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Cardiac Neuroablation for Vagal-Induced Bradyarrhythmias

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Introduction

Abnormal autonomic nervous system activity plays a substantial role in the occurrence of clinical bradyarrhythmias like vasovagal syncope (VVS), sinus node dysfunction (SND), and functional atrioventricular block (AVB).

In patients with symptomatic and refractory vagal-induced bradyarrhythmia, pacemaker implantation may become essential to prevent bradycardic episodes.[1] Altering autonomic innervation through the radiofrequency catheter ablation of ganglionated plexi, a process known as *cardiac neuroablation*, can potentially lessen the effects of excessive vagal tone on the heart.[2]

Vasovagal Syncope

Vasovagal syncope is the most prevalent form of syncope. It is defined as an abrupt autonomic nervous system disruption that results in an insufficient blood pressure or heart rate to maintain cerebral perfusion.[1] Reflex syncope can result from a purely vasodepressor effect, a solely cardioinhibitory response, or a mixed type of response.[3] Cardiac neuroablation in VVS theoretically works to prevent the vagal efferent arm of the reflex arc in the cardioinhibitory type of VVS or the mixed type of VVS with a predominant cardioinhibitory response.[1] Sinus node dysfunction is often associated with age-related fibrosis of the sinus nodal tissue. It is essential to differentiate between intrinsic SND and vagal-induced SND when choosing proper treatment for patients. An atropine challenge can help confirm vagal-induced SND. A positive response indicated by a sinus rate increase of at least 25% or a sinus rate of at least 90/min within 15 minutes of administration confirms vagal-induced SND. Lack of response to atropine suggests intrinsic SND.[4]

Atrioventricular Block

Atrioventricular block, typically caused by intrinsic disease, presents with prodromal symptoms lasting up to 5 seconds. Vagal-induced or functional AVB is influenced by the parasympathetic nervous system and associated with longer prodromal symptoms (>5 s) and sinus node slowing before and during AVB.[1]

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Diagnostic Tools and Patient Selection

A complete evaluation, including history, physical examination, and supine and standing blood pressure, is needed for accurate diagnosis and patient selection for cardiac neuroablation. An electrocardiogram followed by a tilt table test and implantable loop recorder may further clarify the diagnosis or classification of VVS[5]:

- **Tilt table test** is used to induce a response similar to VVS in laboratory conditions. The test has a high specificity of 92% to 94%. The VVS is classified into the following groups based on heart rate and blood pressure changes during syncope:
  - **Type 1, mixed.** Heart rate declines at the time of syncope, but the ventricular rate does not drop to less than 40/min or it falls to less than 40/min for less than 10 seconds with or without asystole of less than 3 seconds.
  - **Type 2A, cardioinhibition without asystole.** Heart rate declines to a ventricular rate of less than 40/min for more than 10 seconds, but asystole of more than 3 seconds does not occur. Blood pressure drops before the heart rate drops.
  - **Type 2B, cardioinhibition with asystole.** Asystole occurs for more than 3 seconds. Heart rate drop coincides with or precedes blood pressure drop.
  - **Type 3, vasodepressor.** Heart rate does not fall more than 10% from its peak during syncope.[6]
- **The implantable loop recorder** continuously records electrocardiographic data, which can identify arrhythmic events in patients whose cause of syncope was not detected during routine follow-up.

Cardiac Neuroablation—Unknowns and Patient Selection

Clinical knowledge of cardiac neuroablation is still limited in some respects, and there are some unknown questions that further studies should answer. These questions include the best method for identifying ganglionated plexi, the most effective approach to selecting a suitable candidate for the procedure, defining an optimal ablation strategy, and evaluating the long-term outcomes of complete and partial denervation. Patients with VVS who have a cardioinhibitory response to tilt table testing (type 1, 2A, or 2B) and refractory symptoms, despite physical and drug therapy, are currently deemed suitable candidates for cardiac neuroablation.

