LETTERS TO THE EDITOR

To the Editor—Atropine: Hero or villain in cardioneuroablation?

We want to congratulate the authors for their case report,[1] stressing their dedication to obtaining the best treatment for the patient; however, there was a relapse after supposed successful cardioneuroablation (CNA). Several reasons should be considered.

First, unfortunately, atropine at CNA beginning was the villain of this case. Unfortunately, the residual effect of atropine, a powerful vagal blocker, hampered the authors' work, masking denervation that was poor enough to allow rapid reinnervation. Nevertheless, diagnostic atropine testing may be a hero if made not less than 2 days before. Case atropine is accidentally administered at CNA beginning the procedure must not be performed.

Second, denervation confirmation during CNA by extracardiac vagal stimulation is essential.[2] Cardiac innervation is extensive, far beyond the ganglionated plexi (GP), and long-term denervation depends on the denervation validation.[3] CNA must be finished only after complete vagal response abolishment, and no CNA may be considered successful without this confirmation as the main endpoint. In case of residual vagal response, CNA must be expanded, ablating additional atrial fibrillation nests,[4–6] until complete abolishment. Residual innervation must be disclosed to the patient, as reinnervation/recurrence may occur.

Third, it is impossible to stimulate GP by high-frequency stimulation with 1–20 millivolts. It is likely a typing error. We have abandoned CNA controlled by high-frequency stimulation[4] because extracardiac vagal stimulation typically shows intense residual vagal response in these cases.

Fourth, high heart rate from the beginning suggests the undesirable residual atropine effect hampering the authors' work.

Finally, for lasting denervation, additional P-point and Waterston's groove ablation must always be performed.[6,7] A huge number of micro-GPs exist in these areas.

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Author's Reply—Atropine: Hero or villain in cardioneuroablation?

We thank Drs Pachon for their interest in our recent report. Collaboration is critical in novel procedures.

The comment "atropine at CNA beginning was the villain" is unclear; there was no "rapid innervation." Rather, we objectively demonstrated persistent denervation. Fundamentally, an interesting observation of our report is not the recurrence itself, but the nature of the recurrence. Heart rate (HR) and HR variability slowly normalizing over an extended time course does not suggest a simple procedural failure, but perhaps that more complex physiology is at play.

In this early stage, no cardioneuroablation (CNA) protocols have garnered sufficient evidence for widespread adoption. We recognize a school of thought advocating for earlier procedural atropine administration, as acknowledged in our report. However, during the procedure, the patient's HR drifted back down to the upper 60 beats per minute range, near the baseline in the upper 50s. As such, both the subsequent 36% HR increase produced by radiofrequency delivery and the blunted HR response to postablation atropine remain reliable indicators of efficacy. Further, our lab has since generated unpublished data from a repeat atropine challenge in this same patient 10 months later, in which no HR increase could be provoked. It is not clear based on available data how earlier atropine administration would have changed the localization or ablation of ganglionated plexi.

"Abandonment" of high-frequency stimulation has not been prevalent, less so at the time of this procedure early in 2021, and labs that exclude high-frequency stimulation generally do so in favor of an electrogram-only approach, rather than replacing it with extracardiac vagal stimulation, as implied.[1–3] We are interested in the potential of extracardiac vagal stimulation to optimize denervation assessment; however, its incorporation in mainstream CNA workflows has been, as Drs Pachon cite, quite limited.

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In addition, the typographical error has been corrected, and the anatomic sites in question were indeed covered by the initial lesion set.

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