

Characteristics of a large-scale cohort with accessory pathway(s): A cross-sectional retrospective study highlighting over a twenty-year experience

Aksesuar yolu bulunan geniş ölçekli bir kohortun karakteristikleri: Yirmi yılı aşkın deneyimi vurgulayan retrospektif kesitsel bir çalışma

Suat Görmel, M.D.¹ , Salim Yaşar, M.D.¹ , Serkan Asil, M.D.¹ , Erhan Bozkurt, M.D.² ,
Serdar Fırtına, M.D.¹ , Hatice Tolunay, M.D.¹ , Veysel Kutay Vurgun, M.D.³ , Erkan Yıldırım, M.D.¹ ,
Yalçın Gökoğlan, M.D.¹ , Barış Buğan, M.D.¹ , Murat Çelik, M.D.¹ , Uygur Çağdaş Yüksel, M.D.¹ ,
Hasan Kutsi Kabul, M.D.¹ , Basri Amasyalı, M.D.⁴ , Cem Barçın, M.D.¹ , Sedat Köse, M.D.³ 

¹Department of Cardiology, Gülhane Training and Research Hospital, Ankara, Turkey

²Department of Internal Medicine, Afyonkarahisar Health Sciences University School of Medicine, Afyonkarahisar, Turkey

³Department of Cardiology, Liv Hospital, Ankara, Turkey

⁴Department of Cardiology, TOBB Economics and Technology University School of Medicine, Ankara, Turkey

ABSTRACT

Objective: Catheter ablation following electrophysiologic study (EPS) is the mainstay of diagnosis and treatment for patients with atrioventricular reentrant tachycardia (AVRT), demonstrating excellent long-term outcome and a low rate of complications. In this study, our aim was to assess our experience in patients with accessory pathway (AP) and to compare our data with the literature.

Methods: We included 1,437 patients who were diagnosed and treated for AP in our hospital between 1998 and 2020. The demographic data of all the patients, AP location, and periprocedural results were recorded.

Results: Of the 1,437 patients, 1,299 (90.4%) were men; and the mean age of the population was 26.67 years. The location of 1,418 APs were along the left free wall (647 [45.6%] patients), in the posteroseptal region (366 [25.3%] patients), in the anteroseptal region (290 [20.4%] patients), and along the right free wall (115 [8.1%] patients). The ratio of the second AP existence was 3.0% and AVNRT co-existence was 2.0%. A total of 55 (3.8%) patients had recurrent sessions for relapse. Our center's total success rate was 95.5%, and total complication rate was 0.26%.

Conclusion: According to our retrospective analysis, EPS is a highly functional tool in the diagnosis and management of arrhythmias such as AVRT for high-risk patient groups like military personnel with the aim of risk stratification and medical management.

Patients with accessory pathway (AP) have an alternative conduction to the atrioventricular (AV)-His-Purkinje system, bypassing the AV node and typically resulting in pre-excitation in the electrocardiogram (ECG). The types of APs are classi-

ÖZET

Amaç: Elektrofizyolojik çalışmayı (EPS) takiben kateter ablasyonu, Atriyoventriküler Reentrant Taşikardisi (AVRT) olan hastalar için tanı ve tedavinin temel dayanağıdır ve mükemmel uzun vadeli sonuç ve düşük bir komplikasyon oranı gösterir. Çalışmamızın amacı, aksesuar yolaklı hastalardaki deneyimlerimizi değerlendirmek ve verilerimizi literatür ile karşılaştırmaktır.

Yöntemler: Hastanemizde 1998-2020 yılları arasında aksesuar yol (AP) tanısı alan ve tedavisi olan 1437 hastayı dahil ettik. Tüm hastaların demografik verileri, aksesuar yolun konumu ve işlemle ilgili sonuçlar kaydedildi.

Bulgular: 1437 hastanın 1299'u (%90.4) erkekti ve çalışma popülasyonunun ortalama yaşı 26.67 idi. 1418 AP'nin lokasyonu; sol serbest duvar boyunca (647 hasta, %45.6), posteroseptal bölgede (366 hasta, %25.3), anteroseptal bölgede (290 hasta, %20.4) ve sağ serbest duvar boyunca (115 hasta, %8.1) idi. İkinci AP var olma oranı %3.0 ve AVNRT birlikte var olma oranı %2.0 idi. 55 (%3.8) hastada relaps sebebiyle tekrarlayan işlemler yapıldı. Merkezimizin toplam başarı oranı %95.5 ve toplam komplikasyon oranı %0.26 idi.

