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Noninvasive characterization of atrioventricular conduction in patients with atrial fibrillation

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Abstract The atrioventricular (AV) node plays a fundamental role in patients with atrial fibrillation (AF), acting as a filter to the numerous irregular atrial impulses which bombard the node. A phenomenological approach to better understand AV nodal electrophysiology is to analyze the ventricular response with respect to irregularity. In different cohorts of AF patients, such analysis has been performed with the aim to evaluate the association between ventricular response characteristics and long-term clinical outcome and to determine whether irregularity is affected by rate-control drugs. Another approach to studying AV nodal characteristics is to employ a mathematical model which accounts for the refractory periods of the two AV nodal pathways. With atrial fibrillatory rate and RR intervals as input, the model has been considered for analyzing data during (i) rest and head-up tilt test, (ii) tecadenoson and esmolol, and (iii) rate-control drugs. The present paper provides an overview of our recent work on the characterization and assessment of AV nodal conduction using these two approaches.

Keywords: Atrioventricular node; beta Blockers; Calcium channel blockers; Irregularity; Entropy; Head-up tilt

Introduction

The atrioventricular (AV) node plays a fundamental role in patients with atrial fibrillation (AF) as it acts as a filter to the irregular atrial impulses that bombard the node itself. One of the current approaches to treat AF is to allow the arrhythmia to continue, but to prevent rapid ventricular rates by the use of rate-controlling drugs [1]. To achieve optimal rate control, however, better understanding of the AV nodal properties is highly desirable. A phenomenological exploration of AV nodal electrophysiology is offered by the analysis of ventricular response during AF. Although the response is highly irregular during AF, it is not completely random and therefore assessment of variability and irregularity of the RR series can provide useful insights. We have recently analyzed RR irregularity in various cohorts of AF patients with the aim to evaluate (i) the association between ventricular response characteristics and long-term clinical outcome in patients with mild to moderate congestive heart failure, and (ii) the extent with which irregularity is affected by commonly used rate-control drugs.

Direct assessment of AV nodal characteristics is usually performed during electrophysiological studies by means of pacing protocols in patients during sinus rhythm. Since conventional electrophysiological techniques for assessment of refractory period or conduction velocity of the AV node are not applicable during AF, we have recently developed a model-based method for noninvasive (ECG-based) assessment of AV nodal characteristics. The significance of the novel method has been investigated by analyzing data acquired during (i) rest and head-up tilt test, (ii) administration of tecadenoson and esmolol, and (iii) administration of beta blockers and calcium channel blockers.

This paper reviews our recent work on noninvasive characterization of the AV node, expressed either in terms of variability and irregularity of the ventricular response or refractory periods of the two AV nodal pathways. The results obtained from analyzing data of the RATAF, MUSIC and MADIT-II studies are reviewed.

AV nodal analysis

Estimation from surface ECG

While electrophysiological properties of the AV node can be assessed invasively during sinus rhythm at different

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stages of drug development and in clinical settings, an atrial pacing protocol cannot be applied during AF. Yet, it is desirable to assess the effect of a drug on AV nodal electrophysiology during AF, especially for rate-control drugs acting on the AV node.

We have recently proposed a method to noninvasively estimate five parameters characterizing the AV node in patients with AF, namely the refractory periods of the two AV nodal pathways, the probability of an impulse not passing through the fast pathway, and the prolongation of the refractory periods [2,3]. Atrial impulses are considered to arrive randomly to the AV node with a mean arrival rate proportional to the atrial fibrillatory rate (AFR), determined from the f-wave pattern [4]. The definition of the absolute refractory period (aRP) includes both the effective refractory period of the AV node and the AV conduction interval, and therefore aRP may serve as an indirect estimate of the functional refractory period. The ECG is processed so that the RR series and the AFR are produced, i.e., the two quantities that constitute the complete basis for estimation of the AV node parameters (Fig. 1). It should be emphasized that the estimates of the AV node parameters are indirect, i.e., they are determined from the ECG.

