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ORIGINAL ARTICLE

Diagnosis and management of phantom tachycardias based on an electrophysiologically guided approach

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Abstract *Background:* Non-documented palpitations, or phantom tachycardias, are palpitations deemed to be of unknown origin after evaluation with conventional diagnostic tools, such as 12-lead electrocardiogram and Holter recordings. Our aim was to determine the diagnostic value of an electrophysiologic study (EPS) and its role in the management of patients presenting with non-documented palpitations.
Methods: We performed EPS in 78 consecutive patients with repeatable, poorly tolerated symptoms of paroxysmal, non-documented tachycardia, the absence of structural heart disease and at least one 24-h Holter recording. The duration and frequency of palpitations was registered in each patient.
Results: Long-lasting palpitations (>1 hour) were present in 15.4% of patients. Half of patients reported symptoms less often than once per week. Only 13/78 patients (16.6%) had normal EPS findings, while dual pathways at the AV node ± echo beats were identified in another 13 patients without inducible tachycardia. At least one tachycardia event was induced in 52 patients (66.6%). AVNRT was provoked in 32 patients (41.2%). Ablation was performed in 14/52 patients with inducible tachycardia (26.9%). Slow pathway ablation was also performed in three patients with dual AV pathways and atrial echo-beats but without provoked tachycardia. Follow-up data were available in 52 patients, and 84.6% had fewer or no clinical recurrences.

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Conclusions: EPS is safe and of enhanced diagnostic value in patients with unexplained palpitations because only 1/6 had negative results. EPS also provided an explanation about the mechanism of arrhythmia and successfully guided the management of these patients, as well as enhanced improvement in the quality of life.

1. Introduction

Although palpitation is a common referral symptom among outpatients who consult cardiologists, a definitive or at least probable diagnosis of its cause is often not reached.[1] For up to 16 percent of such patients, the sensation of a rapid or irregular heartbeat remains unexplained after initial evaluation with history, physical examination and electrocardiogram, inducing anxiety and frequent visits to the emergency department.[2]

Non-documented palpitations or phantom tachycardias are palpitations that are deemed to be of unknown origin after evaluation with conventional diagnostic tools, such as 12-lead electrocardiogram and Holter recordings.[2] According to current diagnostic practice, an electrophysiologic study (EPS) as an invasive procedure; it is usually considered at the end of the diagnostic work-up.[2,3] Only in patients with significant heart disease and those with palpitations that precede syncope, does EPS generally precede the use of ambulatory ECG monitoring.[2] Additionally, few data exist on the value of EPS when it is performed as part of the diagnostic algorithm of nondocumented palpitation in patients without structural heart disease[4,5]. The aim of the present study was to determine the diagnostic value of EPS and its role in the management of patients presenting with non-documented palpitations.

2. Methods

A retrospective, single-center study was performed to assess the value of EPS on the diagnosis and treatment of patients with non-documented palpitations. Informed consent was obtained from all patients before EPS.

From January 2004 to December 2014, 78 consecutive patients, who were referred for repeatable poorly tolerated symptoms of paroxysmal non-documented tachycardia and with a negative routine initial evaluation, including history, physical examination, 12-lead electrocardiogram, transthoracic echocardiography, blood chemistry examinations and at least one 24-h Holter recording, underwent EPS. The duration and frequency of palpitations was registered in each patient. Patients with sustained tachycardia that was detected during noninvasive testing, a history of documented arrhythmias and other known medical causes of the symptoms were excluded from the study. Patients with significant structural heart disease (coronary artery disease, decreased [<50%] left ventricular ejection fraction and at least moderate valvulopathies) and systematic illnesses were also excluded.

Event loop recorders, external loop recorders and implantable loop recorders (ILRs) were not used in any patient.