Sonuç: Retrospektif analizimizin ışığında elektrofizyolojik çalışma, risk sınıflandırması ve tıbbi karar amacıyla askeri personel gibi yüksek riskli hasta grupları için AVRT gibi aritmilerin tanı ve yönetiminde oldukça işlevsel bir araçtır.

fied as AV bypass tracts (best known, Kent fibers), atrionodal tracts (James fibers), atriohisian tracts (Breckenmacher fibers) and Hisian-fascicular tracts (Mahaim fibers).^[1]



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Correspondence: Suat Görmel, M.D. Department of Cardiology,

Gülhane Training and Research Hospital, Ankara, Turkey

Tel: +90 530 691 10 24 e-mail: suatgormel@yahoo.com

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The clinical significance of these APs is AV re-entrant tachycardias (AVRT) by re-entrant circuits. These circuits consist of two anatomically defined limbs; AV-His-Purkinje system and AP, with different refractoriness and conduction times, which may initiate an AVRT with a critically timed premature atrial or ventricular beat.

In 1930, Wolff, Parkinson, and White first described the bundle of Kent causing pre-excitation on an ECG through an AV bypass tract and named it the “Wolff-Parkinson-White (WPW) pattern.”^[2] In case of paroxysmal tachyarrhythmias, it is called the WPW syndrome.

In the general population, the prevalence of a WPW pattern on surface ECG which means “manifest AP,” ranges from 0.15%-0.25 %; however, concealed AP is not rare,^[3] and not all patients develop supraventricular tachycardia (SVT). Compared with the other SVTs, the pre-excitation population is generally younger, predominantly male, and has less comorbidity.^[4,5] Nowadays, AVRTs are among the most frequently referred SVTs for catheter ablation to specialized centers after atrial fibrillation (AF)/atrial flutter and AV node re-entrant tachycardia (AVNRT).^[6-8] Radiofrequency (RF) catheter ablation or cryo-ablation are the optimal medical procedures for AVRT with high procedural success, which result in significant improvements in the patients’ quality of life.^[9,10]

Although AVRTs are well-known SVTs, most of the studies defining its characteristics are from the beginning of the electrophysiological studies (EPS) consisting of smaller populations. Therefore, the epidemiological studies over the characteristics AVRTs are scarce and insufficient. To address and complete the gaps in evidence, we investigated an AVRT cohort consisting of mainly military personnel with over 8,000 patients for over 20 years retrospectively, and this study represents the results.

METHODS

Our study was a retrospective analysis, and our population consisted of 1,437 consecutive children and adult patients (1,299 [90.4%] men; 26.67±10 years) who underwent EPS between January 1998 and June 2020 at our center. The study group was evaluated for AVRT including clinical and electrophysiologic characteristics. There was no exclusion criterion. The study protocol was approved by the Clinical Research Ethics Committee of Gülhane Training and Research Hospi-

tal (Approval Date: June 30, 2020; Approval Number: 2020-314) and conformed with the principles defined in the Declaration of Helsinki. Written informed consent was obtained from all the individual participants included in the study.

EPS Procedure

All antiarrhythmic drugs were discontinued four to five half-lives before the procedure. EPS was performed under local anesthesia in a

fasting state. Three catheters were introduced through the right femoral vein and were positioned at high right atrium (HRA), coronary sinus, and His region. The catheter at His position was also used for ablation, or the catheter at HRA was shifted to right ventricle when necessary. Intracardiac signals were filtered at 20-500 Hz, amplification gains were 10-80 mm/mV. All signals were displayed and acquired on an electrophysiological recording system. After obtaining baseline basic cycle length (BCL), atrial-His interval (AH), and His-ventricle interval (HV) measurements, interval measurements, programmed electrical atrial and ventricular stimulation was performed. Anterograde and retrograde conduction properties were analyzed. If no tachycardia was inducible, the stimulation protocol was repeated after atropine administration. Ablations were carried out using 7F non-irrigated multi-curve ablation catheter (steerable 4-mm tip ablation catheter, Marinr®, Medtronic, Minneapolis, USA) and Medtronic Atakr II® (Medtronic Inc., Mpls., MN, USA) radiofrequency generator. Patients who had undergone ablation were hospitalized overnight and discharged the day after the procedure. Follow-up visits were performed in the outpatient clinic at one month after ablation.

