asked by e-mail to give an opinion about the opportunity of the ajmaline challenge, I gave my suggestion after thinking that the young man might be the same age as my son, never submitted to ECG and who might also have a similar trace.

Some years ago, Professor Hurst2 wrote ‘it is not possible to justify the study of a patient’s genes, perform an endomyocardial biopsy, perform an MRI, perform an electro-physiological study, and perform a coronary arteriography in every patient in whom the condition is suspected’. This wise assumption must be kept in mind when we decide to translate laboratory research into clinical work, relying on limited evidence-based data.

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References

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The ajmaline challenge and a strange ECG: reply

We have read with interest the letter by Dr Martini and we are grateful for his comments. We would like to reply to some of the issues raised by Dr Martini in his letter.

The authors are aware that ajmaline was used as a diagnostic tool in the past to unmask intraventricular conduction delays. However, nowadays sodium channel blocker challenge is an accepted and established tool to unmask the ECG pattern diagnostic of the Brugada syndrome.3 This test is especially important in the circumstance when the basal ECG in patients with the Brugada syndrome is fluctuating between the diagnostic and non-diagnostic patterns.2 The underlying cellular and pathophysiological mechanisms and the rationale of this test have been described in detail.3–7

The available data by now have shown that patients with a drug-induced Brugada ECG are at risk for sudden cardiac death. However, the risk in the asymptomatic patient without a spontaneous diagnostic ECG is assumed to be low.3–5

The question is whether to perform the ajmaline test in the asymptomatic patient presenting with a saddle-back type ECG. From the authors’ point of view, the test may offer the chance to exclude an underlying Brugada ECG. In the case of a positive test, the patient has to be risk stratified as mentioned in the manuscript guided by the recommendations of the Brugada consensus conference.6,7 At least repetitive ECG recordings to test for a spontaneous diagnostic Brugada pattern are indicated. Furthermore, general recommendations like avoidance of certain drugs (www.brugadadrugs.org) or lowering of fever can be given.

According to the literature, the prevalence of a saddle-back Brugada type II or type III ECG in European populations is rare ranging from 0.2 to 0.6%.8,9 These data might diverge from Dr Martini’s personal observation.

We presented in the paper the results on consecutive ajmaline challenges performed in tertiary referral centres specialized in primary electrical diseases. The results described were based on a retrospective analysis of all tests conducted between 2001 and 2006. During 6 years, ‘only’ 110 patients were referred for ajmaline challenge in the setting of solely a basal saddle-back type ECG. This indicates that the saddle-back type ECG is a rarity and that we are dealing with a highly selected population.

We agree with Dr Martini that we are still lacking data on the long-term follow-up on...
asymptomatic patients with a Brugada type II or III ECG. As long as these data are not available, we have to treat our patients according the data that we have so far.

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References


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The editorial also suggests that there is a lack of a treatment effect for ICDs in the NYHA class III, based on subgroup analysis of the SCD-HeFT trial. However, it should be remembered that DEFINITE found a greater benefit of ICD therapy among patients with NYHA class III than among patients with class II; and in MADIT-II, there were no significant differences in the survival benefit in subgroup analyses stratified according to NYHA class.8,9 A meta-analysis of all primary prevention studies also failed to confirm a contribution of NYHA class (or mean age or mean left ventricular ejection fraction) to statistical heterogeneity in all-cause mortality in the relevant trials.10

The editorial notes that there are differences between healthcare systems in Europe, and suggests that Belgium is not representative of Europe in terms of cost. We agree that it is not straightforward to compare reimbursement rates across countries and/or regions given the complexity and diversity in healthcare financing systems, including a variety of diagnosis-related group (DRG) classifications and special arrangements for funding medical devices. Some countries cluster ICD and CRT-D devices in the same DRGs, others do not; some countries have multiple DRGs corresponding to patterns of disease severity or patient co-morbidities, others do not; and some DRG systems incorporate capital equipment and facility costs, others do not. We believe that overall, the Belgium costs adequately represent most European countries and are certainly likely to be more relevant than North American models.

Is the battery longevity in our model similar to real-world observed longevity? The editorial cites a study of ICD longevity in 153 patients implanted from 2000 through 2002.11 When we examined this study, we found evidence to support the longevity in our model: eight patients had a Medtronic Gem II VR device, and seven of these patients had not had a replacement after 5.4-year follow-up; and the longevity for three Medtronic Gem devices was 6.75 years. A recent study in Belgium with a mixed sample of 143 Medtronic ICD/CRT-D devices replaced July 2007–September 2008 confirmed an average longevity of 6.19 years (P. Galloo, personal communication). Meine et al. incorrectly stated that we assumed a longevity of 6.5 years—we used a survival distribution for Gem II VR devices with a mean of 6.3 years, truncated at the right-hand side of the distribution at 6.5 years (the maximum follow-up available at that time).

The editorial also suggests that we underestimated mortality in the ICD group. Eight-year follow-up from MADIT II (recently reported at