Ultrasound-guided extracardiac vagal stimulation—
New approach for visualization of the vagus nerve
during cardioneuroablation

Roman Piotrowski, MD, PhD, Anna Zuk, MD, Jakub Baran, MD, PhD,
Agnieszka Sikorska, MD, PhD, Tomasz Krynski, MD, Piotr Kulakowski, MD, PhD

From the Department of Cardiology, Centre of Postgraduate Medical Education, Grochowski Hospital,
Warsaw, Poland.

BACKGROUND  Fluoroscopy-guided extracardiac vagal stimulation (ECVS) from the internal right and left jugular veins (RIJV and LIJV) is routinely used to document vagal response (sinus arrest and/or atrioventricular block) during cardioneuroablation. Ultrasound-guided ECVS allows direct visualization and selective stimulation of the vagus nerve (VN).

OBJECTIVES  The objectives of this study were to assess the feasibility of ultrasound-guided ECVS and to compare it with fluoroscopy-guided ECVS.

METHODS  The study group consisted of 48 patients (25 men [52%]; mean age 38 ± 15 years) in whom fluoroscopy-guided ECVS and ultrasound-guided ECVS were performed. For fluoroscopy-guided ECVS, a pacing electrode was introduced into the RIJV and into the LIJV under fluoroscopic guidance. For ultrasound-guided ECVS, the VN and electrode were visualized using ultrasonography. Partial vagal response was defined as induction of sinus arrest or atrioventricular block, whereas full vagal response was defined as induction of both.

RESULTS  ECVS was performed in all patients from the RIJV and in 45 from the LIJV. Visualization of the VN using ultrasound was possible in 44 patients (92%). During ECVS from the RIJV, partial vagal response was obtained in 39 (81%) using fluoroscopy-guided ECVS vs 45 (94%) using ultrasound-guided ECVS (not significant) whereas full vagal response was obtained in 27 patients (56%) using fluoroscopy-guided ECVS vs 40 (83%) using ultrasound-guided ECVS (P = 0.0071). For ECVS from the LIJV, partial vagal response was achieved in 40 (89%) vs 44 (98%) patients (not significant) whereas full vagal response was achieved in 30 (67%) vs 40 (89%) patients (P = 0.021) (fluoroscopy-guided ECVS vs ultrasound-guided ECVS, respectively).

CONCLUSION  Ultrasound-guided ECVS is feasible and full vagal response is achieved significantly more frequently than using fluoroscopy-guided ECVS.

KEYWORDS  Cardioneuroablation; Extracardiac vagal stimulation; Fluoroscopy-guided; Ganglionated plexi; Ultrasound-guided; Vagal response; Vagus nerve

Introduction
Cardioneuroablation (CNA) is a promising method for the treatment of cardioinhibitory vasovagal syncope (VVS) or functional atrioventricular (AV) block (AVB). Both VVS and functional AVB are caused by the hyperactivity of the parasympathetic part of the autonomic nervous system, and ablation of ganglionated plexi, known as CNA, may abolish hypervagotonia and prevent syncope and need for pacemaker implantation. The optimal technique for performing CNA has not yet been established and operators use various approaches.

One of the unresolved issues is what acute end point of the procedure is optimal. It seems that extracardiac vagal stimulation (ECVS) may serve as a tool to assess acute vagal denervation. ECVS is performed from the right and left internal jugular veins (RIJV and LIJV) to demonstrate vagal response such as sinus arrest and AVB at baseline and lack of ECVS effects on cardiac rhythm after successful total vagal denervation.

The recommended technique for ECVS is introducing a pacing electrode under fluoroscopic control into the RIJV and LIJV up to the level of the jugular foramen. Partial vagal response was defined as induction of sinus arrest or atrioventricular block, whereas full vagal response was defined as induction of both.

Funding Sources: The authors have no funding sources to disclose.

Disclosures: The authors have no conflicts of interest to disclose.

Address reprint requests and correspondence: Dr Jakub Baran, Department of Cardiology, Centre of Postgraduate Medical Education, Grochowski Hospital, Grenadierow 51/59 St, 04-073 Warsaw, Poland. E-mail address: jakub.baran1111@gmail.com.
result is due to already very low vagal activity or more probably due to the lack of vagus nerve capture because of anatomical variabilities. These limitations of fluoroscopy-guided ECVS may be eliminated by the use of ultrasound-guided ECVS. Ultrasound-guided approach may be an interesting option because it allows direct visualization of the vagus nerve and placing the pacing electrode under eye control directly adjacent to the vagus nerve, which enables selective vagal stimulation. In the literature, there is only 1 case report describing the potential benefit of using ultrasound during CNA.11

The objectives of this study were to assess the feasibility of ultrasound-guided ECVS performed directly before CNA and to compare vagal response using ultrasound-guided ECVS vs fluoroscopy-guided ECVS.

