Effects of stepwise denervation of the stellate ganglion: Novel insights from an acute canine study

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BACKGROUND The stellate ganglion (SG) is important for cardiac autonomic control. SG modification is an option for treating refractory ventricular tachyarrhythmias. The optimal extent of left- and right-sided SG denervation necessary for antiarrhythmic effect, however, remains to be learned.

OBJECTIVE The purpose of this study was to evaluate the effects of stepwise SG denervation on hemodynamic and electrophysiological parameters in dogs.

METHODS After sequential left and right thoracotomy in 8 healthy dogs, the SG was exposed by dissection. Two pacing wires were placed in the upper SG to deliver high-frequency stimulation. The lower SG, ansae subclaviae, and upper SG were removed in a stepwise manner. The same protocol was performed on the right side. Blood pressure (BP), heart rate, and electrophysiological parameters were recorded at baseline and after 5 minutes of stimulation.

RESULTS Systolic and diastolic BP significantly increased during stimulation of the upper left SG. The mean increase in systolic BP from baseline was 49.4 ± 26.6 mm Hg ($P = .007$), 25.5 ± 14.1 mm Hg after the lower SG was removed ($P = .02$), and 8.6 ± 3.4 mm Hg after resection of the ipsilateral ansae subclaviae ($P = .048$). Heart rate and other electrophysiological parameters did not change significantly. After the complete removal of the left SG, systolic BP increased by 34.0 ± 17.6 mm Hg ($P = .005$) after stimulation of the right SG.

CONCLUSION Sympathetic output remains after the lower SG is removed, and sympathetic output from the right SG remains after the complete resection of the left SG and ansae subclaviae. Thus, some patients who undergo left SG denervation can still have significant sympathetic response via right SG regulation.

KEYWORDS Ansa subclavia; Canine; Cardiac sympathetic denervation; Stellate ganglion; Vagal trunk

(Heart Rhythm 2016;0:1–7)

Introduction

The heart is richly innervated by autonomic nerves. The balance between the parasympathetic and sympathetic effects of the autonomic nervous system has an important role in proper cardiac function.[1] Both aspects of the autonomic nervous system have significant effects on cardiac chronotropy and inotropy.[2] The stellate ganglion (SG) provides important sympathetic nerve inputs into the heart and may predispose the myocardial conduction system and myocardium itself to multiple types of atrial and ventricular arrhythmias.[3]

Cardiac sympathetic denervation (CSD) has been shown to reduce the burden of ventricular arrhythmias acutely.[4] Preganglionic sympathetic efferents arising from the T1-4 spinal cord that project to the heart transit through stellate ganglia via the paravertebral chain. In left-sided CSD procedures, the lower half (T1-4) of the left side of the SG (LSG) is removed.[5] A recent work by Buckley et al[6] showed that T1-2 surgical excision is sufficient to functionally interrupt the central control of peripheral sympathetic efferent activity. However, the upper part of T1 of the LSG and ansae subclaviae remains connected to the heart and can still affect cardiac function through these remaining sympathetic innervations. Studies defining the role of the remaining segments after left CSD are scarce. Furthermore, the balance between the sympathetic and parasympathetic nervous systems is dynamic and is altered after left CSD procedures. Thus, we investigated the effects of stepwise SG denervation with subsequent stimulation of the remaining nerve tissue in dogs to assess the physiological effects on blood pressure (BP), heart rate (HR), and electrophysiological intervals.

The study was supported by Small Grant from Mayo Clinic and Foundation and National Natural Science Foundation of China (grant no. 81270305, to Dr Wu). **Address reprint requests and correspondence:** Dr Yong-Mei Cha, Division of Cardiovascular Diseases, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905. E-mail address: ycha@mayo.edu.

  http://dx.doi.org/10.1016/j.hrthm.2016.03.010

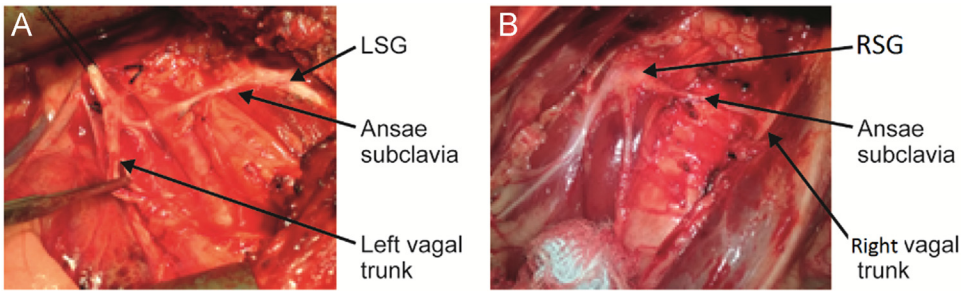

Figure 1 Anatomy of the stellate ganglion, vagal trunk, and ansae subclaviae. **A:** Left stellate ganglion (LSG), left vagal trunk, and left ansa subclavia. **B:** Right stellate ganglion (RSG), right vagal trunk, and right ansa subclavia.

