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Effects of ganglionated plexi ablation on ventricular electrophysiological properties in normal hearts and after acute myocardial ischemia

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ABSTRACT

Background: Ganglionated plexi (GP) ablation has been shown to play an important role in atrial fibrillation (AF) initiation and maintenance. Also, GP ablation increases chances for prevention of AF recurrence. This study investigated the effects of GP ablation on ventricular electrophysiological properties in normal dog hearts and after acute myocardial ischemia (AMI).

Methods: Fifty anesthetized dogs were assigned into normal heart group (n = 16) and AMI heart group (n = 34). Ventricular dynamic restitution, effective refractory period (ERP), electrical alternans and ventricular fibrillation threshold (VFT) were measured before and after GP ablation in the normal heart group. In the AMI heart group, the incidence of ventricular arrhythmias and VFT were determined.

Results: In the normal heart group, GP ablation significantly prolonged ERP, facilitated electrical alternans but did not increase ERP dispersion, the slope of restitution curves and its spatial dispersion. Also, GP ablation did not cause significant change of VFT. In the AMI heart group, the incidence of ventricular arrhythmias after GP ablation was significantly higher than that in the control group or the GP plus stellate ganglion (SG) ablation group ($P<0.05$). Spontaneous VF occurred in 8/12, 1/10 and 2/12 dogs in the GP ablation group, the GP plus SG ablation group and the control group, respectively ($P<0.05$). VFT in the GP ablation group showed a decreased trend though a significant difference was not achieved compared with the control or the GP plus SG ablation group.

Conclusions: GP ablation increases the risk of ventricular arrhythmias in the AMI heart compared to the normal heart.

1. Introduction

Recently, basic and clinical studies have revealed the critical contribution of the intrinsic cardiac autonomic nervous system (ICANS) in atrial fibrillation (AF) initiation and maintenance [1–8]. Ganglionated plexi (GP) within epicardial fat pad serves as the most important component in the ICANS [9–12]. GP ablation has been shown to increase the success rate of AF ablation, particularly in addition to pulmonary vein isolation procedures [5–7,13].

Although considerable evidence has confirmed the efficacy of GP ablation for the prevention of AF, the effects of GP ablation on ventricular electrophysiological properties remain unknown. It is well known that cardiac autonomic modulation significantly influences the initiation of ventricular arrhythmias (VA) and sudden cardiac death. An increase in parasympathetic activity or a reduction in sympathetic activity significantly decreases the susceptibility of the heart to ventricular fibrillation (VF), while an enhancement of sympathetic activity or an impairment of parasympathetic activity increases it [14,15]. As cell bodies of parasympathetic postsynaptic neurons innervating the heart are mainly located on the atrial GP, destruction of cardiac autonomic innervation at the atria may also damage ventricular autonomic innervation [9–11]. Recently, Osman et al. [16] reported a case of a patient with AF undergoing pulmonary vein isolation with a profound vagal response, subsequently developed VF after programmed ventricular stimulation. Thus, we hypothesized that destruction of the major cardiac parasympathetic elements by GP ablation might predispose the heart to VA. In the present

Abbreviations: AF, atrial fibrillation; AMI, acute myocardial ischemia; AP, action potential; APD, action potential duration; APD_{90}, an APD at 90% repolarization; CV, coefficient of variation; DI, diastolic interval; ERP, effective refractory period; GP, ganglionated plexi; ICANS, intrinsic cardiac autonomic nervous system; LVA, left ventricular apex; LVB, left ventricular base; LVM, the median area between LVA and LVB; RVA, right ventricular apex; RVB, right ventricular base; RVM, the median area between RVA and RVB; SG, stellate ganglion; S_{max}, the maximum slope of restitution curve; VA, ventricular arrhythmias; VF, ventricular fibrillation; VFT, ventricular fibrillation threshold; VPC, ventricular premature contraction; VT, ventricular tachycardia.

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study, we investigated the effects of GP ablation on ventricular electrophysiological properties in normal dog hearts and after acute myocardial ischemia (AMI).

2. Methods

2.1. Animal preparation

All animal studies were reviewed and approved by the animal experimental administration of Wuhan University, China. The investigation conforms to the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1996). Fifty adult mongrel dogs weighing 18–25 kg were randomly assigned into a normal heart group (n = 16) which consisted of 8 dogs without GP ablation and 8 dogs with GP ablation and an AMI heart group (n = 34) which consisted of 12 dogs without GP ablation, 12 dogs with GP ablation and 10 dogs with GP plus stellate ganglion (SG) ablation. All dogs were anesthetized with 30 mg/kg Na-pentobarbital and ventilated with room air by a positive pressure ventilator. Additional maintenance doses of 2 mg/kg Na-pentobarbital were administrated at the end of each hour during the procedure. Systemic arterial pressure was monitored during the whole procedure using a computer-based Lab System (Lead 2000B, Jingjiang Inc., China). A heating pad was used to maintain the core body temperature of the dogs at 36.5 ± 1.5 °C.

2.2. GP ablation

High-frequency electrical stimulation (20 Hz, 0.1 ms duration, 0.6–5 V) was applied to identify the 4 major GP [1,2]: (1) anterior right GP located at the right superior pulmonary vein–atrial junction; (2) inferior right GP located at the junction of inferior vena cava and both atria; (3) superior left GP located adjacent to the left superior pulmonary vein–atrial junction between the left atrial appendage and left pulmonary artery; and (4) inferior left GP located at the left inferior pulmonary vein–atrial junction. An irrigated large-tip (3.5 mm) electrode catheter (Biosense-Webster Inc. Diamond Bar, CA, USA) was used for ablation. Radiofrequency current (≤35 W) was immediately delivered to the sites showing sinus rate slowing or atrioventricular conduction block during high-frequency electrical stimulation. Complete ablation was verified by elimination of sinus rate slowing or atrioventricular conduction block when applying maximal strength of stimulation to the ablated area. We also ablated the ligament of Marshall which is also richly innervated by both sympathetic and parasympathetic neural elements and serves as an important part of ICANS.