Statistical Analysis

This was a descriptive study in which the categorical variables were represented as absolute numbers and

Abbreviations:

| | |
|-------|--------------------------------|
| AF | Atrial fibrillation |
| AP | Accessory pathway |
| AS | Anteroseptal |
| AV | Atrioventricular |
| AVNRT | AV node re-entrant tachycardia |
| AVRT | AV re-entrant tachycardias |
| CHD | Congenital heart disease |
| ECG | Electrocardiogram |
| EPS | Electrophysiological studies |
| HRA | High right atrium |
| LA | Left anterior |
| LAL | Left anterolateral |
| LL | Left lateral |
| LP | Left posterior |
| LPL | Left posterolateral |
| LPS | Left posteroseptal |
| MS | Midseptal |
| RA | Right anterior |
| RAL | Right anterolateral |
| RF | Radiofrequency |
| RL | Right lateral |
| RP | Right posterior |
| RPL | Right posterolateral |
| RPS | Right posteroseptal |
| SVT | Supraventricular tachycardia |
| WPW | Wolff-Parkinson-White |

percentages. Continuous variables were represented as mean±standard deviation. Statistical analyses were performed using SPSS for Windows version 20.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Between 1998 and 2020, we evaluated 8,233 patients who underwent EPS. The characteristics of the patients are summarized in Table 1. Among all the patients, we established 1,437 patients with 1497 APs. Our population was unusually predominant of the male sex (90.4%) and consisted of young adults (26.67±10 years) (Figure 1). Most of the patients had manifest AP (69.2%).

In our study, we found two (0.14%) patients with Ebstein anomaly as congenital heart disease in our population. Both patients had right-sided APs, a right posteroseptal AP and a right midseptal AP, which were ablated successfully.

The periprocedural results of the 1,437 patients who underwent EPS for diagnostic evaluation or ablation therapy are displayed in Table 2. We classified the AP distribution according to location, and 1,418 APs are illustrated in Figure 2. In addition, there were 36 patients with atrio-fascicular pathway. AP localization of 43 patients was unknown because of missing data. Of the 1,418 APs, 647 (45.6%) were located along the left free wall, 366 (25.3%) in the posteroseptal region, 290 (20.4%) in the anteroseptal region, and 115 (8.1%) along the right free wall respectively.

Among 1,437 cases, 1,352 patients had single AP, and 42 patients had double APs; the ratio of the second AP existence was 3.0%. Co-existence of AVNRT was observed in 30 (2.0%) patients. For most of the patients (1,382 [96.1%]), a single EPS procedure was enough for diagnosis and/or ablation. However, for complete evaluation, 50 (3.5%) patients had to undergo a second procedure and five (0.3%) patients a third procedure.

We classified our population according to EPS indications and showed that 17.3% asymptomatic patients with pre-excitation had undergone EPS for medical evaluation. Considering the EPS results of 1,437 patients, 999 (69.0%) had successful ablation and 47 (3.2%) had failed ablation; 143 (9.9%) patients with indistinct complaints and borderline ECG findings who were admitted for assessing health sufficiency for military service had innocent APs not causing any inducible tachycardia; and therefore, ablation was

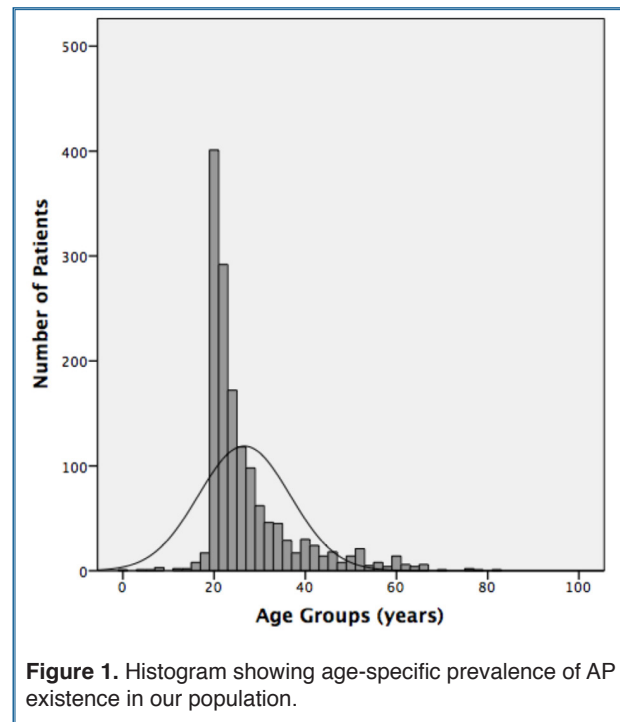


Figure 1. Histogram showing age-specific prevalence of AP existence in our population.

