

Opinion

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# The Effect of Low-Level Electrical Stimulation of the Aortic Root Ventricular Ganglionated Plexi on the Treatment of Heart Failure



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## Opinion

Congenital heart failure (HF) is one of the most popular heart disease, which is often accompanied by arrhythmia especially atrial fibrillation (AF). Both HF and AF share the similar underlying pathogenesis such as structural, neurohormonal, and electrical atrial or ventricular remodeling. Unfortunately, traditional pharmacological therapy may not be as useful for the treatment of HF in patients with AF as it is in patients in normal sinus rhythm. Because imbalanced tone of autonomic nervous system (ANS) plays the key role in the initiation of AF in patient with HF [1], modulation of ANS became a hotly debated point in the current research and practice.

Strong vagal stimulation had long been used to induce AF and high level nerve stimulation is considered to facilitate both AF and HF. Recently, Li et al. [2] gave a novel idea that low-level electrical stimulation (LL-ES) of vagal nerve VNS could suppress AF by inhibiting the intrinsic cardiac autonomic nervous system (ANS) and prevent episodic AF arising from pulmonary vein or non-pulmonary vein. Following Li's study, increasing evidences suggested that LL-ES of vagal nerve, with voltage levels 10-50% below threshold showed an antiarrhythmic effect [3-5]. Furthermore, Stavrakis et al. [6] demonstrated that transcatheter LL-ES suppresses AF and decreases inflammatory cytokines in patients with paroxysmal AF. These results indicated LL-ES of autonomic nerve could bring both anti- arrhythmia and anti-inflammation effect.

Intrinsic ANS are mainly connected by some GPs that located in the epicardial fat pads, and these GP co-operated with each other. So we assumed that the atrial GP and the ventricular GP connected with each other over nerve axon. To confirm the hypothesis, Avidin Biotin Complex staining were performed to study the efferent autonomic pathway from the aortic root

ventricular GP to the pulmonary veins, and the results showed that Avidin Biotin Complex positive nerve fibers that contained both cholinergic and adrenergic neurotransmitters penetrated directly from the aortic root ventricular GP to the left pulmonary veins [7]. Moreover, He et al. [8,9] claimed that electrical stimulation of atrial GP influenced the electrophysiology of the ventricle and ventricular arrhythmogenic properties. These results indicated that atrial GP and ventricular GP may cooperate with each other and act as a single functional unit. Therefore, we proposed that modulation of the ventricular GP would also affect the electrophysiology of the atrium. Our recent study [10] demonstrated that stimulation of aortic root ventricular GP provoked robust AF in the absence of extrinsic cardiac nerve activity using an isolated perfused heart model. These findings suggested that ventricular GP innervated PVs and contribute to the initiation of AF with the exception of atrial GP. Finally, our latest study [11] showed that LL-ES of the aortic root ventricular GP attenuated the tone of autonomic nerves and reduce the inducing rate of AF mediated by ANS, which demonstrated that LL-ES of the aortic root ventricular GP presented an antiarrhythmic effect.

Because arrhythmia, especially AF is one of the common complications accompanied with HF. AF induces atrial enlargement and electrical remodeling, which aggravates HF. Several studies demonstrated that the rise of sympathetic tone facilitated myocardial fibrosis and electrical remodeling, therefore offered an essential substrate for the development and maintenance of AF [12,13]. It is well known that ANS and inflammation played important role in both HF and AF, and these two syndromes were often presented in the same patients. The rise of ANS tone especially the sympathetic tone combined the release of inflammatory factors such as C-protein made

it even harder to cure these kinds of patients. For this reason, modulation of the local intrinsic cardiac GP was proposed these years and had made some progress. Li [14] stated that vagal nerve stimulation can modulate the inflammatory response and affect specific inflammatory mediators. As a result, vagal nerve stimulation may present beneficial effects that are independent from heart rate or AV conduction in HF. Kobayashi et al. [15] found that endovascular cardiac GP stimulation selectively improved the contractility of left ventricle without increasing heart rate. Efforts to optimize electrode placement and fixation will improve the reproducibility of endovascular cardiac GP stimulation. These studies demonstrated that the decreasing tone of ANS could also benefit to HF. It is therefore plausible to hypothesize that LL-ES of the aortic root ventricular GP would be antiarrhythmic and anti-inflammation, which might reverse the structural remodeling of myocardial fibrosis and atrial enlargement following HF by attenuating the sympathetic tone.