2.3. SG ablation

After a left or a right thoracotomy was performed, high-frequency electrical stimulation (20 Hz, 0.1 ms duration, 30–50 V) was applied to identify the left or right stellate ganglion. Ablation was considered complete when stimulation of each ablated ganglion no longer produced any changes of heart rate and/or blood pressure. The ablation procedure was the same as that of GP ablation.

2.4. Cardiac electrical recording

Both left and right thoracotomies were performed at the 5th intercostal space to expose the heart. Two multi-electrode catheters with 2 mm interelectrode distance were sutured to record electrogram at 8 epicardial sites from the apex to the base in the left and right ventricular free walls (Fig. 1). A custom-made Ag–AgCl electrode was used to record monophasic action potentials (AP) from the epicardial surface of the left and right ventricular free walls (Figs. 1, 2A) at 6 sites: left ventricular apex (LVA), left ventricular base (LVB), the median area between LVA and LVB (LVM), right ventricular apex (RVA), right ventricular base (RVB), and the median area between RVA and RVB (RVM). Standard surface electrocardiograms (leads I, II, III, aVR, aVL and aVF, Fig. 1C) were continuously monitored. A computer-based Lab System (Lead 2000B, Jingjiang Inc., China) was used to display all recordings and to perform all pacing protocols. The monophasic APs were filtered at 0.05 to 1200 Hz and local cardiac electrograms between 30 and 500 Hz.

2.5. Stimulation protocol

Ventricular pacing was performed to determine the effective refractory period (ERP) of the ventricular myocardium. The ventricular ERP was determined using an 8-beat drive train (S1, 300 ms cycle length) followed by an extrastimulus (S2) and repeated with progressively shorter S1–S2 intervals [from 250 ms to ventricular ERP]. Ventricular ERP was defined as the longest S1–S2 interval that failed to capture the ventricles. ERP dispersion was defined as the coefficient of variation (CV, standard deviation/mean) of the ERP at all 8 sites.

A dynamic steady state pacing protocol (S1S1) with a series of pulse trains at constant pacing cycle length [17,18] was performed to obtain monophasic AP duration (APD) of each site (Fig. 2B). The distal pair of the electrodes attaching to the left or right ventricular apex was used for pacing at twice the diastolic threshold. The pulse train was delivered at an initial cycle length just slightly shorter than the sinus cycle length and then repeated with progressively shorter cycle length in an initial stepwise fashion by 20 or 30 ms and a subsequent stepwise fashion by 10 ms until APD alternans occurred (Fig. 2C). Each pulse train was maintained for 30 s to achieve a steady state. After each pulse train was delivered, the pacing was interrupted for 2 min to minimize the pacing memory effects

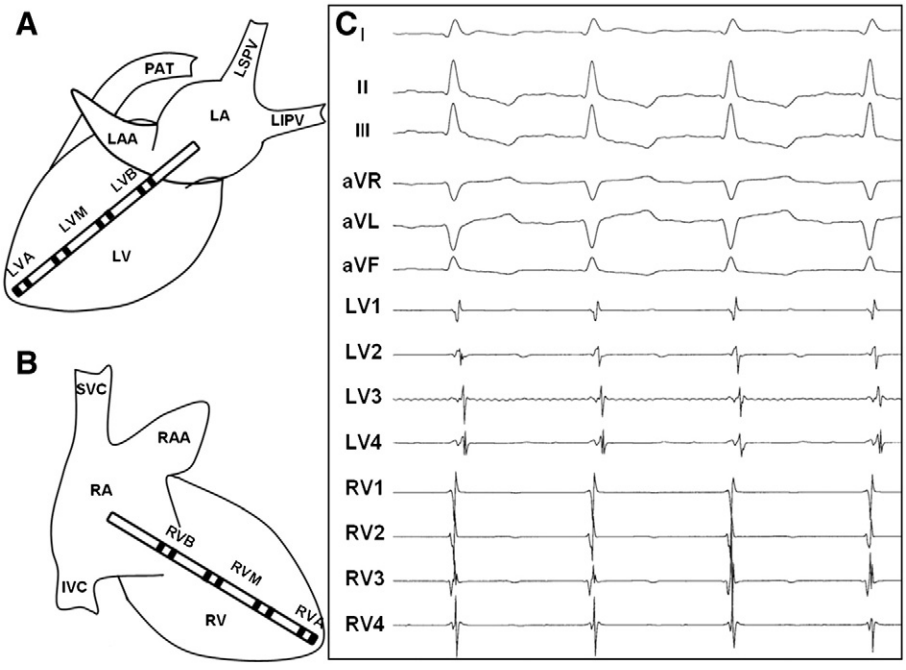

Fig. 1. Schematic representation and catheter positions in the left (A) and right (B) ventricular free walls and simultaneous surface and intracardiac electrocardiogram recording (C). I, II, III, aVR, aVL and aVF are surface electrocardiogram leads. LV, left ventricle; RV, right ventricle; LA, left atrium; RA, right atrium; LAA, left atrial appendage; RAA, right atrial appendage; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; PAT, pulmonary artery trunk; SVC, superior vena cava; IVC, inferior vena cava; LVA, left ventricular apex; LVB, left ventricular base; LVM, the median area between LVA and LVB; RVA, right ventricular apex; RVB, right ventricular base; RVM, the median area between RVA and RVB.