EDITORIAL COMMENTARY

Advantages and pitfalls of selective cardioneuroablation targeting the atrioventricular node

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Swallowing syncope is a relatively rare reflex syncope that is mostly conditioned by a pure cardioinhibitory response to swallowing and esophageal passage. Therefore, until recently, the predominant and effective treatment method was permanent cardiac pacing. With the current availability of cardioneuroablation (CNA) for the treatment of functional bradyarrhythmias, it is logical to also consider this option, especially in young patients. Although some patients may have a subclinical intrinsic sinoatrial (SA) or atrioventricular (AV) node disorder that is only potentiated by a reflex mechanism, in most cases the functional component is prevailing. Nevertheless, atropine testing is highly desirable before CNA, thus verifying sufficient parasympathetic reserve, and ideally documenting the atropine-induced disappearance of the cardioinhibition due to swallowing.

In the case report "Selective cardioneuroablation of the posteromedial left ganglionated plexus for drug-resistant swallow syncope with functional atrioventricular block" by Yoneda and colleagues,[1] investigators correctly examined the patient and indicated very selective CNA, which is the subject of this commentary.

The electrocardiogram (ECG) phenotype corresponding to swallowing syncope—sinus arrest or AV block—is decisive for the specific ablation strategy. If the clinical manifestation is sinus arrest, it is not clear how the AV node would respond to vagal irritation. In such a situation, both SA and AV node denervation is a reasonable choice, as vagal hyperactivity is frequently shared. Although standalone ablation of the superior right ganglionated plexus (GP) (SRGP) has a significant impact on the AV node, complete AV nodal denervation in many patients is only achievable by additional ablation of the posteromedial left GP (PMLGP).[2] Nevertheless, SRGP ablation alone can be clinically successful, even with ablation limited to the right atrial aspect of the superior interatrial septum, as we demonstrated previously.[3]

If the clinical manifestation is AV block, it is possible to target the PMLGP only. This approach has some advantages, but also disadvantages. A clear advantage is the absence of sinus rhythm (SR) acceleration that may be responsible for postprocedural symptomatic sinus tachycardia. Another advantage may be shorter procedural and radiofrequency time. The disadvantage is an increased risk of incomplete denervation and/or reinnervation of the AV node. Certainly, the vagal modulation of the SA node is not significantly affected by this approach, given the dominant craniocaudal hierarchy of cardiac vagal innervation.

The procedural endpoint was the loss of AV nodal response to balloon esophageal dilatation. Since this response was not very intense at baseline, its disappearance was not a strong indicator of sufficient denervation of the AV node. If the authors had used extracardiac vagus nerve stimulation (ECVS),[4] they might have been surprised that the AV node would not be denervated after their lesion set. In our series with the systematic use of ECVS, complete denervation of the AV node after standalone PMLGP ablation was achieved in only 40% of patients (unpublished data). However, the ECVS method is not widely used because a dedicated neurostimulator is not commercially available. The authors used endocardial high-frequency stimulation (HFS) to localize PMLGP. Therefore, after the CNA, they could repeat HFS in the ablated region, which could bring some information about the CNA effects, but this was not reported. Nevertheless, endocardial HFS is known for its low sensitivity, specificity, and reproducibility, so even the disappearance of the vagal responses after ablation cannot be considered a reliable indicator of denervation.

In case of insufficient AV nodal denervation, the solution would be either to further expand the original ablation cluster targeting the PMLGP or to ablate the superior left GP or the Marshall tract GP, both of which significantly affect the vagal modulation of the AV node and, at the same time, have a negligible impact on the SA node. If even this strategy did not result in AV nodal denervation, it would be necessary to ablate the SRGP. This would already be associated with unwanted SR acceleration. In any case, achieving maximal

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ECVS-guided denervation of the AV node would certainly be a desirable goal. While such a procedural endpoint does not guarantee clinical success because reinnervation occurs in every patient, it is plausible to speculate that incomplete rather than complete procedural denervation is associated with a higher rate of late reinnervation and clinical failure.

Regardless of these "technical" concerns, the procedure was clinically successful, although late recurrence cannot be excluded, since the 11-month follow-up does not fully cover the period in which reinnervation with subsequent clinical manifestation can occur.

The authors of the case report correctly pointed out episodes of junctional rhythm during swallowing after the CNA, which were caused by the denervation of the AV node and missing denervation of the SA node. Although AV block was the predominant disorder at baseline, their Figure 2 ("breakfast" ECG) shows that during swallowing, slowing of instant SR from 82 to 72 beats per minute with a rapid return to baseline occurred concomitant to AV block. During the swallowing after the CNA, a similar slowing of the SR occurred with subsidiary accelerated junctional rhythm from the denervated AV node (their Supplemental Figure 2, "lunch" ECG). Theoretically, SR dynamics during swallowing may be more prolonged or pronounced after CNA, because preablation AV block caused hemodynamic deficit and subsequent counter-regulatory vagal withdrawal owing to the baroreflex. After CNA, this mechanism is absent in the setting of a junctional rhythm. Fortunately, in the described case, these episodes were short and asymptomatic.

The authors are to be commended for a highly educational case report that is important not only in demonstrating again the utility of CNA instead of pacemaker implant to treat recurrent swallowing syncope but also in showing that selective AV nodal denervation can be performed in the case of a dominant AV nodal phenotype and thereby avoid excessive SR acceleration, like in the recently published case report.[5] In our practice, we use a similar principle in selected patients with functional bradyarrhythmias and a dominant AV nodal phenotype, in whom we perform complete denervation of the AV node followed by gentle ablation of the SRGP so that this main vagal entry is partially modified with moderate SR acceleration. Such a strategy is especially appropriate for patients with a high resting SR and/or considerable SR acceleration after atropine administration. Of course, "titration" of ablation is purely empirical. The interrelationship between procedural SA nodal denervation, procedural SR acceleration, reinnervation rate, and clinical outcomes has not been comprehensively investigated so far. The ablation strategy must always be tailored to the individual patient and should balance the benefit and risks. The effort to achieve the perfect procedural endpoint is always associated with the risk of "overtreatment." In this context, we should keep in mind that although the reinnervation processes are considerably potent, some ablation effects remain irreversible. Therefore, resigning to the ideal procedural endpoint and waiting for clinical outcomes with the possibility of re-CNA can sometimes be a reasonable strategy.

A short terminological remark: Throughout the text of the commentary, we have adhered to the GP nomenclature that was used in the original case report. However, the SRGP indeed merges almost indistinguishably with the anterior right GP and this entire complex can be targeted from the right and left atrial aspect of the superior interatrial septum. Therefore, the unifying term of "superior paraseptal GP" seems more appropriate. Similarly, the term "inferior paraseptal GP" would be more appropriate than PMLGP, which is not purely "left-sided" but can be targeted from the left and right atrium and the proximal coronary sinus. Such a unifying nomenclature was proposed in a recently published consensus document that addresses the methodology and indication of CNA for the treatment of reflex syncope.[6]

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