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Renal sympathetic denervation suppresses atrial fibrillation induced by acute atrial ischemia/infarction through inhibition of cardiac sympathetic activity

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ABSTRACT

Objective: This study aims to explore the effects of renal sympathetic denervation (RSD) on atrial fibrillation (AF) inducibility and sympathetic activity induced by acute atrial ischemia/infarction.
Methods: Acute ischemia/infarction was induced in 12 beagle dogs by ligating coronary arteries that supply the atria. Six dogs in the sham-RSD group did not undergo RSD, and six dogs without coronary artery ligation served as controls. AF induction rate, sympathetic discharge, catecholamine concentration and densities of tyrosine hydroxylase-positive nerves were measured.
Results: Acute atrial ischemia/infarction resulted in a significant increase of AF induction rate, which was decreased by RSD compared to controls ($P < 0.05$). The root-mean-square peak value, peak area and number of sympathetic discharges were significantly augmented by atrial ischemia relative to the baseline and control ($P < 0.05$). The number of sympathetic discharges was significantly reduced in the RSD group, compared to the control and sham-RSD groups ($P < 0.05$). Norepinephrine and epinephrine concentrations in the atria, ventricle and kidney were elevated by atrial ischemia/infarction, but were reduced by RSD ($P < 0.05$).
Conclusions: Sympathetic hyperactivity was associated with pacing-induced AF after acute atrial ischemia/infarction. RSD has the potential to reduce the incidence of new-onset AF after acute atrial ischemia/infarction. The inhibition of cardiac sympathetic activity by RSD may be one of the major underlying mechanisms for the marked reduction of AF inducibility.

1. Introduction

New-onset atrial fibrillation (AF) is a common complication of acute myocardial infarction, which has an estimated prevalence that ranges between 7% and 21%. It has been suggested that transient AF in this setting increases the risk of AF recurrence, heart failure, stroke and mortality [1,2]. Remodeling of the cardiac sympathetic nervous system after myocardial infarction (MI) contributes to the pathogenesis of arrhythmias in animal models and in humans [3–5]. Clinical [6] and experimental [7] studies have demonstrated that renal sympathetic denervation (RSD) has potential atrial anti-arrhythmic and anti-remodeling effects, which might be related to the suppression of atrial electrophysiology and cardiac sympathetic activity. No studies have previously evaluated the influence of sympathetic hyperactivity associated with ischemia/infarction on AF genesis. Moreover, whether RSD can reduce AF inducibility and sympathetic activity induced by acute atrial ischemia/infarction remains unknown. In this study, we induced new-onset AF after acute ischemia/infarction in a canine model to evaluate the mechanism of sympathetic hyperactivity contributing to AF genesis. In particular, we aim to explore the effects of RSD on AF induction rate, sympathetic nerve discharge and catecholamine concentration.

2. Methods

2.1. Ethics statement

This study was carried out in strict accordance with the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health.

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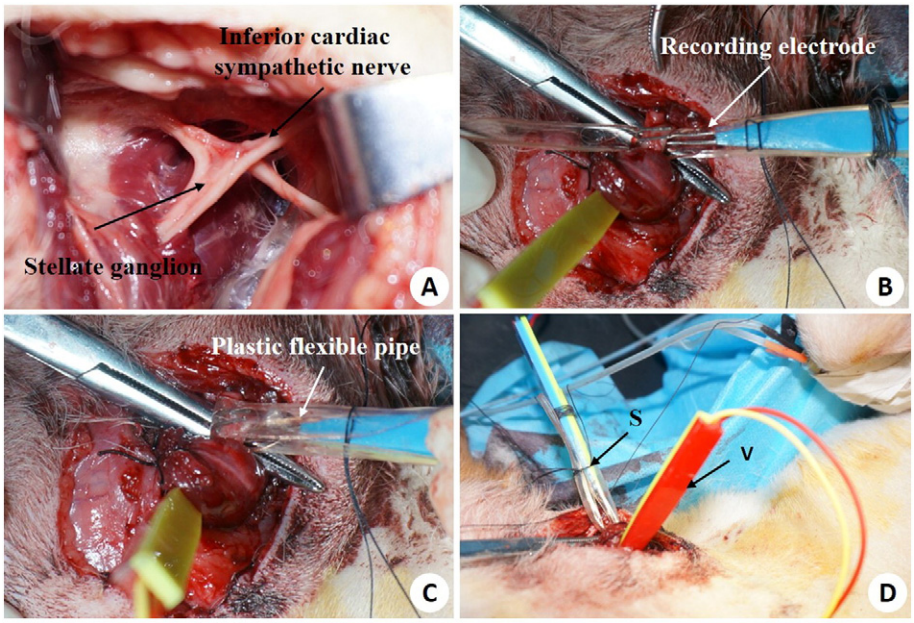

