CASE REPORT

A new and simple technique for vagal ganglia ablation in a patient with functional atrioventricular block: Electroanatomical approach

Fonksiyonel atriyoventriküler bloklu bir hastada vagal gangliyonların ablasyonu için yeni ve basit bir teknik: Elektroanatomik yaklaşım

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Summary– Increased parasympathetic tone may cause symptomatic functional atrioventricular block (AVB) and necessitate pacemaker implantation. In these patients, where there is no structural damage to the conduction system, removal of the vagal activity using radiofrequency ablation seems to be a theoretically rational approach. Several methods have been used to determine suitable areas for vagal ganglia ablation. The aim of this report was to describe a new method to detect parasympathetic innervation sites without the need to use additional equipment or extend procedure time. A 51-year-old man was referred to the clinic for implantation of a permanent pacemaker because of symptomatic second-degree AVB and recurrent syncope. The functional nature of the AVB and a supra-Hisian location were verified with standard electrocardiography, Holter recordings, atropine sulfate test, and a standard electrophysiological study. Using conventional recordings, the electrograms were divided into 3 subgroups and sites demonstrating a fractionated pattern were targeted. All of the fractionated electrogram sites considered suitable for usual ganglion settlement were ablated. Biatrial ablation was initiated from the left atrial side. During left atrial ablation, the intrinsic basic cycle length of sinus node accelerated to 800 milliseconds despite AVB persistence. Subsequently, 1:1 atrioventricular conduction was achieved when ablation was applied around the coronary sinus ostium. The patient was completely asymptomatic, experiencing no episodes of dizziness or syncope, and was taking no medications at the end of 9 months of follow-up. In conclusion, electroanatomically guided vagal ganglia ablation may be a good alternative to pacemaker implantation in well-selected patients with functional AVB.

Özet– Artan parasempatik tonüs, semptomlu fonksiyonel atriyoventriküler blok (AVB) gelişmesine ve kalıcı kalp pili yerleştirilme gereksinimine neden olabilir. İletim sisteminde yapısal hasarın olmadığı bu grup hastalarda radyofrekans ablasyon ile vagal aktivitenin ortadan kaldırılması teorik olarak akılcı bir yaklaşım gibi gözükmektedir. Şimdiye kadar vagal gangliyonların ablasyonu için uygun alanın saptanmasında farklı yöntemler kullanılmıştır. Biz ek donanım gerektirmeden ve işlem süresini uzatmaksızın parasempatik innervasyon alanlarını belirleyen yeni bir yöntem tanımlamayı amaçladık. Elli bir yaşında erkek hasta semptomlu ikinci derece AVB ve tekrarlayan senkop nedeni ile kalıcı kalp pili takılması için merkezimize yönlendirildi. AVB'nin fonksiyonelliği ve His-üstü yerleşimi standart EKG, Holter kayıtları ve atropin sülfat testi ve standart elektrofizyolojik çalışma ile doğrulandı. Geleneksel kayıtlar kullanılarak elektrogramlar 3 alt gruba bölündü ve fraksiyonlu patern gösteren alanlar hedeflendi. Gangliyon yerleşimi için uygun alanlardaki tüm fraksiyonlu elektrogramlar ablate edildi. İşleme sol atriyumdan başlandı ve sağ atriyum ablasyonuyla devam edildi. Sol atriyum ablasyonu esnasında sinüs düğümünün hızı 800 milisaniyeye çıkmasına rağmen AVB devam etti. Koroner sinüs ağzının etrafındaki ablasyon ile bire bir atriyoventriküler iletim sağlandı. Dokuz aylık ilaçsız takip sonunda hasta tümü ile semptomsuzdu, baş dönmesi ve senkop atağı yoktu. Elektroanatomik yaklaşımla vagal gangliyonların ablasyonu fonksiyonel AVB'li seçilmiş hastalarda kalp pili takılmasına iyi bir alternatif olabilir.