Table 1. Baseline characteristics of population

| | |
|---------------------------------|--------------|
| Population, n | 1,437 |
| Accessory pathway, n | 1,497 |
| Sex, male, n (%) | 1,299 (90.4) |
| Age (years) | 26.67±10 |
| Pre-excitation existence, n (%) | 891 (69.2) |
| CHD | |
| Ebstein anomaly, n (%) | 2 (0.14) |

CHD: congenital heart disease.

deferred. Seventy nine (5.4%) patients who were military staff at the same time had undergone diagnostic EPS for medical evaluation but did not demand ablation at our center, and 122 (8.4%) patients had para-hisian AP and did not prefer any high-risk procedure. As a result, our success rate for catheter ablation in the treatment of AVRT was 95.5%.

Our overall total major complication rate was 0.26%. The most common complication encountered after procedure was persistent AV block requiring pacemaker implantation in two patients. Another major complication in one patient was anaphylactic shock against the local anesthetic drug, who recovered after medical treatment. Finally, one patient with cardiac tamponade who had hemodynamic instability underwent surgical pericardial drainage.

Table 2. Periprocedural results

| AP number (n=1,437) | No. of patients | % of patients |
|---|-----------------|---------------|
| Single AP | 1,352 | 94.1 |
| Double AP | 42 | 2.9 |
| Missing data | 43 | 3.0 |
| AVNRT co-existence (%) | 30 | 2.0 |
| Recurrent EPS (1,437) | | |
| Single | 1,382 | 96.1 |
| Twice | 50 | 3.5 |
| Thrice | 5 | 0.3 |
| EPs indications (n=1,497) | | |
| WPW patients with cardiac arrest and pre-excited AF | 7 | 0.4 |
| Symptomatic patients with documented SVT | 287 | 19.0 |
| Patients with complaints and induced tachycardia | 938 | 62.0 |
| Asymptomatic patients with pre-excitation and innocent AP | 260 | 17.3 |
| No data | 5 | 0.3 |
| EPS results (n=1,437) | | |
| Successful ablation | 999 | 69.0 |
| Failed ablation | 47 | 3.2 |
| Innocent AP | 143 | 9.9 |
| Diagnostic EPS | 79 | 5.4 |
| Postponed ablations | 39 | 2.7 |
| High risk procedure - ablation canceled | 122 | 8.4 |
| No data | 8 | 0.5 |
| Complications (n=1437) | | |
| Third-degree AV block | 2 | 0.13 |
| Cardiac tamponade | 1 | 0.06 |
| Anaphylactic shock | 1 | 0.06 |