AV nodal properties: drug administration and tilt testing

Changes in AV nodal properties were investigated during drug administration [5–7]. The hypothesis is that the estimates of AV nodal refractory periods reflect overall changes in AV nodal properties previously reported on in studies accomplished invasively during sinus rhythm.

We recently investigated the effect of tecadenoson and esmolol in a small cohort of patients [5]. Tecadenoson prolongs the effective refractory period of the AV node and slows down its conduction [8]. Similarly, esmolol prolongs refractoriness and conduction time in both pathways during AV nodal reentrant tachycardia [9]. In [5], the parameter aRP, including both the effective refractory period and the conduction interval, was prolonged for both tecadenoson and esmolol. The increase in aRP of both pathways suggested either prolonged effective refractory period or prolonged AV conduction, or both. In addition, tecadenoson was shown to affect heart rate but not AFR, suggesting that a decrease in heart rate may be attributed to tecadenoson affecting the AV node.

We investigated changes in AV nodal properties during administration of beta blockers (carvedilol and metoprolol) and calcium channel blockers (diltiazem and verapamil) in a controlled setting, i.e., data from the RATe control in Atrial Fibrillation (RATAF) study [10]. In patients with permanent AF, the RATAF study compared the effects of four once-daily drug regimens (metoprolol, diltiazem, verapamil and carvedilol) on heart rate and arrhythmia related symptoms. While the results of this study are not directly comparable to previous studies, the changes in estimated AV nodal properties are in agreement with previous electro-

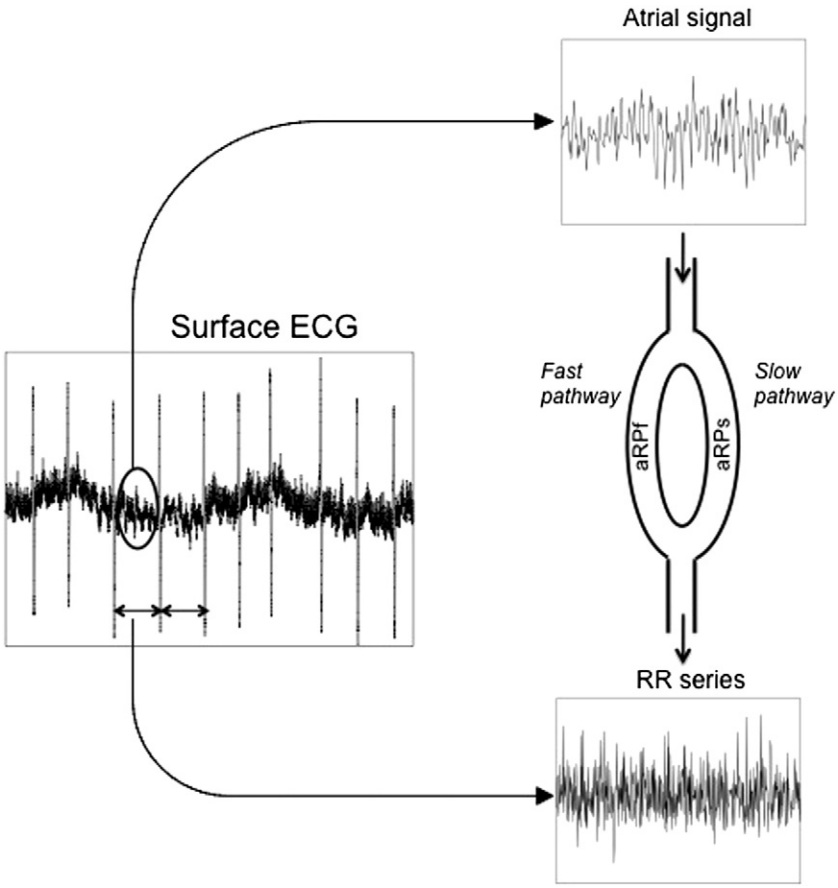

Fig. 1. Scheme of the method for characterize the AV node: the ECG is processed to produce the RR series and the atrial signal that form together the basis for estimation of the AV node parameters. aRPs = absolute refractory period of the slow pathway; aRPf = absolute refractory period of the fast pathway.