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Some forms of bradyarrhythmia, such as sinus node dysfunction in young patients, functional atrioventricular block (AVB), carotid sinus syndrome, and neurally mediated reflex syncope, may be related to inadvertently increased parasympathetic tone rather than any structural disease or a rare ventricular nodal pathway interfering with atrioventricular conduction.[1,2] Unlike the sympathetic system, the postganglionic neuronal body of the parasympathetic system is located on or near the target organ.[3] Therefore, the postsynaptic parasympathetic neurons are either very close to or embedded in the heart, and are also known as vagal ganglia, whereas the neural body of the postganglionic sympathetic and sensory neurons is located far from the heart. Theoretically, if the localization of these vagal ganglia could be precisely detected, radiofrequency catheter ablation in this area could provide a permanent damage of parasympathetic effect, whereas the sympathetic and sensory systems would not be permanently affected because they only have postganglionic nerve fibers in this region, which can be repaired through the axonal regeneration process in the long term.[3–6] Despite this theoretical background, determining the exact location of vagal ganglia during an electrophysiological study (EPS) is not always possible. Three different approaches have been used to identify vagal ganglia in the atria: (1) high frequency stimulation (HFS), (2) spectral analysis (SA), and (3) anatomical approach (AA).[7] All of these methods have some limitations and to compensate for these limitations, an alternative modality is needed.

In the present case, we used a combination of electrogram characteristics and anatomical prediction and called it electroanatomically guided ablation. Described in the present case is use of electroanatomically guided vagal ganglia ablation in a patient with second-degree AVB due to increased vagal tone and the potential therapeutic role of this technique.

CASE REPORT

Patient history

A 51-year-old man was referred to the clinic for implantation of a permanent pacemaker due to symptomatic second-degree AVB. For 4 months, the patient had experienced recurrent episodes of dizziness and syncope. Repeated Holter recordings indicated variable degree AVB with a minimum heart rate of 26 bpm (Fig. 1). There was no 1:1 atrioventricular conduction during 72 hours of recording. Mobitz type I and 2:1 AVB were detected on his admission electrocardiograms (ECGs) (Fig. 2). The AVB gradually disappeared following an atropine sulfate infusion (0.04 mg/kg). During stage 2 of a treadmill exercise test, his ventricular rate suddenly increased and stable 1:1 atrioventricular conduction with a rate of 120 bpm was achieved. There was no chronotropic incompetence. When all of these findings were evaluated together, the AVB was considered to be functional; therefore, vagal ganglia ablation was planned. The patient provided written informed consent for the ablation procedure. The procedure was performed with the patient in a non-sedated state.

Abbreviations:

AA	*Anatomical approach*
AVB	*Atrioventricular block*
ECG	*Electrocardiography*
EPS	*Electrophysiological study*
HAFE	*High-amplitude fractionated electrogram*
HFS	*High frequency stimulation*
LAFE	*Low-amplitude fractionated electrogram*
SA	*Spectral analysis*

Pre-procedural electrophysiological study

A standard electrophysiology catheter was placed via venous puncture into the right atrium, right ventricle, and His-bundle region. Supra-Hisian level AVB was

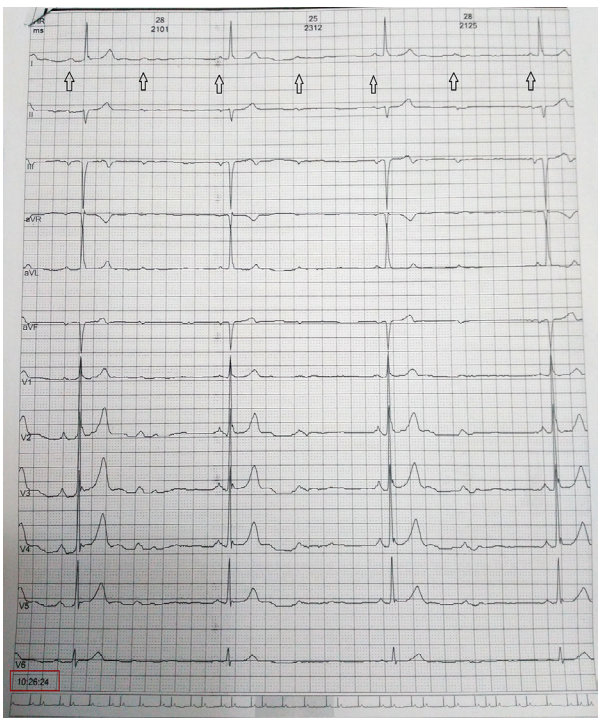

Figure 1. A Holter monitor strip demonstrating 2:1 atrioventricular block. Arrows indicate p waves. Please note that the time of the event is 10:26 am.

