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EDITORIAL COMMENT

Ablation of Atrial Gangionated Plexi to Treat Symptomatic Sinus Bradycardia*

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A long history of research into the function of the autonomic nervous system exists. Geis et al. (1) and Lazzara et al. (2) described individual autonomic pathways innervating the atria, sinus, and atrioventricular (AV) nodes in canine experiments 45 years ago. Randall and Ardell (3) showed that the neural pathways could be surgically interrupted, thereby selectively denervating these structures. Chiou et al. (4) found that vagal fibers were located in the atrial epicardium and subendocardium, and funneled through a central fat pad; they achieved denervation using topical phenol application and radiofrequency ablation. The finding that hexamethonium and tetradotoxin superfusing the atrial epicardium after pericardial instillation achieved neural blockade established the superficial location of the nerves and ganglia (5).

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In this issue of *JACC: Clinical Electrophysiology*, Qin et al. (6) have capitalized on this wealth of previous scientific information—exactly as they should—to translate those bench observations to the bedside for better patient care. Remarkably, Oklahoma has been an exemplary "hotbed" of superb autonomic observations over many years, and this is another creative contribution, collaborating with a skilled group in Shanghai.

In this study of 62 patients with symptomatic sinus bradycardia, the authors found that catheter ablation of atrial ganglionated plexi (GP), particularly of the right anterior GP and the GP at the junction of the aorta and superior vena cava, increased the mean and minimal sinus rates most effectively in patients <50 years of age for as long as a year, with improved quality of life in those <50 years of age. Older patients had less heart rate increase that disappeared by 1 year, and less improvement in quality-of-life indices (6).

Pacemaker therapy has been the only reliable long-term treatment for patients with symptomatic bradycardia, whether due to sinus node disease or AV conduction abnormalities. While such device implantation has become a routine choice for patients of all ages, long-term complications, especially with leads, along with required pulse generator changes, can be problematic. However, it might be appropriate to pause for a moment to put this life-saving technology into perspective: Arne Larsson, the first person in the world to receive an implantable cardiac pacemaker for life-threatening bradycardia in 1958, died in 2002 of a skin melanoma at 86 years of age after 26 implants (the first pacemaker replacement was required several hours after the initial implant), and outlived his implanting surgeon, Ake Senning, and the pacemaker inventor, Rune Elmqvist (7). Now, of course, we have leadless pacing (8) to obviate lead problems. Biologic pacing still seems a distant application (9), beset with its own list of problems.

Several aspects of this study are very appealing. First, as with catheter ablation of arrhythmias, altering the patient's own body to improve his or her health without implanting devices or leaving surgical footprints is a great achievement and, as long as the manipulation has no negative consequences, a preferred treatment approach. Second, finding a differential response in younger versus older aged patients is intriguing, and might provide clues to

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understanding the pathophysiology of sinus bradycardia in the future. Third, noting a different impact of ablating particular GPs provides important physiological understanding of cardiac innervation.

What are the potential drawbacks? First, though avoided in this study by a skilled ablation team, serious procedural complications in less experienced hands can result. This is not a trivial procedure. Second, might regeneration of nerves occur in the future and blunt or eliminate the sinus rate increase? The authors focused on ablating autonomic neurons that, they tell us, are unlikely to regenerate. Persistence of ablation effect after a year in patients <50 years of age supports their conclusion. But why did the effect disappear in the older patients at 1 year? Will the younger patients lose their response as they age? Longer follow-up will validate whether the authors were right. Third, the authors presented no measures of AV conduction, but if the AV node is vagally denervated along with the sinus node, it is possible that in the future some patients might develop atrial fibrillation with very rapid ventricular responses that may be difficult to control. Fourth, denervation supersensitivity is an established physiologic mechanism after neural denervation (10). It is possible that if these patients were exposed to vagomimetic stimuli, they might develop exaggerated symptomatic sinus slowing. Fifth, given the superficial location of the GP, transmural endocardial ablation of atrial muscle is necessary unless an epicardial approach is used. Widespread ablation might affect atrial function. Finally, and most importantly, while this is a well-done and important study, it is of a small and very selective group of patients. As such, it should be considered a hypothesis-generating pilot study, and be followed by a larger, well-controlled, and randomized trial, as the authors recommend. Only this way can we establish whether GP ablation deserves a proper place in treatment selection for patients with symptomatic sinus bradycardia.

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