2.1. Electrophysiological study

An EPS was performed using the standard protocol. Shaped quadripolar catheters were inserted via the femoral vein using the Seldinger technique and they were advanced to the high right atrium for registration and atrial stimulation as well as the right ventricular apex and His bundle position for His registration and ventricular/para-hisian stimulation, respectively.[6,7] A decapolar deflectable-tip catheter was positioned in the coronary sinus via the femoral vein. A typical protocol of an incremental right atrial pacing and extrastimulus testing was performed in all patients. The protocol used a drive train of six paced beats at a fixed cycle length (500-600 ms), which was followed by 1-3 extrastimuli. The drive train was repeated, while the coupling interval of the extrastimulus was progressively decreased until the atrium was no longer captured. In cases without induced tachycardia, the protocol was repeated after the infusion of isoprotenerol. Programmed ventricular stimulation with $\leq$ 3 extrastimuli was also performed in the absence of supraventricular tachycardia induction.

The diagnosis of supraventricular tachycardia and, in particular, of atrioventricular reentrant tachycardia (AVRT) or atrioventricular nodal reentrant tachycardia (AVNRT) was based on standard criteria.[7,8] The diagnosis of atrial tachycardia was supported when a "VAAV" response to ventricular stimulation during tachycardia or the lack of VA linking was identified.[9] Induced runs of atrial flutter or atrial fibrillation were included in the same group. Furthermore, the diagnosis of dual A-V nodal pathways was based on the induction of discontinuous A-V nodal conduction curves with programmed atrial extrastimulation.[10]

The EPS result was considered positive when supraventricular and/or ventricular tachyarrhythmia were induced. The EPS findings were also characterized as positive when dual AV nodal pathways with or without atrial echo beats were present.

Radiofrequency ablation was proposed in patients with induced tachycardia. Ablation was not always performed on the same day.

2.2. Follow up

Follow up of the patients with positive or negative EPS results by direct or telephone interviews was performed in 52

patients. The severity of symptoms before and after EPS, according to EPS findings and subsequent treatment, was assessed.

All data were analyzed by using SPSS, version 18 (SPSS Inc., Chicago IL). The results of the aforementioned variables were compared using chi-square analysis. P values $\leq$0.05 were considered statistically significant.

3. Results

Among the 78 patients with phantom tachycardias undergoing EPS, 47 were females (60.2%) and 31 males (39.8%) with a mean age of 40.8 years. Hypertension was present in 10/78 patients.

The majority of patients reported symptoms lasting for more than 5 minutes. Specifically, the duration of palpitations was <1 min in 23.1% of patients, 1-5 min in another 23%, between 5 min and 1 hour in 38.5%, and long-lasting (>1 hour) in 15.4%. Regarding the frequency of episodes, 12.8% of patients reported symptoms less often than once at six months, 21.8% had > 1 episodes at six months but less often than 1 per month, 15.4% had >1 episode/month but fewer than 1/week and 50% had >1 episode/week. The sudden onset of symptoms was reported by 67% of the patients and sudden termination by 71% patients.

Only 13/78 patients (16.6%) had normal EPS findings, while dual pathways at the AV node ± echo beats were identified in another 13 patients without inducible tachycardia. At least one tachycardia event was induced in 52 patients (66.6%). AVNRT was provoked in 32 patients (41.2%). Orthodromic reentrant tachycardia via a concealed accessory pathway was induced in 3 patients. Atrial tachycardia was induced in 9 patients and atrial flutter/atrial fibrillation in 2 patients. Both AT and AVNRT were provoked in 2 patients. Sustained ventricular tachycardia was detected in 2 patients and sinus node reentry tachycardia was detected in 2 patients (Figure 1). Tachycardias were induced after isoproterenol infusion in 7/52 patients. The mean tachycardia cycle length was 320±64 msec. No complications related to EPS were observed.

Ablation was performed in 14/52 patients with inducible tachycardia (26.9%). Ablation was performed on the same day in 8 of these 14 patients. The ablated induced tachycardias were mostly AVNRT (10/14). Slow pathway ablation was also performed in 3 patients with drug-refractory symptoms and dual AV pathways with atrial echo-beats but without provoked tachycardia.