Therefore, our further study used programmed electrical stimulation, burst electrical stimulation, immunohistochemistry, PCR and Western Blot, Ellesa, and patch clamp skills to investigate the anti-cardiac remodeling effect of LL-ES of the aortic root ventricular GP. After 4h of LL-ES of the aortic root ventricular GP, ventricular effective refractory period (VERP) and the dispersion of VERP (dVERP) were measured. Bioactive factors of HF, including angiotensin II, TGF- $\beta$  mitogen-activated protein kinase (MAPK), and matrix metalloproteinase (MMP), were assessed. Furthermore, ventricle size, cardiac fibrosis as well as left ventricular ejection fraction were also determined. And the results indicated that Long term LL-ES of the aortic root ventricular GP improved acute cardiac structural and electrical remodeling induced by rapid pacing.

In conclusion, LL-ES of local cardiac GP seems to be an excellent choice in the treatment of both AF and HF. However, the neuron net work of intrinsic ANS is just the lower nerve center, whose activity was controlled by the higher nerve center- cranial nucleus. Therefore, further studies should deepen into the brain neuron to disclose the mechanism of LL-ES of intrinsic ANS in the treatment of HF or AF.

## References

1. Chen PS, Chen LS, Fishbein MC, Lin SF, Nattel S (2014) Role of the autonomic nervous system in atrial fibrillation: pathophysiology and therapy. *Circ Res* 114: 1500-1515.

2. Li S, Scherlag BJ, Yu L, Sheng X, Zhang Y, et al. (2009) Low-level vagosympathetic stimulation a paradox and potential new modality for the treatment of facl atrial fibrillation. *Circ Arrhythm Electrophysiol* 2(6): 645-651.
3. Chen M, Zhou X, Liu Q, Sheng X, Yu L, et al. (2015) Left-sided noninvasive vagus nerve stimulation suppresses atrial fibrillation by up-regulating atrial gap junctions in canines. *J Cardiovasc Pharmacol* 66(6): 593-599.
4. Stavrakis S, Nakagawa H, Po SS, Scherlag BJ, Lazzara R, et al. (2015) The role of the autonomic ganglia in atrial fibrillation. *JACC Clin Electrophysiol* 1(1-2): 1-13.
5. Liao K, Yu L, Zhou X, Saren G, Wang S, et al. (2015) Low-level baroreceptor stimulation suppresses atrial fibrillation by inhibiting ganglionated plexus activity. *Can J Cardiol* 31(6): 767-774.
6. Stavrakis S, Humphrey MB, Scherlag BJ, Hu Y, Jackman WM, et al. (2015) Low-level transcatheter electrical vagus nerve stimulation suppresses atrial fibrillation. *J Am Coll Cardiol* 65(9): 867-875.
7. Wang H, Fan B, Su FF, Zeng D, Liu X, et al. (2015) Autonomic Innervation from the Aortic Root Ventricular Ganglionated Plexi to the Pulmonary Vein: A Novel Pathway. *J Cardiovasc Med Cardiol* 2: 21-25.
8. He B, Lu Z, He W, Huang B, Yu L, et al. (2013) The effects of atrial ganglionated plexi stimulation on ventricular electrophysiology in a normal canine heart. *J Interv Card Electrophysiol* 37(1): 1-8.
9. He B, Lu Z, He W, Wu L, Cui B, et al. (2013) Effects of ganglionated plexi ablation on ventricular electrophysiological properties in normal hearts and after acute myocardial ischemia. *Int J Cardiol* 168(1): 86-93.
10. Wang HT, Li ZL, Fan BY, Su FF, Zhao JB, et al. (2014) The independent role of the aortic root ganglionated plexi in the initiation of atrial fibrillation: an experimental study. *J Thorac Cardiovasc Surg* 148(1): 73-76.
11. Wang HT, Xu M, Fan B, Liu XT, Su FF, et al. (2015) Low-level electrical stimulation of aortic root ventricular ganglionated plexi attenuates autonomic nervous system-mediated atrial fibrillation. *JACC Clin Electrophysiol* 1(5): 390-397.
12. Tang RB, Yan XL, Dong JZ, Kalifa J, Long DY, et al. (2014) Predictors of recurrence after a repeat ablation procedure for paroxysmal atrial fibrillation: role of left atrial enlargement. *Europace* 16(11): 1569-1574.
13. De Jong AM, Maass AH, Oberdorf-Maass SU, Van Veldhuisen DJ, Van Gilst WH, et al. (2011) Mechanisms of atrial structural changes caused by stretch occurring before and during early atrial fibrillation. *Cardiovasc Res* 89(4): 754-765.
14. Li W, Olshansky B (2011) Inflammatory cytokines and nitric oxide in heart failure and potential modulation by vagus nerve stimulation. *Heart Fail Rev* 16(2): 137-145.
15. Kobayashi M, Sakurai S, Takaseya T, Shiose A, Kim HI, et al. (2012) Effects of percutaneous stimulation of both sympathetic and parasympathetic cardiac autonomic nerves on cardiac function in dogs. *Innovations (Phila)* 7(4): 282-289.



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