Methods

Study population
The study group consisted of 48 consecutive patients (25 [52%] men; mean age 38 ± 15 years) who underwent CNA in our center between December 2020 and October 2021. The inclusion criteria were as follows: (1) VVS (cardioinhibitory or mixed) or symptomatic bradycardia and (2) positive response to atropine challenge, meaning increase in sinus rate ≥ 30%, measured 2 minutes after 2 mg atropine injection or 0.04 mg of atropine per kg of body weight if the patient weighed < 50 kg. Patients gave written informed consent to undergo CNA and to use their demographic and clinical data for research purposes. The study protocol was approved by the Local Ethics Committee of the Centre of Postgraduate Medical Education, Warsaw, Poland (No. 108/2021).

ECVS
The protocol of ECVS used in our laboratory has been described previously.10,12 During ECVS, the vagus nerve was captured from the decapolar steerable electrode placed in the RIJV or LIJV up to the level of the jugular foramen. Stimulation was delivered from the distal and the third pole of the electrode using pulsed electric field with a pulse amplitude of 1 V/kg of body weight up to 70 V, 50 μs width, and 30 Hz frequency, delivered over 5–8 seconds (neurostimulator designed by Pachon JCM, São Paulo, Brazil). An extremely short pulse duration with the current limitation is used for preventing tissue lesion. The device settings were established by the inventor, and the recommended parameter of ECVS guarantees reproduction and safety even in obese patients.10

According to our protocol, first ECVS was performed from the RIJV and second from the LIJV. Fluoroscopy-guided ECVS was always performed first, followed by ultrasound (USG)-guided ECVS.

In the fluoroscopy-guided ECVS approach, a decapolar electrode was introduced up to the jugular foramen and the optimal site for pacing (reproducible sinus arrest and/or AVB) was obtained under fluoroscopic guidance (Figure 1). In the ultrasound-guided ECVS approach, the electrode was initially introduced under fluoroscopic control up to the middle of the neck; however, from this point, USG was used for optimal positioning of the electrode and the vagus nerve was visualized in the long- and short-axis views (ACUSON SC2000 ultrasound MACHINE, Siemens, Erlangen, Germany) with a linear transducer probe, at a depth of ~3.5 cm. High-resolution smart-part transducers with frequencies >10 MHz were used. Examinations were performed in the supine position with head extension. The probe was placed in the transverse plane several centimeters above the medial edge of the sternocleidomastoid muscle. The cervical 10–15 cm segment of the vagus nerve is usually visible in the caudocranial direction on the neck. First, the nerve and its course were identified on the first quick overview and scanned in the axial position. Next, the vagus nerve was scanned in the transverse plane from the carotid bifurcation to the level of the clavicle in ultrasound B-mode imaging and the place where the nerve was in the closest distance to

Figure 1  Position of the pacing electrode during extracardiac vagal stimulation from the (A) right interior jugular vein and (B) left interior jugular vein.
the internal jugular vein (IJV) was chosen for ECVS (Figure 2 and Online Supplemental Video 1).

The typical response to ECVS is a massive vagal response during high-frequency stimulation, resulting in sinus arrest and complete AVB, with the latter demonstrated during atrial pacing from the coronary sinus (Figure 3). In the present study, 2 types of vagal response were analyzed: partial—induction of sinus arrest or AVB; and full—induction of both. For the present analysis, we compared only baseline fluoroscopy-guided ECVS with baseline ultrasound-guided ECVS because usually there is no vagal response after successful CNA.

The ECVS settings were the same for all ECVS attempts in an individual patient. First, ECVS was performed during sinus rhythm, and when no P waves were visible, sinus arrest was identified. If ECVS did not cause sinus arrest but there was no AV conduction during sinus rhythm, AVB without sinus arrest (partial response) was identified. Next, ECVS was performed during atrial pacing from the CS catheter, and when no AV conduction was observed, AVB was identified.