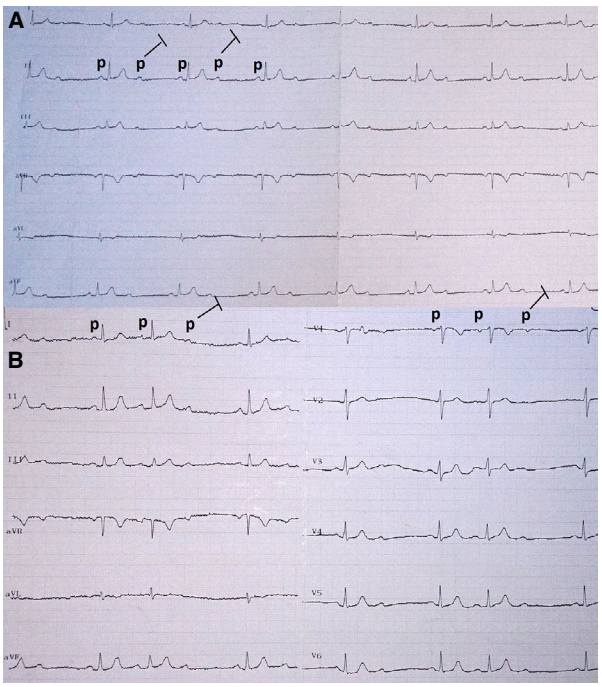

Figure 2. **(A)** The patient's 12-lead electrocardiogram (ECG) from the initial consultation to consider pacemaker implantation demonstrates 2:1 atrioventricular block (AVB); **(B)** A12-lead ECG recorded during hospitalization shows Mobitz type I AVB. P indicates p waves.

confirmed in a baseline recording. The intrinsic basic cycle length was 950 milliseconds. At several different pacing rates, the longest sinus node recovery time and corrected sinus node recovery time were determined to be 1350 milliseconds and 400 milliseconds, respectively, and within the normal range. Atrial pacing at a cycle length of 600 milliseconds generated 2:1 atrioventricular conduction.

Mapping of vagal ganglia

Using a 4-mm, open-tip, irrigated radiofrequency ablation catheter (FlexAbility; St. Jude Medical, St. Paul, MN, USA), the geometry of both atria was drawn with a 3-dimensional electroanatomical mapping system (EnSite NavX; St. Jude Medical, St. Paul, MN, USA). Bipolar endocardial electrograms were displayed at filter settings of 30–500 Hz and 300–500 Hz (for EPS and online spectral analysis, respectively) and measured at a sweep speed of 400 mm/second. All of the recordings were stored on an optical disk (EP-Workmate Recording System; St. Jude Medical, St. Paul, MN, USA).

The electrograms were divided into subgroups as previously defined by Lellouche et al.:[8] (1) Normal electrogram, which demonstrates fewer than 4 deflections, (2) low-amplitude fractionated electrogram (LAFE) with 4 or more deflections and an amplitude of less than 0.7 mV, and (3) high-amplitude fractionated electrogram (HAFE), which reveals 4 or more deflections and an amplitude of 0.7 mV or more. Schematic views of the electrograms are provided in Figure 3. If the fractionated electrogram (HAFE or LAFE) sites were in a region compatible with the probable location of the vagal ganglia as previously defined (Fig. 3), these sites were tagged as ablation targets. Other sites demonstrating a LAFE pattern were accepted as scar tissue and excluded from the assessment. There was no HAFE electrogram pattern

