International Journal of Cardiology 171 (2014) 259–264

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Transverse versus longitudinal electrical propagation within the atrioventricular node during dual pathway conduction: Basis of dual pathway electrophysiology and His electrogram alternans (Zhang's phenomenon)☆

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ARTICLE INFO

Article history:
Received 30 September 2013
Received in revised form 25 November 2013
Accepted 14 December 2013
Available online 22 December 2013

Keywords:
Atrioventricular node
His bundle
Dual pathway electrophysiology
His electrogram alternans
Action potential

ABSTRACT

Background: We have discovered and validated that AV node dual pathway conduction results in a new phenomenon termed His electrogram alternans (HEA), which indicates dual inputs rather than a final common pathway from the AV node into the His bundle. However, the electrophysiological basis for AV node dual pathway conduction and HEA has not been clarified. This study was designed to elucidate the electrophysiological basis for dual pathway conduction and HEA.

Methods: By using HEA as an index of dual pathway electrophysiology, action potentials from multiple locations in the superior and inferior AV nodal domains were obtained to monitor electrical propagation during dual pathway conduction in 8 isolated rabbit hearts.

Results: Fibers inside the AV node were generally aligned along the AV conduction axis. During fast pathway (FP) conduction, electrical excitation in the AV node was propagated in a superior to inferior direction across the major fiber orientation. In contrast, slow pathway (SP) conduction occurred when the superior–inferior propagation failed within the superior nodal domain, permitting electrical propagation to proceed in the inferior nodal domain along the fiber orientation in a posterior to anterior direction. In effect, FP activated first the superior distal node, while SP activated first the inferior distal node. This functional dissociation of superior-fast and inferior-slow domains in distal node produced dual inputs into the His bundle.

Conclusions: Transverse versus longitudinal electrical propagation within the AV node produces functional dissociation in the distal node, resulting in superior-fast and inferior-slow inputs into the His bundle and HEA during dual pathway conduction.

1. Introduction

AV node dual pathway electrophysiology is accepted as the mechanism for AV nodal reentrant tachycardia (AVNRT), the most common type of paroxysmal supraventricular tachycardia [1,2]. The current textbook model of AV node dual pathway electrophysiology was initially proposed by Moe and colleagues in the 1960s [3]. According to the model, the upper part of the node can be functionally and spatially dissociated into two (fast and slow) pathways, which communicate with a final common pathway before reaching the His bundle. The model has provided a convenient explanation of reentrant circuit responsible for AVNRT, and eventually provided the framework from which the fast pathway (FP) and slow pathway (SP) ablations have been developed to cure AVNRT in patients [4,5]. Despite these enormous advancements, the substrate and electrophysiological basis for dual pathway electrophysiology remain elusive [1,6,7].

In a series of experiments, we have discovered and validated that dual pathway conduction results in a novel phenomenon, termed His electrogram alternans (HEA) [8–12]. This phenomenon has been reproduced by other investigators [13]. It also has been demonstrated in isolated human hearts [14]. The phenomenon indicates that there are 2 temporally and spatially discrete (superior-fast and inferior-slow) inputs, rather than a final common pathway from the AV node into the His bundle during dual pathway conduction. Considering the anatomical locations of superior-fast and inferior-slow pathway ablations [4,5], we hypothesized that the AV node is functionally dissociated into superior-fast and inferior-slow domains. The FP wave front initiated at the "superior/anterior approach", propagates in a superior to inferior direction across the major fiber orientation in the AV node, resulting in an early activation of the superior AV nodal domain (especially the superior distal node) and subsequently the superior His bundle domain. In contrast, the superior–inferior propagation would fail within the

☆ This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and the discussed interpretation.

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http://dx.doi.org/10.1016/j.ijcard.2013.12.032

superior nodal domain at short prematurity (at least partly due to across fiber orientation propagation), permitting electrical propagation initiated at the "inferior/posterior approach" to proceed in the inferior nodal domain along fiber orientation in a posterior to anterior direction to first reach the inferior His bundle domain.

This study has provided electrophysiological and histological evidence supporting that transverse versus longitudinal electrical propagation within the AV node produces functional dissociation in the distal node, resulting in superior-fast and inferior-slow dual inputs into the His bundle and consequently HEA during dual pathway conduction.

2. Methods

The use of animals was approved by the Institutional Animal Care and Use Committee and is in compliance with the "Guide for the Care and Use of Laboratory Animals" (NIH Publication No. 85-23, Revised 1996).

2.1. In vitro rabbit AV node preparation

The experiments were conducted on 8 atrial-AV node preparations from adult New Zealand White rabbits of both sexes. The preparations were instrumented as previously described [8]. Briefly, after sodium pentobarbital (50 mg/kg) anesthesia, the heart was removed and placed in a standard oxygenated Tyrode's solution saturated with 95% O_2/5% CO_2 at a flow rate of 35 mL/min. After trimming, the AV node preparation contained the triangle of Koch and the surrounding right atrial and ventricular tissues.

2.2. Electrical recordings and stimulation protocols

Custom-made bipolar electrodes (0.2 mm spacing) were used to record atrial electrograms and for atrial pacing. Roving bipolar electrodes were used to record the superior and inferior His electrograms as described previously [8]. All electrodes were positioned with micromanipulators (M330, WPI, Sarasota, FL). An 8-channel, programmable stimulator (Master-8, AMPI, Jerusalem, Israel) was used for pacing. The electrical signals were amplified, filtered at 30 to 3000 Hz (CyberAmp 380, Axon Instruments, Union City, CA), recorded and analyzed by AxoScope (Axon Instruments).