Fig. 1. Surgical procedure and setup for electrophysiological recordings. (A) Anatomical position of the inferior cardiac sympathetic nerve and stellate ganglion. (B) The inferior cardiac sympathetic nerve trunk and cervical vagus trunk were connected to a pair of modified bipolar neural recording electrodes. (C) Modified bipolar electrodes were surrounded by flexible plastic tubes. (D) The recording electrodes for the sympathetic nerve trunk (S) and vagus trunk (V) were embedded into the tissue to maintain the physiological state of the nerve.

This study protocol was approved by the Institutional Animal Care and Use Committee of the First Affiliated Hospital of Xinjiang Medical University (Permit number: IACUC-20131105010), and conformed to the guidelines of the Association for Assessment and Accreditation of Laboratory Care (AAALAC). All surgical procedures were performed under sodium pentobarbital anesthesia, and all efforts were made to minimize animal suffering [8].

2.2. Animals and study design

Eighteen beagle dogs of either sex, weighing 12–15 kg, were included in this study. Animals were randomly divided into three groups: RSD group, comprised of six dogs that underwent coronary artery occlusion and RSD; sham-RSD group, comprised of six dogs that underwent coronary artery occlusion, but did not undergo

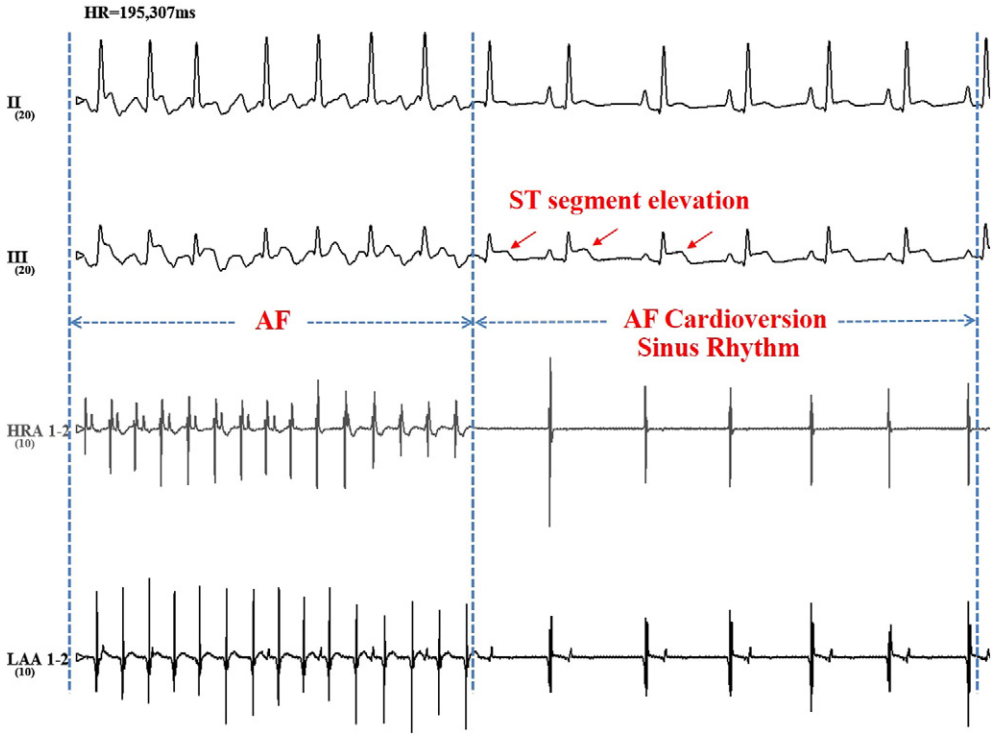

Fig. 2. New-onset spontaneous AF after acute atrial ischemia/infarction and AF cardioversion. A representative ECG shows ST segment depression after acute MI following coronary artery occlusion.