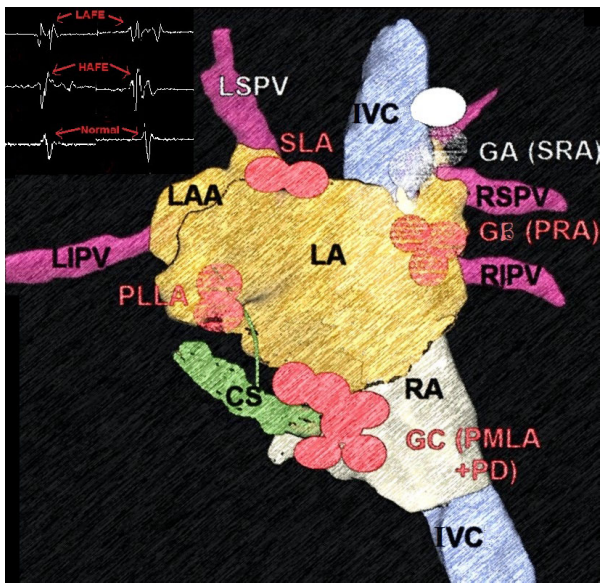

Figure 3. The comparative schematic view of vagal ganglia from our previous work was used with the permission of the editor-in-chief.[9] Pachon et al.[10] re-named 3 fat pads in their study. Ganglia A, B, and C correspond to the superior vena cava-aorta fat pad, right pulmonary vein fat pad, and inferior vena cava-left atrium fat pad, respectively. Please note the similar anatomical localization of the superior vena cava-aorta fat pad and the superior right atrial vagal ganglion, the right pulmonary vein fat pad and the posterior right atrial vagal ganglion, and the inferior vena cava-left atrium fat pad and the posteromedial left atrial vagal ganglion. CS: Coronary sinus; GA: Ganglion A; GB: Ganglion B; GC: Ganglion C; IVC: Inferior vena cava; LA: Left atrium; LAA: Left atrial appendage; LIPV: Left inferior pulmonary vein; LSPV: Left superior pulmonary vein; PD: Posterior right atrial vagal ganglion; PMLA: Posteromedial left atrial vagal ganglion; PLLA: Posterolateral left atrial vagal ganglion; PRA: Posterior right atrial vagal ganglion; RA: Right atrium; RIPV: Right inferior pulmonary vein; RSPV: Right superior pulmonary vein; SLA: Superior left atrial vagal ganglion; SRA: Superior right atrial vagal ganglion; SVC: Superior vena cava.

in any site that was incompatible with the location of the vagal ganglia.

Ablation of vagal ganglia

The ablation endpoint was the almost complete elimination of atrial electrical potentials (<0.1 mV) in all targeted sites. Radiofrequency current was delivered point by point at a power of 35 W (maximum 40 W) and applied in temperature-controlled mode. The target temperature was 40°C, with a cooling rate of 18 mL/minute. Continuous flow during mapping was 2 mL/minute. The ablation procedure was first performed through the left atrium, targeting the superior left atrial, posterolateral left atrial, and posteromedial left atrial vagal ganglia from the left side, and the superior right atrial and posterior right atrial vagal ganglia from the right side (Fig. 4). Then, the procedure continued with ablation of the superior right atrial and posterior right atrial vagal ganglia from the superior side and ablation of the posterior descending vagal ganglia from the inferior side (Fig. 4). During left atrial ablation, the intrinsic basic cycle length of sinus node accelerated to 800 milliseconds despite the persistence of AVB (Fig. 4). Subsequently, 1:1 atrioventricular conduction was achieved when ablation was applied around the coronary sinus ostium (Fig. 4).

Post-procedural electrophysiological study

The 1:1 atrioventricular conduction continued during a 30-minute waiting period. The atrioventricular Wenckebach point was reached at 270 milliseconds.

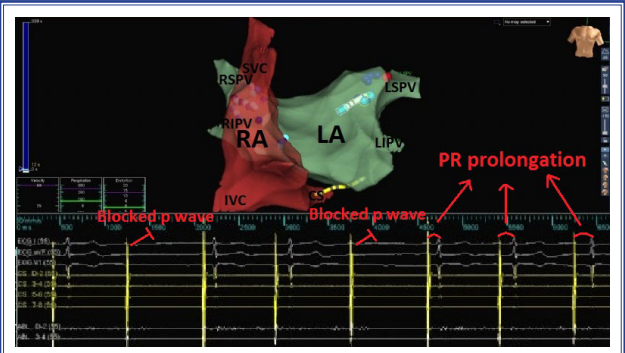

Figure 4. A 3-dimensional anatomical map (Ensite NavX; St. Jude Medical, St. Paul, MN, USA) of the left and right atria in an anteroposterior view during left atrial ablation. Spheres indicate ablation lesions. Red lines demonstrate blocked p waves and PR prolongation at the bottom of the figure. CS: Coronary sinus; IVC: Inferior vena cava; LA: Left atrium; LIPV: Left inferior pulmonary vein; LSPV: Left superior pulmonary vein; RA: Right atrium; RIPV: Right inferior pulmonary vein; RSPV: Right superior pulmonary vein; SVC: Superior vena.