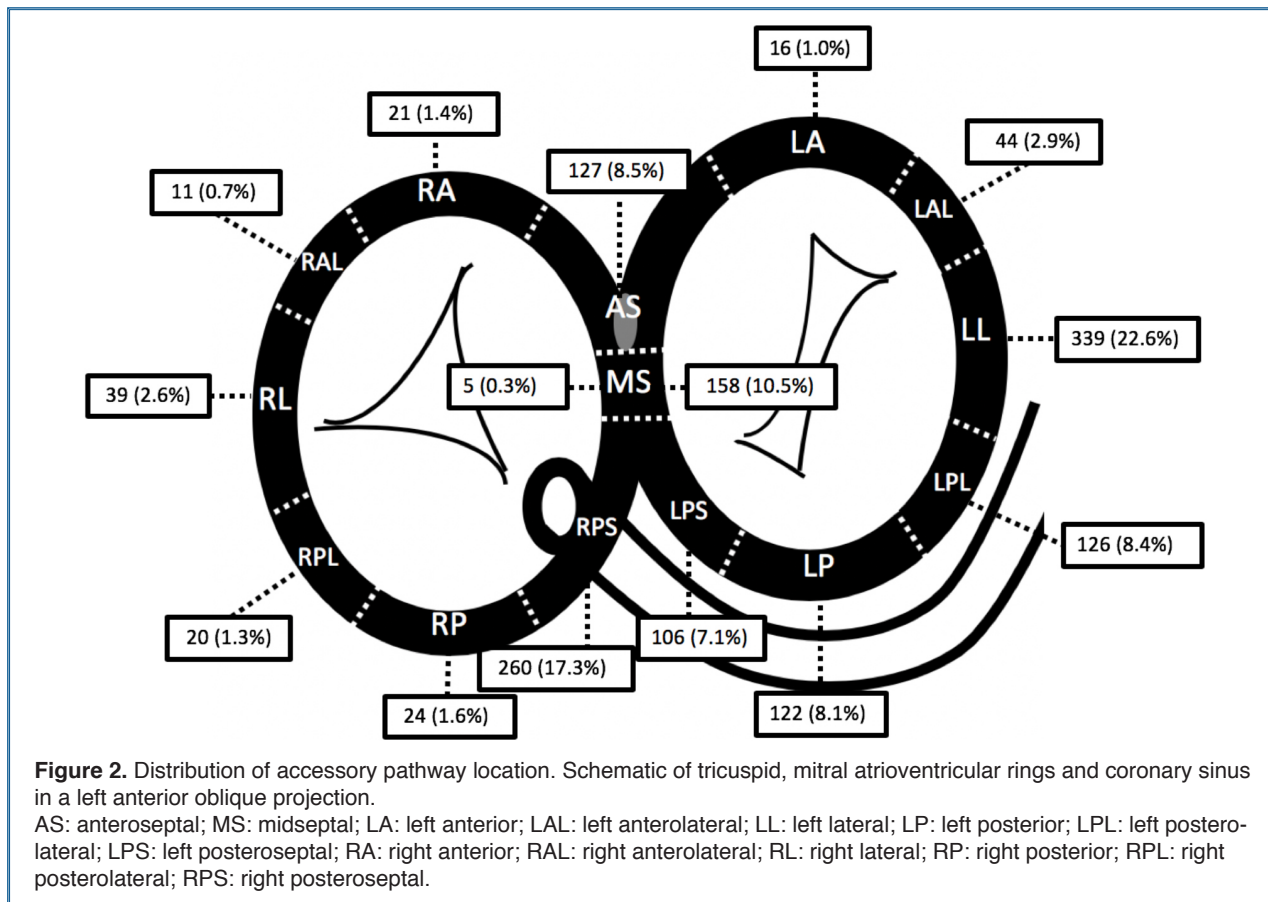
AP: accessory pathway; AV: atrioventricular; AVNRT: AV node re-entrant tachycardia; EPS: electrophysiological study; SVT: supraventricular tachycardia.

DISCUSSION

Our hospital used to be a military hospital, and every 20-year-old male military service candidate plus military staff were referred here nationwide for further medical evaluation until August 2016. Therefore, our center's archives contain one of the largest and longest series of patients with AVRT in Turkey.^[11] Because it was a military hospital, the patient population here was unusually predominantly male. However, similar to previous literature of Taiwanese (mean age 26.8 years) and Spanish (mean age 20.9 years) cohorts and differently from the Swedish (mean age 41.0 years) cohort, our population's mean age was 26.67±10 years.^[4,6,8]

Approximately one-third of the AP tachycardias are because of concealed Aps with an incidence of 15%-42%.^[12] In our study, 546 (30.8%) patients had concealed AP which is consistent with the literature.

Most APs in Ebstein's are associated with the tricuspid valve. As we expected, the AVRTs in both of our patients with Ebstein anomaly were right-sided; a right posteroseptal AP and a right midseptal AP. Because of lower acute success rates and higher recurrence rates compared with the general population, ablation in this population is challenging. The leading causes for difficulties are altered right heart anatomy and common electrophysiological problems such as



additional APs, AP variants such as Mahaim fibers, other tachycardia mechanisms, and so forth.^[13-15]

Aps are commonly located along the tricuspid or mitral annulus or within the subepicardial pyramidal space in the inferoseptal region.^[16] In this study, we classified the APs according to anatomical localizations and demonstrated that the most common AP area was the septal area and the area surrounding the coronary sinus, referring to nearly two-third of all the APs. This was similar to previous studies, which have demonstrated the most frequent AP distribution was along the left free wall, in the posteroseptal region, in the anteroseptal region, and along the right free wall, respectively.^[17] Rarely, an AP has an alternative conduction from the atria to the ventricles other than atrioventricular (AV)-His-Purkinje system, bypassing the AV node; atrionodal tracts, atriohisian tracts and Hisian-fascicular tracts. We had 36 (2.4%) patients with fascicular pathway, which was more frequent in our population in comparison to the previous results. However, our population consisted of mainly incidental patients admitted for medical evaluation and few

symptomatic patients. Fascicular pathways seldom cause an inducible arrhythmia and are generally encountered incidentally. This paradigm was demonstrated by LaRocca et al.^[18] in their study with similar results; fascicular pathway existence in incidental APs was 12.2% and 1.1% in patients with WPW syndrome.