Standard glass microelectrodes were used to record the intracellular action potential (AP) from AV nodal fibers (typically from 2 sites simultaneously). Anatomic location, AP morphology and amplitude, and dV/dt (~10–50 V/s), as well as cycle-length dependency, were used to identify signals originating from different nodal regions [15].

All preparations were paced at a basic cycle length (A1A1) of 300 ms and a standard AV nodal conduction curve was generated by interposing a premature A2 stimulus after every 20th basic beat A1. The prematurity coupling interval A1A2 was progressively shortened (in steps of 10–5 ms) until the occurrence of AV block. The AV nodal effective refractory period (ERP) was defined as the longest A1A2 which failed to conduct by the AV node.

Programmed A1A2 pacing protocol with a fixed short prematurity, typically 20 ms longer than the AV nodal ERP (which was conducted by the SP judged by the HEA as described below), was delivered during recording of AV nodal AP at various locations. In this way, the AV nodal conduction sequence can be traced from AP recordings at various locations during both FP conduction at basic beat A1 and SP conduction at premature beat A2.

2.3. Monitoring of AV nodal fast and slow pathway propagation by HEA

HEA was used to monitor FP and SP conduction, as previously reported [8–12]. His electrogram recorded from the superior His bundle domain (superior His electrogram, SHE) is high in amplitude during FP conduction and the amplitude becomes low during SP conduction. In contrast, His electrogram recorded from the inferior His bundle domain is always from low amplitude during FP to high amplitude during SP conduction.

2.4. Slow pathway ablation

Surgical ablation of the SP was performed as previously reported [9]. Successful SP ablation in the inferior AV nodal approaches resulted in a longer AV nodal ERP and elimination of HEA.

2.5. Histology

The AV nodal preparations were immersion-fixed with 4% formalin and then processed by paraffin embedding. The AV conduction system was studied by serial sectioning. To reveal the major fiber orientation within the AV node, serial sections (6.0-μm-thick) were cut parallel to the endocardial surface along the AV conduction axis and stained with hematoxylin and eosin (H&E), and Masson's trichrome stain.

2.6. Statistical analysis

Data are expressed as mean ± SD where appropriate. Comparisons before and after SP modification were performed by paired Student's t-test. A value of $P < 0.05$ was required for statistical significance.

3. Results

3.1. Histology and the working model

The AV node was situated adjacent to the tricuspid valve with its superior/anterior and inferior/posterior approaches on the right AV septal junction, as previous reported [8]. Serial sections revealed that AV nodal fibers, including the transitional layers, are aligned longitudinally along the AV conduction axis (Fig. 1). It was also noticed that atrial fibers coming from the crista terminalis and the fibers in the inferior part of the AV node (inferior/posterior approaches, posterior nodal extension) were generally aligned longitudinally. In contrast, atrial fibers in the anterior atrial septum and the fibers in the superior/anterior transitional layers were not so well aligned (not shown).

Based on histological architecture, we developed the following working hypothesis (Fig. 2). Electrical excitation coming from atrial myocytes arrives at the transitional layers. At basic beats or long prematurities, electrical propagation can cross the fiber orientation in the superior/anterior AV node domain. Once the superior part of the node is activated, electrical excitation can proceed in 2 directions: 1) from the superior AV node domain along the fiber orientation to activate the superior His bundle domain (Fig. 2A, green arrows) resulting in an early, large SHE (green dots); and 2) continuing superior to inferior propagation within the AV node to activate the inferior nodal domain, in particular the distal part of the inferior AV node, preventing longitudinal conduction coming from the inferior/posterior approach (Fig. 2A, yellow arrow). This is the case of FP conduction.

At short prematurities, the "superior to inferior" propagation could easily fail within the superior AV nodal domain due to across fiber propagation [16,17]. The failing across fiber excitation in the superior AV nodal domain (Fig. 2B, green curved arrows) permits electrical excitation formed at inferior/posterior approaches to proceed along the fiber direction to activate the inferior part of the node (posterior nodal extension, compact node/lower nodal cells) to reach the inferior His bundle domain (Fig. 2B, large yellow arrows) resulting in an early, high-amplitude IHE (yellow dots). Meanwhile excitable fibers in the superior AV nodal domain could be invaded retrogradely by the slow wave front

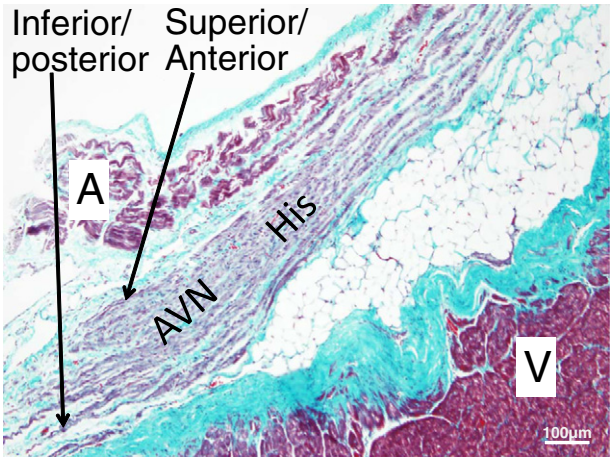

Fig. 1. Photomicrograph of the AV septal junction showing the major components of the AV conduction system (AV node and the His bundle) in a longitudinal axis. Note that fibers in the AV node and the His bundle are aligned longitudinally. AVN: AV node, A: atrial myocardium, His: His bundle, V: ventricular myocardium. Masson's trichrome staining.