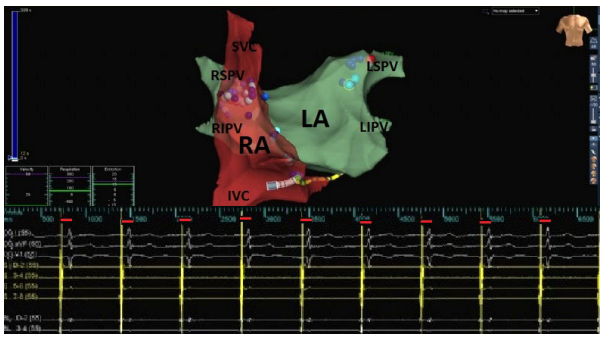

Figure 5. A 3-dimensional anatomical map (Ensite NavX; St. Jude Medical, St. Paul, MN, USA) of the left and right atria in an anteroposterior view during right atrial ablation. Spheres indicate ablation lesions. Red lines demonstrate the 1:1 and constant atrioventricular conduction at the bottom of the figure. CS: Coronary sinus; IVC: Inferior vena cava; LA: Left atrium; LIPV: Left inferior pulmonary vein; LSPV: Left superior pulmonary vein; RA: Right atrium; RIPV: Right inferior pulmonary vein; RSPV: Right superior pulmonary vein; SVC: Superior vena cava.

The post-procedural basic cycle length was 700 milliseconds. At several different pacing rates, the longest sinus node recovery time and corrected sinus node recovery time was 960 milliseconds and 300 milliseconds, respectively. Total procedural, fluoroscopy, and ablation times were 88 minutes, 12 minutes, and 280 seconds, respectively. The total number of ablation lesions was 48, of which 21 were in the left atrium and 27 in the right atrium (Fig. 5).

Follow-up

The patient has been completely asymptomatic, experiencing no episodes of dizziness or syncope, and was taking no medications at the end of a 9-month follow-up period. All follow-up ECGs and Holter recordings demonstrated normal atrioventricular conduction. The minimum and mean heart rates changed from 68 and 81 bpm at 1 month to 65 and 79 bpm, 56 and 75 bpm, and 52 and 70 bpm at 3 months, 6 months, and 9 months post procedure, respectively.

DISCUSSION

The primary finding of the present case is that vagal ganglia ablation may be used with great success in well-selected, functional AVB cases. Secondly, the present case demonstrated that fractionated electrograms may be used in addition to an empirical anatomical approach to define the location of vagal ganglia without the need for spectral analysis or high

frequency stimulation. Lastly, ablation in different parts of the atria may cause different effects on the sinus node or atrioventricular conduction system.

Vagal ganglia ablation was first studied as an alternative to pacemaker implantation by Pachon et al.[10] in a mixed population consisting of patients with functional, intermittent high-degree AVB, reflex syncope, and sinus node dysfunction. To detect parasympathetic innervation sites, they converted conventional atrial electrograms to atrial spectra using fast Fourier transformation analysis. After ablation of all of the regions demonstrating parasympathetic spectra, the procedure was continued in the regions of 3 epicardial fat pads named ganglion A, B, and C (Figure 3). Contrary to the present report, all of the patients included in that study demonstrated 1:1 atrioventricular conduction at the beginning of procedure.

Rivarola et al.[11] investigated critical atrial regions responsible for the major autonomic changes. They performed ablation in empirically identified anatomic locations of both atria (Fig. 3). Four of 9 patients (all with transient AVB) did not demonstrate any clinical improvement after ablation and required pacemaker implantation. The septal aspect of the superior vena cava junction and the posterior aspect of the interatrial septum, which are compatible with ganglions A and C, respectively, were determined to be critical for vagal denervation in 36% of the studied patients. In a previous report, we investigated the clinical effectiveness of a selective right atrial approach in 7 patients (4 with intermittent AVB and the remainder with permanent AVB) using a combination of SA, HFA, and additional anatomical ablation.[6] Our procedural approach was successful in 6 of 7 patients. Looking at the clinical features of the failed case, that patient was the oldest in the study population (69 years old) and demonstrated partial resolution of atrioventricular conduction after an atropine sulphate infusion. It was thought that the AVB may have been related to structural disease of the atrioventricular conduction system and not functional. In the present case, although we performed biatrial ablation, improvement of AVB during radiofrequency application around the coronary sinus from the right atrial side may be further evidence of our earlier hypothesis that a right atrial approach would suffice in patients with AVB.