Follow-up data were available in 52 patients. The mean follow up period was 84±37 months. Among the 52 patients with available follow-up data, only 1 patient mentioned deterioration of the palpitation frequency, 7 reported no change in the palpitation frequency, 26 patients (50%) had a lower frequency and 18 patients (34.6%) had no clinical recurrence (Figure 2). All but one patient who underwent ablation reported amelioration of clinical symptoms.

Thirty-five out of the 52 patients received medical treatment. Specifically, 15 patients received class II antiarrhythmics, 11 subjects class IV, 6 class I and 3 class III. Discontinuation of calcium channel blockers was observed in 3 patients due to side effects. Nine patients out of 11 had no clinical recurrence or amelioration of their symptoms with channel Ca antagonist administration; 10/15 patients under b-blockers and all six patients who received class I antiarrhythmic remained symptom free. Moreover, 3/5 (60%) untreated patients with negative EPS results remained symptom free at follow up despite the absence of any treatment.

4. Discussion

The results of this study provide useful information about the role of EPS on phantom tachycardias. First, we have demonstrated that EPS is safe and of enhanced diagnostic value in patients with unexplained palpitations because

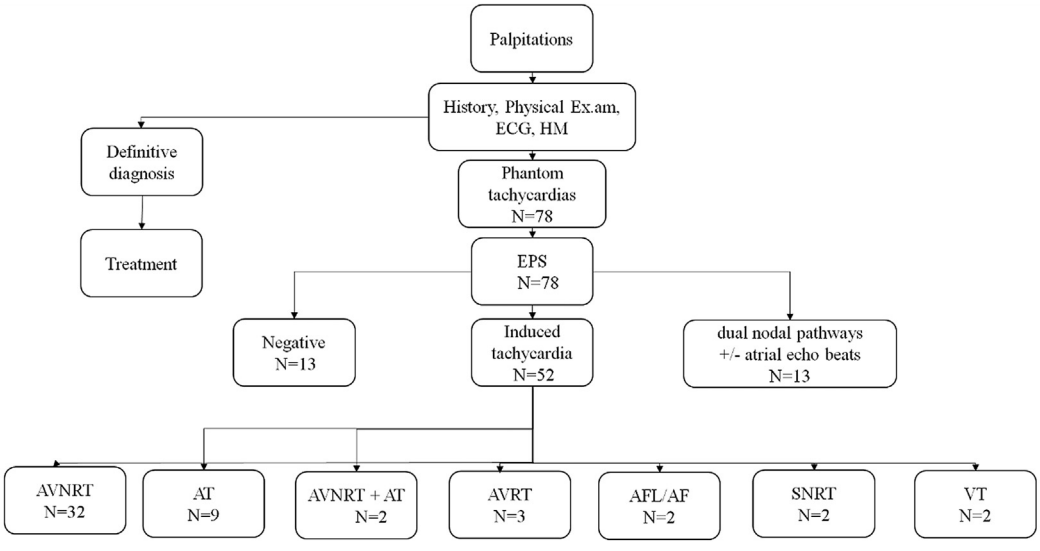

Figure 1 Flow diagram of the diagnostic algorithm and EPS results for non-documented palpitations. ECG: electrocardiogram, HM: Holter monitoring, EPS: electrophysiological study, AVNRT: atrioventricular nodal reentrant tachycardia, AT: atrial tachycardia, AVRT: atrioventricular reentry tachycardia, AFL: atrial flutter, AF: atrial fibrillation, SNRT: sinus node reentrant tachycardia, and VT: ventricular tachycardia.