Sinus arrest was defined as lack of P waves during ECVS, and AVB was defined as no AV conduction during sinus rhythm and/or atrial pacing during ECVS. The minimal duration of vagal stimulation–induced sinus arrest that was considered positive was 3 seconds. A similar cutoff was used to assess the minimal duration of AVB.
Table 1  Demographic and clinical characteristics of the study group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>48</td>
</tr>
<tr>
<td>Age (y)</td>
<td>38 ± 15</td>
</tr>
<tr>
<td>Male sex</td>
<td>25 (52)</td>
</tr>
<tr>
<td>No. of syncopeces per year</td>
<td>4 ± 3</td>
</tr>
<tr>
<td>No. of presyncopeces per year</td>
<td>6 ± 4</td>
</tr>
<tr>
<td>VVS cardiodepression</td>
<td>19 (40)</td>
</tr>
<tr>
<td>VVS mixed</td>
<td>4 (8)</td>
</tr>
<tr>
<td>AVB</td>
<td>12 (25)</td>
</tr>
<tr>
<td>Sinus bradycardia</td>
<td>13 (27)</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD or n (%).

AVB = atrioventricular block; VVS = vasovagal syncope.

All procedures of CNA with ECVS were conducted with general anesthesia with total muscle relaxation. The details of our protocol of CNA have been published elsewhere.

**Statistical analysis**
The results are presented as mean ± SD or number and percentage. Numerical variables were compared using the Fisher test and Student t test, where appropriate. A P value of <.05 was considered significant.

**Results**
The demographic and clinical characteristics of the studied population are presented in Table 1.

In all 48 patients (100%), ECVS was performed from the RIJV and in 45 (94%) from the LIJV. In 3 patients (6%), ECVS was not performed from the LIJV because of difficulties in vessel cannulation due to an acute angle between the LIJV and the subclavian vein. In the ultrasound-guided ECVS method, perfect visualization of the vagus nerve was possible in 44 patients (92%) and took <1 minute whereas in 4 patients (8%) 3 images of the RIJV [6%] and 1 image of the LIJV [2%] the optimal ultrasound images were difficult to obtain because of anatomical difficulties (short and thick neck) and the decapolar pacing catheter was placed in the most probable place of the course of the vagus nerve.

In the case of RIJV, the mean duration of sinus arrest was 8 ± 6 seconds ranging from 3 to 33 seconds under fluoroscopic guidance and 7 ± 3 seconds ranging from 3 to 11 seconds under ultrasound guidance (not significant) while the mean duration of AVB was 8 ± 4 ranging from 3 to 23 seconds under fluoroscopic guidance and 8 ± 3 seconds ranging from 3 to 13 seconds under ultrasound guidance (NS). In the case of LIJV, the mean duration of sinus arrest was 7 ± 3 ranging from 3 to 17 seconds under fluoroscopic guidance and 7 ± 3 ranging from 3 to 17 seconds under ultrasound guidance (NS) while the mean duration of AVB was 8 ± 5 seconds ranging from 3 to 13 seconds under fluoroscopic guidance and 8 ± 3 seconds ranging from 3 to 13 seconds under ultrasound guidance (NS).

Partial vagal response during pacing from the RIJV was obtained in 39 patients (81%) in the fluoroscopy-guided ECVS group vs 45 patients (94%) in the ultrasound-guided ECVS group (NS). Similar results were obtained when pacing from the LIJV: 40 patients (89%) vs 44 patients (98%) had partial vagal response, respectively (NS). When analyzing the components of partial vagal response, sinus arrest was induced in 42 patients (87%) when pacing from the RIJV and in 41 patients (91%) when pacing from the LIJV whereas AVB was induced in 46 (96%) and 43 (96%) patients, respectively (NS) (Figure 4).

Full vagal response, when pacing from the RIJV, was achieved in 27 patients (56%) in the fluoroscopy-guided ECVS group vs 40 patients (89%) in the ultrasound-guided ECVS group (P = .0071). Similar results were obtained when pacing from the LIJV: 30 patients (67%) vs 40 patients (89%) had full vagal response, respectively (P = .021) (Figure 4).

In summary, in 42 patients any or full vagal response was obtained using both fluoroscopy-guided ECVS and ultrasound-guided ECVS, in 5 patients using only ultrasound-guided ECVS, and in 1 patient using only fluoroscopy-guided ECVS. In 1 patient, vagal response was not obtained using both fluoroscopy-guided ECVS and ultrasound-guided ECVS.

According to analysis the type of vagal response (partial vs complete), the mean follow-up duration was 10 ± 3 months (range 5–13 months). During this period, 3 patients experienced syncpe recurrence. The first patient had full vagal response using both fluoroscopy-guided ECVS and ultrasound-guided ECVS. The second patient had full vagal response in the RIJV using fluoroscopy-guided ECVS and ultrasound-guided ECVS, whereas partial vagal response was observed in the LIJV using both approaches. The third patient had no vagal response in the RIJV using both approaches, and full vagal response was observed in the LIJV using fluoroscopy-guided ECVS and ultrasound-guided ECVS. Because the number of patients with syncpe recurrences was low and the duration of follow-up was rather short, it was not possible to assess the value of partial vs complete vagal response in predicting syncpe recurrences.