The limitations mentioned below suggest that we need an alternative modality to define the exact localization of vagal ganglia:

(1) In SA, the whole atrial endocardium needs to be scrutinized using computer-aided mapping. This process requires additional equipment and prolongs the procedure.

(2) In HFS, the procedure should be applied in all atrial sites. The areas demonstrating positive vagal response are targeted for ablation. Then, the disappearance of vagal response in those sites should be checked. Therefore, this is a very time consuming method. Also, the application may require general anesthesia due to sensation of chest discomfort. Furthermore, it may cause negative dromotropic or chronotropic effects, like vagal response due to nonspecific excitation of nociceptors within the wall of the atria, superior vena cava, or coronary sinus.[12] Lastly, it may cause inadvertent atrial fibrillation stimulation.

(3) In AA, ablation is performed in empirically identified sites. It may cause an unnecessary or larger than necessary area of ablation. In a recently published meta-analysis, we compared the recurrence rate of these 3 approaches in with vasovagal syncope and demonstrated that only AA is associated with higher syncope recurrence.[7]

To address these limitations, we tried to define a new and simple method that does not require additional equipment, is easily applicable, and has a high degree of accuracy. Fractionated electrograms were first studied in relation to atrial fibrillation. Although the exact underlying mechanisms of these patterns (normal, LAFE, and HAFE) are unproven, there are several hypotheses. The normal electrogram is assumed to be associated with healthy atrial tissue and is sharply inscribed due to rapid and uniform conduction.[13] The LAFE pattern is a low-amplitude electrogram with slow conduction and is usually associated with atrial fibrosis.[14] There is no clear explanation for the origin of the HAFE pattern. In Lellouche's study,[8] fractionated electrograms were found to be associated with the parasympathetic response during atrial fibrillation ablation. They demonstrated that both patterns may predict vagal response, although it was more visible in the HAFE pattern. A similar relationship was detected in our previous work.[6] So, in the present case, we targeted all fractionated electrograms. The

most important advantage of this new technique seems to be that it allows for ablation in specifically selected sites without the need for additional equipment. Therefore, we can avoid unnecessary ablation, which can be seen when performing empirical AA. In 2 previous studies using spectral guided ablation, a mean of 36.8±5 and 28.7±15 endocardial points were treated per patient.[6,10] Since the total number of ablation lesions in the present work was 48, it suggests that the use of electrograms may also be effective in showing target regions.

Limitations

The present study consists of the clinical data of only 1 case. A larger patient cohort and randomized controlled trials are needed to confirm the safety and efficacy of this new approach in patients with functional AVB. In this case, the patient follow-up was only 9 months, and the long-term pertinence of vagal denervation has not yet been clearly determined. Although there was no AVB seen on follow-up ECGs and Holter recordings, we may have missed transient AVB episodes. Implantable loop records may be used to deal with this dilemma in the near future. Also, there is still a theoretical concern about possible adverse effects of unrequited sympathetic activity. Although we previously demonstrated clinical success with an isolated right atrial approach in functional AVB cases, we used a biatrial approach in the present case. We need comparison studies to understand the individual effects of each vagal ganglion and the potential effectiveness of selective vagal ganglia ablation. We did not take some LAFE areas into consideration and accepted them as scar tissue when they were detected outside the usual settlements of vagal ganglia. This may have caused an inadvertent bias. As previously mentioned, the HAFE pattern is better at predicting vagal response than the LAFE pattern. However, since in our study we did not attempt HAFE-only targeted ablation, it is not possible to assess whether this will be sufficient.

Conclusion

Our report indicates that vagal ganglia ablation may be a good alternative modality in a patient with functional AVB, regardless of whether the block is transient or permanent, when conventional modalities are inadequate or pacemaker implantation is declined. Instead of SA or HFS, analysis of electrogram characteristics in terms of the presence of fractionated patterns may be used to define parasympathetic innervation sites. Further larger and randomized, controlled studies with a sham procedure are required to demonstrate the efficiency and reliability of vagal ganglia ablation.

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Keywords: Atrial fibrillation; atrioventricular node; bradycardia; parasympathetic; sinus node; syncope.

Anahtar sözcükler: Atriyum fibrilasyonu; atriyoventriküler düğüm; bradikardi; parasempatik; sinüs düğümü; senkop.