Abbreviations

AVB, atrioventricular block
SND, sinus node dysfunction
VVS, vasovagal syncope

Targets of Cardiac Neuroablation

Ganglionated plexi, located in the epicardial atrial fat pads, connect preganglionic and postganglionic nerve fibers, influencing heart rate, refractoriness, and cardiac function. Radiofrequency energy can effectively reach ganglionated plexi through the atria, enabling endocardial ablation for autonomic denervation. Ganglionated plexi in the left or right atrium are the primary targets.[7]

Approaches to Identifying Ganglionated Plexi

Anatomical guidance, high-frequency stimulation, and spectral mapping can be used to identify and target ganglionated plexi during cardiac neuroablation. Anatomical guidance alone, however, is insufficient because of the individual variability of ganglionated plexi sites in many patients, so commonly used identification approaches currently include high-frequency stimulation and spectral-guided methods[8]:

- **Anatomically guided approach.** Some electrophysiologists use an anatomically guided approach to conduct the ablation of ganglionated plexi. Ganglionated plexi can be identified based on the routine anatomical locations in the 3-dimensional electroanatomic mapping of the right and left atria. Debruyne et al[8] used a computed tomographic scan and electroanatomic mapping to pinpoint the ganglionated plexi sites.
- **High-frequency stimulation approach.** High-frequency stimulation was originally created to locate ganglionated plexi during circumferential pulmonary vein isolation for atrial fibrillation. This method applies high-frequency stimulation to each ganglionated plexi site with a frequency of 20 Hz, a voltage of 10 V to 20 V, and a pulse duration of 5 milliseconds. The presence of a positive vagal response, defined as transient ventricular asystole, AVB, or a 50% increase in R-R interval,

indicates vagal innervation sites. One drawback of this approach is the inadvertent induction of atrial fibrillation. To mitigate this risk, programmed high-frequency stimulation may be used during the atrial refractory period (10-20 milliseconds following the initially designed atrial stimulation) for 3 to 5 seconds. Even in cases of induced atrial fibrillation, a mean R-R interval increase of more than 50% can be used to assess a positive vagal response.[8]

- **Spectral-guided method.** Aksu et al[1] simplified the process of finding the ganglionated plexi by targeting fractionated electrograms in routine anatomical ganglionated plexi locations. They evaluated bipolar endocardial atrial electrograms for amplitude and number of deflections at filter settings of 200 Hz to 500 Hz and a sweep speed of 200 mm/s. The electrograms were divided into the following categories: normal (<4 deflections), low-amplitude fractionated (≥4 deflections, <0.7 mV amplitude), or high-amplitude fractionated (≥4 deflections, ≥0.7 mV amplitude). The technique allows for performance with conventional electrophysiologic equipment by adjusting filter settings.[8]

Ablation End Point of Cardiac Neuroablation

There is no standardized method to evaluate the completeness of vagal denervation after cardiac neuroablation, but several end points have been proposed in different studies:

- **Elimination of positive vagal response.** High-frequency stimulation is used to assess vagal response, and the ablation will continue until high-frequency stimulation shows no vagal response.
- **Absence of heart rate response to atropine.** The denervation is assumed to be successful in the absence of a heart rate response to atropine. Because of its long-lasting effects, atropine should be used at the end of the procedure.
- **Extracardiac vagal stimulation.** A quadripolar electrode catheter is placed through the jugular foramens to stimulate the vagus nerves. Positive responses (asystole or AVB) indicate incomplete denervation. Extracardiac vagal stimulation can be repeated during cardiac neuroablation, and ultrasonographic guidance could be used to localize the vagus nerve and find the best position for the catheter.[9]

Conclusion

The role of cardiac neuroablation in treating different kinds of bradyarrhythmia is rapidly evolving. The procedure is a promising treatment for patients with refractory symptoms in select populations, but its long-term efficacy and safety are not yet completely understood. Future research directions in implementing cardiac neuroablation include recognizing optimal candidates, finding the best ablation strategies, and creating standardized procedural end points.

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