Multiple Aps can be identified in 3%-13% of the patients undergoing EPS for tachycardias mediated by APs, and its prevalence is as high as 52% in patients with Ebstein anomaly. According to literature, a high prevalence of multiple APs has been observed, especially in pediatric populations with structural heart disease (SHD) predominance.^[19,20] Our study population had a majority of adults and very few patients with SHD. As a result, we had relatively less patients (3%) with multiple APs.

Sometimes, AVRT and AVNRT may present concurrently up to 8% as reported by Zardini et al.^[21] in a retrospective analysis of 402 patients. Although our cohort had a larger study group, co-existence was lower than expected (2%). This inconsistency may be owing to the retrospective design of both studies. Our

clinic's repeat ablation rate for AVRT was compatible with the previous studies.^[8]

In asymptomatic patients, catheter ablation of APs successfully eliminates the low risk of sudden death associated with the condition. However, a generalized referral of every asymptomatic patient for ablation could also carry serious and potentially life-threatening complications.^[22] Therefore, to date, the decision to refer an asymptomatic patient with pre-excitation for ablation remains a dilemma. Currently, there is no agreement among the European and American Cardiology Societies in the management of asymptomatic athletes or high-risk professionals with a WPW ECG pattern. The consensus recommends that upon discovery of ventricular pre-excitation, first line non-invasive diagnostic methods like exercise stress test should be done to assess the persistence of pre-excitation. However, if the results of first line methods are not satisfactory, risk stratification with invasive methods is recommended.^[23,24] Our population consisted of a large number of asymptomatic military staff with WPW ECG pattern referred for medical evaluation. Therefore, the asymptomatic patient ratio enrolled for diagnostic assessment was as high as 17.3% in our study group unlike the general EPS populations.^[6-8]

In our study group, there was a patient population of 17.3% with pre-excitation on the surface ECG but clinically asymptomatic. In this group, although the indications for diagnostic EPS were not clear according to the current literature, the majority were military personnel working in the high-risk business group, which increased our diagnostic EPS rate. These patients were pre-diagnosed with incidental arrhythmia during routine periodic examinations and had no previous cardiac history. Therefore, we aimed to prevent possible adverse cardiac events by basic medical evaluation, including standard 12-lead ECG followed by EPS evaluation if needed. In countries with compulsory military service as in our country, a baseline resting ECG is an important tool in the diagnosis and management of arrhythmias such as AVRT for discriminating the high-risk group.

Radiofrequency catheter ablation (RCA) for APs is often considered as a first-line approach because of its high success rates (approximately 95%) and low-risk profile (complication rates of 3%).^[25-27] Our center's total success rate (95.5%) and total complication rate (0.26%) were consistent with the previous studies.

Limitations

This study was a single-center retrospective study in which the epidemiological characteristics of the patients and the findings of electrophysiological procedures were retrieved from institutional archives. Therefore, it lacked follow-up data and did not include long-term outcomes. In addition, a vast majority of our study group was male military staff referred for medical evaluation, inconsistent with the general population.

Conclusion

To the best of our knowledge, this study is probably the largest and the longest to demonstrate a nationwide epidemiological profile of military service patients with APs in Turkey. We investigated the patient characteristics, AP location, and periprocedural results in our population. Our outcomes of EPS and RCA showed acceptable success rates, similar to those in the literature. The complication rate in our cohort was as low as shown in other studies. As a result, based on our retrospective analysis, EPS seems to be a functional tool in the diagnosis and management of arrhythmias, such as AVRT for high-risk patient groups like military personnel.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Research Ethics Committee of Gülhane Training and Research Hospital (Approval Date: June 30, 2020; Approval Number: 2020-314)

Informed Consent: Written informed consent was obtained from all the individual participants who participated in this study.

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