**Discussion**
This study showed that (1) good-quality imaging of the vagus nerve using USG is feasible in the vast majority of patients and (2) ultrasound-guided placement of the pacing electrode to perform ECVS is at least as good as standard fluoroscopy-guided ECVS in inducing sinus arrest or AVB and probably better to evoke full vagal response.

Over the last years, high-resolution USG has become a basic tool for the visualization of the peripheral nerves. It enables the morphological analysis of the nerves better and sometimes gives information that is not seen in magnetic resonance imaging. The commonly used parameters for peripheral nerve description are cross-sectional area on axial scans, nerve width (medial to lateral diameter), and thickness (anterior to posterior diameter). Therefore, it is not surprising that vascular USG may be used for vagus nerve...
visualization; however, its use to guide ECVS was mentioned in only 1 case report.\textsuperscript{11}

The vagus nerve is a round, thin structure of honeycomb-like appearance that is centrally hypoechoic and peripherally hyperechoic. The nerve is located between the common carotid artery and the IJV in the carotid sheath. Visualization of the vagus nerve may be difficult in patients with a short and large neck as it was the case in 4 of our 48 patients. USG is an accepted method for visualization of vessels and the surrounding tissue\textsuperscript{16}; thus, both the IJV and the vagus nerve may be adequately imaged.

In our study, the vagus nerve was identified as a hypoechoic structure surrounded by a hyperechoic border like a “honeycomb” appearance. When it was not obvious if the structure was a nerve, color Doppler was used to distinguish it from the small vessel. The vagus nerve was paced when it was in the closest place of the IJV next to the wall of the vein, stretching the vein’s wall.

Usually, the vagus nerve travels along the IJV in the close proximity to the vessel wall. When the course of the IJV is not typical, additional USG views are necessary to localize the nerve. This was the case in 2 of 4 patients in whom the vagus nerve had slight course variation and the distance between the nerve and the vein wall was probably too long to achieve the optimal ECVS effect\textsuperscript{18–20} and was probably the main reason for not achieving satisfactory vagal response in some patients.

USG may offer additional advantages over fluoroscopy. For example, in our cohort, in 3 patients there was a problem with introducing the decapolar catheter into the LIJV using fluoroscopy because the guidewire and catheter always tended to enter the external jugular vein. USG helped to manipulate the guidewire and cannulate proper vessel (Figure 5 and Online Supplemental Video 2).

Whether ultrasound-guided ECVS is associated with lower fluoroscopy time and radiation dose than fluoroscopy-guided ECVS is not known. Perhaps it is, because in patients

![Figure 4](image-url)  
**Figure 4** Comparison between fluoroscopy-guided extracardiac vagal stimulation (F-ECVS) and ultrasound-guided ECVS (USG-ECVS) for inducing vagal response from the right and left jugular veins (RIJV and LIJV). Any vagal response = sinus arrest or atrioventricular block; full vagal response = sinus arrest and atrioventricular block; NS = not significant.

![Figure 5](image-url)  
**Figure 5** Ultrasound image during left inferior jugular vein cannulation showing that the guidewire first introduced into the left external jugular vein (A) and after ultrasound-guided repositioning introduced into the left internal jugular vein (B).
in whom multiple attempts of fluoroscopy-guided repositioning of the pacing electrode were necessary to achieve vagal response, this could have been achieved more precisely and without fluoroscopy if USG would have been used. In order to demonstrate whether there are differences between fluoroscopy-guided ECVS and ultrasound-guided ECVS in fluoroscopy duration, a randomized study is needed.

The main limitation of the present study is lack of randomization; thus, the question whether ultrasound-guided ECVS may replace fluoroscopy-guided ECVS or may become an additive tool for vagus nerve imaging when the standard approach with fluoroscopy fails has not yet been answered. Another limitation is the lack of the test of the threshold in an individual patient; however, as we mentioned above, the device settings were established before by the inventor and the recommended parameter of ECVS guarantees reproducibility; thus, the question whether ultrasound-guided ECVS can replace fluoroscopy if USG would have been used. In order to demonstrate whether there are differences between fluoroscopy-guided ECVS and ultrasound-guided ECVS in fluoroscopy duration, a randomized study is needed.

Conclusion Ultrasound-guided ECVS is feasible and full vagal response is achieved significantly more frequently than using standard fluoroscopy-guided ECVS.

Appendix Supplementary data
Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2022.04.014.

References