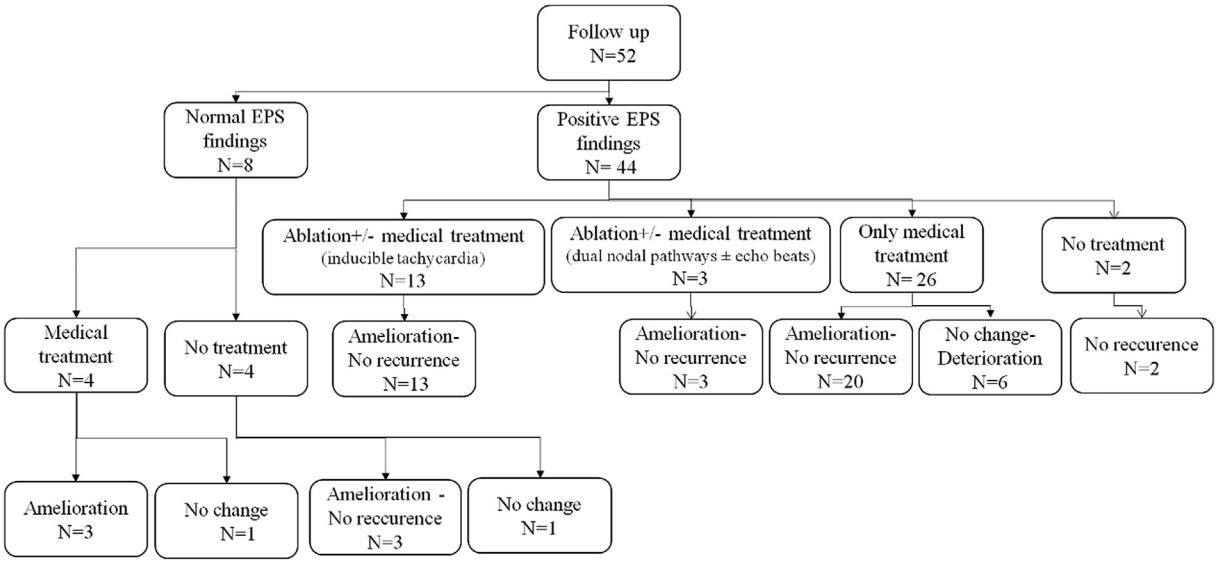

Figure 2 Flow diagram of the therapeutic outcomes of patients with non-documented palpitations. EPS: electrophysiological study.

only 1/6 had negative results. Second, EPS provided an explanation of the mechanism of arrhythmia. Moreover, EPS successfully guided the management of these patients and enhanced improvement in the quality of life. Finally, this study confirmed the therapeutic power of radiofrequency ablation in patients with inducible tachycardia and supported the empirical slow pathway ablation when the frequent and refractory (to medical treatment), unexplained palpitations were associated with EPS detected dual nodal pathways and atrial echo beats, even in the absence of induced AVNRT.

In our study, we did not use external or implantable loop recorders for diagnosing unexplained palpitations. In patients with frequent palpitations of unknown origin and with negative Holter monitoring results, new external loop recorders with auto-trigger functions and mobile cardiac outpatient telemetry had a high diagnostic yield of 86% and a better cost-effectiveness ratio than Holter devices.[11] Monitoring cannot be performed for more than 3-4 weeks and continual maintenance is required, while the devices are uncomfortable. Furthermore, with external loop recorders, the identification of underlying arrhythmogenic mechanism is not always feasible. Finally, ambulatory ECG monitoring necessitates the patient have a recurrence of symptoms, which delays the diagnosis. Apart from these, ILRs have been successfully used to study syncope, and they can be useful for studying palpitations of unknown origin.[2,12] The recurrent unexplained palpitations (RUP) study recently demonstrated the superiority of ILRs over the conventional diagnostic strategy of Holter and event recorder monitoring as well as external loop recorders in evaluating patients with infrequent palpitations; both had a higher diagnostic value (73% vs. 21%) and better cost/effectiveness ratio.[13] However, the study population was limited. Moreover, patients enrolled in the study had infrequent symptoms (i.e., monthly frequency), and the mean time interval to the first palpitation recurrence during monitoring with ILR was 279 days, which could have been overestimated because the ILRs detected both clinical and non-clinical events.[13] Implantation of ILRs constitutes an invasive procedure with a risk of local complications at the implantation site. Limited memory and sensitivity are also usual unsolved problems for ILRs. Therefore, ILR use is restricted in selected patients with severe and infrequent palpitations (inter-symptom interval 4 weeks) and when all other modalities are ineffective.[2,12]