Methods

Animal preparation and anesthesia

The study were approved by the Mayo Clinic Institutional Animal Care and Use Committee and performed under the guidelines of the National Institutes of Health *Guide for the Care and Use of Laboratory Animals*. Eight male mongrel dogs (weight 30–40 kg) were anesthetized with ketamine/diazepam for induction and intubation, and intravenous isoflurane (1%–3%) and propofol (7–15 mg/(kg·min)) were used to provide adequate anesthesia during nerve stimulation as well as to maintain an adequate anesthetic plane during thoracotomy to access the nervous structures. After visualization of these structures, isoflurane was reduced to the lowest level possible, and propofol was increased to maintain adequate anesthesia. This was done to allow for adequate evaluation of the sympathetic system during stimulation testing, because propofol has a small effect on autonomic tone than isoflurane.[7,8]

HR and heart rhythm were monitored continuously throughout the study. BP was monitored continuously via a femoral arterial line and was recorded at 15-minute intervals when not measured as part of the stimulation aspect of the study. Core body temperature was monitored and maintained euthermic throughout the study. Vascular access was obtained percutaneously, and sheaths were placed using an over-the-wire technique. Femoral veins, arteries, and external jugular veins were used for the placement of 9–12F sheaths to access the monitoring and stimulation electrodes.

Catheter placement for the electrophysiology study

A Boston Scientific Blazer II XP Temperature Catheter (8F, 4-mm tip, 2.5-mm electrode spacing) was placed at the right ventricular apex for both ventricular recording and stimulation. A multipolar catheter (CS catheter, 6F, Biosense Webster Inc, South Diamond Bar, CA) was inserted into the internal jugular vein and placed in the coronary sinus under fluoroscopic guidance (Axiom Artis dTA, Siemens Inc, Malvern, PA). Electrocardiography, arterial BP, and multichannel intracardiac electrograms were continuously stored using the Prucka CardioLab recording system (GE Healthcare, Chicago, IL).

Electrophysiological parameters were collected from the Prucka system using coronary sinus and ventricular recording catheters. These included the PR, QRS, and QT intervals. Pacing from the coronary sinus and right ventricle was done using a Bloom Stimulator (Fischer Medical Technologies LLC, Wheat Ridge, CO). The atrial and ventricular effective refractory periods (ERPs) were determined by pacing the left atrium and right ventricle, noting the refractory period from a drive train of 8 pulses with a subsequent early S2 stimulus at twice the pacing threshold of the tissue. The left atrial conduction time was taken as the time for signal to travel from the distal to the proximal coronary sinus when the left atrium was captured. The left ventricular (LV) conduction time was determined as the traveling time from the distal to the proximal coronary sinus when the LV was captured.

Approach to thoracotomy and nerve dissection

The methods of thoracotomy and nerve dissection have been previously reported in detail.[9–11] In brief, thoracotomy was performed through the left third intercostal space. The pericardium was opened to expose the left atrial appendage and the base of the LV. The LSG, vagal trunk, and left ansae subclaviae were identified (Figure 1A). After the left-sided procedure and protocol was completed, the wound was closed and a similar surgical procedure was performed on the right side via thoracotomy through the right third intercostal space. The right side of the SG (RSG), right vagal trunk, and right ansae subclaviae were then identified (Figure 1B).

Experimental procedure and stimulation sequence

A standard Grass Stimulator (Grass Technologies, Warwick, RI) with 10-Hz, 2-ms pulse duration, and 10-V output was connected directly to the nervous structures via a pair of electrically active epicardial pacing suture wires. Before and after stimulation, electrophysiological and hemodynamic measurements were recorded.

The process of nerve dissection and stimulation is illustrated in Figure 2. The stimulation sequence included the initial stimulation of the intact LSG. Recordings were taken at baseline and 5 minutes after continuous stimulation. The left vagal trunk was stimulated next. Thereafter, the lower half of the LSG along with T2-3 was resected. The stimulation wires were placed into the upper half of the LSG, and stimulation recordings were then performed.