Reinnervation after cardioneuroablation: When on the run for best intraprocedural endpoints, be aware of possible ablation overdose

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“The heart is not a slave and can’t be manacled or forced to behave.”

Adam Mickiewicz

Treatment of recurrent vasovagal syncope (VVS) is challenging. A new promising method called cardioneuroablation (CNA), or neuromodulation, brought a new hope for this group of patients.1–3 By attenuation of parasympathetic tone using classic radiofrequency catheter ablation near the ganglionated plexi (GP), CNA can lead to very rapid symptom relief, even in some severe forms of VVS.

Each intervention in cardiology requires some periprocedural endpoints that indicate to performing physicians if they are done with the case, or if perhaps there is a need of, for example, additional lesions or improvement of any procedural parameters. This applies also to CNA. Because lesion sets around GPs obviously cannot be extended to infinity, some periprocedural parameters, mainly related with acute responses in heart rate (HR) during radiofrequency catheter ablation or high-frequency stimulation are carefully observed and serve as indicators for long-term clinical success. However, as with each test performed in medicine, these assessments have their limitations.

In this issue of HeartRhythm Case Reports Thurber and colleagues4 show a follow-up failure of initially effective CNA in a patient with VVS. After initial success of the procedure, the gradual decrease in the CNA-induced attenuation of vagal tone, called parasympathetic reinnervation, was documented by implantable loop recorder recordings. These tracings showed the values of ventricular rate and HR variability, which returned to preprocedural values during the course of follow-up, up to the recurrence of syncopal event.

This leads to the question whether the initial approach of CNA could have been somehow altered.

The main problem with intraprocedural assessment of CNA efficacy is which method is used to do so. Thurber and colleagues used 2 parameters—HR acceleration after the procedure and lack of HR increase following atropine injection after the procedure. These parameters suggest that vagal response was completely abolished. Unfortunately, none of these parameters is 100% sensitive and specific to be sure that full vagal denervation was achieved. The only currently available reliable method to accurately assess these effects is extracardiac vagal stimulation (ECVS), routinely used in some laboratories. In our experience even very significant increase of HR following ablation of 1 or more GP areas is not always associated with full vagal denervation because ECVS still can provoke sinus arrest or atrioventricular block in some patients. It could have been the case in the presented patient—although atropine and HR suggested full vagal denervation, it might have not been necessarily 100% true. In addition, baseline atropine test was performed at the beginning of the procedure, which further blunted the HR response after postprocedural atropine injection. This is the reason why baseline atropine test is usually performed at least 1–2 days before the CNA procedure.

Although ECVS is a very elegant and concrete endpoint of the procedure, we still do not know whether full vagal denervation, confirmed by ECVS, is absolutely needed in all patients in order to prevent syncope recurrences. Preliminary data in literature suggest that this is the case; however, there are no prospective randomized trials comparing the outcome between patients in whom ECVS was used and those in whom only HR and atropine effects were measured. In addition, a study comparing the outcome of patients with full vs partial vagal denervation, both assessed by ECVS, is warranted.

Another issue should be raised following the report from Thurber and colleagues. Clearly, initially effective CNA in this patient simultaneously caused poorly tolerated sinus tachycardia. This complication affects around 5%–10% of patients undergoing can, and long-term impact of such
adverse event remains unknown. The beneficial regulatory effects of parasympathetic activity on the human heart have been well documented. The long-term effects of persistent increase in HR and parasympathetic denervation remain unknown. In order to effectively manage post-CNA increased sinus rate, beta blockers or $I_h$ channel blockers may be prescribed and may be effective, although at the cost of the need for taking permanent medication for an unknown period of time—in some extreme situations lifelong pharmacological control may be required.

The authors should be commended on their efforts of careful elevation of symptoms in their patient. Still, the question remains, what to offer her in the future? Clearly, any effective CNA causes poorly tolerated sinus tachycardia in this patient, and any future “redo-CNA” will probably cause recurrence of tachycardia-related symptoms. This should prompt the discussion on the proper “dosage” of CNA in patients with VVS.

In summary, this very educative case report shows us how suboptimal CNA may lead to syncope recurrence and how implantable loop recorder recording may explain this procedural failure—cardiac parasympathetic reinnervation depicted by HR and HR variability trends.

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