Interestingly, in our study population only 16% of EPS evaluations were negative. This percentage, which is similar to previous results[6], is indicative of the high sensitivity of the method. More than half patients with negative EPS results had no additional palpitation recurrences. One cannot exclude a placebo effect of EPS itself. Moreover, the reassurance of the presence of a "healthy" heart might have improved the patient quality of life by reducing anxiety.

EPS detected the cause of palpitation in 2/3 of our subjects. This percentage, which is similar to findings from a recent registry, justifies and enhances the use of EPS for these patients who have distinct clinical characteristics.[4] They usually had frequent episodes of palpitations (more than 1/week), which last for more than 5 minutes. The more common underlying arrhythmia of non-documented palpitations is AVNRT, which is in accordance with findings from previous prospective studies.[4,5] We acknowledge that our study population consisted of young patients (mean age 40.8 years old) who lacked structural heart disease. Furthermore, our EPS revealed dual AV nodal pathways with or without atrial echo beats, which is the functional substrate for AVNRT in 1/6 of our patients, as has previously been reported among patients undergoing EPS.[14] Atrial tachycardia as the cause of undocumented palpitations was the second most common inducible tachycardia in our population study. Apart from this, AVRT, atrial flutter, atrial fibrillation and sinus reentry tachycardia were also occasionally provoked during the EPS procedure, bridging the diversity of underlying mechanisms. The low incidence of atrial fibrillation, in concordance with a previous registry,[4] may be explained by the low mean age of the study

population and its easy detection because it is usually characterized by a long duration. Moreover, AVNRT and atrial tachycardia were both induced in 2 patients, highlighting the complex functional substrate of undocumented palpitations and the diagnostic and therapeutic challenges for the cardiologist. Our data suggest that EPS is a safe, direct and precise tool for diagnosing non-documented palpitations. It is noteworthy to mention that the identification of these tachyarrythmias allows for individualized, effective management of each patient.

Focusing on follow-up, the vast majority of people who underwent ablation reported reduced or a lack of episodes of palpitations. Documentation of tachyarrhythmia during EPS is necessary to ablate AVRT and atrial tachycardia. However, management of dual nodal pathways with atrial echo beats in the absence of inducible supraventricular tachycardia remains controversial. A reasonable approach, as supported by our data, consists of performing empirical slow pathway ablation in patients with frequent and intolerable symptoms who have a suspected (non-inducible) AVNRT substrate during EPS. Medical treatment, as expected, was less effective than radiofrequency ablation. Antiarrhythmic drugs of all Vaughan Williams classes were administered.

The major limitations of our study included the limited number of enrolled patients, retrospective character of the study and absence of available follow-up data in 1/3 of the patients. Furthermore, the selected population did not represent all patients with a sensation of palpitations. Therefore, the real prevalence of underlying inducible tachyarrhythmia of phantom tachycardia is probably lower.

EPS constitutes a safe and feasible tool in the diagnostic approach of phantom tachycardias. Of utmost importance, 2/3 of patients with non-documented palpitations had some form of inducible tachycardias, and AVNRT was the most frequent underlying arrhythmic mechanism. Treatment and management of patients with undocumented palpitations can safely be based on EPS findings. Furthermore, a probable "placebo effect" of EPS itself cannot be excluded. Ablation and non-dihydropyridine calcium channel antagonists seem to be the most promising therapeutic tools for reducing episodes of recurrence.

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