# Current strategy for treatment of patients with Wolff-Parkinson-White syndrome and asymptomatic preexcitation in Europe: European Heart Rhythm Association survey

Jesper Hastrup Svendsen<sup>1,2\*</sup>, Nikolaos Dagres<sup>3</sup>, Dan Dobreanu<sup>4</sup>, Maria Grazia Bongiorni<sup>5</sup>, Germanas Marinskis<sup>6</sup>, and Carina Blomström-Lundqvist<sup>7</sup> conducted by the Scientific Initiatives Committee, European Heart Rhythm Association

<sup>1</sup>Department of Cardiology, The Heart Centre, Section 2012, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK-2100 Copenhagen, Denmark; <sup>2</sup>The Danish National Research Foundation Centre for Cardiac Arrhythmia, DK-2100 Copenhagen, Denmark; <sup>3</sup>Second Cardiology Department, Attikon University Hospital, University of Athens, Haidiri, Greece; <sup>4</sup>Department of Cardiology, Center of Cardiovascular Disease and Transplant, University of Medicine and Pharmacy, Targu Mures, Romania; <sup>5</sup>Second Cardiology Department, University Hospital of Pisa, Pisa, Italy; <sup>6</sup>Clinic of Heart Diseases, Vilnius University Hospital Santariskiu Klinikos and Vilnius University, Vilnius, Lithuania; and <sup>7</sup>Department of Cardiology, Institution of Medical Science, Uppsala University, Uppsala, Sweden

Received 15 March 2013; accepted after revision 27 March 2013

The aims of this survey was to provide insight into treatment activity, the strategy of treatment, and risk stratification of patients with asymptomatic and symptomatic ventricular pre-excitation across Europe. Fifty-eight centres, members of the European Heart Rhythm Association EP research network, covering 20 countries answered the survey questions. All centres were high-volume ablation centres. A younger person with asymptomatic Wolff-Parkinson-White (WPW) pattern has a higher likelihood of being risk-stratified or receiving ablation therapy compared with an older subject. Two-thirds of centres report that they have observed a decline in the number of patients ablated for an accessory pathway during the last 10 years. Pre-excited atrial fibrillation is rarely seen. Discontinuation of a scheduled WPW ablation due to close vicinity of the accessory pathway to the AV node happens very rarely. Patients with a first episode of preexcited atrial fibrillation would immediately be referred for catheter ablation to be performed within weeks by 80.4% of the centres. A significant proportion of responders (50.9%) would use electrical cardioversion to restore sinus rhythm in a patient with pre-excited atrial fibrillation. With respect to the choice of antiarrhythmic medication for a patient with pre-excited AF, the majority (80.0%) would choose class 1C antiarrhytmic drugs while waiting for a catheter ablation. A patient seen in the emergency room with a second episode of orthodromic atrioventricular reentry tachycardia would be referred for immediate ablation by 79.2-90.6% of centres depending on the presence of pre-excitation. The volume of paediatric ablations performed on children younger than 12 years was low (46.4%: 0 patients per year; 46.4%: 1-9 patients per year). The majority of responding centres (61-69%) report that their country lack national guidelines dealing with clinical strategies related to WPW. There is a need for national guidelines dealing with clinical strategy in patients with WPW syndrome. Older individuals with asymptomatic WPW pattern have a higher risk of not receiving risk stratification or curative therapy with ablation compared with younger patients, despite the higher risk of developing atrial fibrillation.

**Keywords** 

WPW • Pre-excitation • Pre-excited atrial fibrillation • Ablation • European Heart Rhythm Association • Survey

#### Introduction

Wolff-Parkinson-White (WPW) syndrome is considered by many electrophysiologists the classical arrhythmic disease but it

still remains a challenge dealing with these patients. The anatomical substrate for WPW syndrome is an additional electrical connection between the atrium and ventricle or part of the conduction system. Patients with WPW syndrome have clinical

<sup>\*</sup> Corresponding author. Tel: +45 3545 2817, E-mail: hastrup@rh.dk

symptoms whereas subjects with signs of ventricular pre-excitation without symptoms have a so-called WPW pattern on the electrocardiogram (ECG).

An European Heart Rhythm Association (EHRA) Scientific Initiative Committee (SIC) survey on this topic from 2009 revealed that 44% of responding centres would choose an invasive electrophysiological test as the first-line approach for risk stratification of asymptomatic WPW patients.<sup>2</sup> Of note, 89% of centres reported that they considered the available guidelines to be insufficient.<sup>2</sup> Seventeen per cent of centres would perform ablation as the first-line strategy in asymptomatic patients whereas, in the other end of the spectrum, 8% did not perform risk stratification at all. Recently, the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS) have released guidelines on how to treat young asymptomatic individuals with WPW pattern.<sup>3</sup>

In this survey, we aimed at elucidating the current strategies in treatment of patients with both symptomatic and asymptomatic WPW syndrome and how these patients are managed across Europe.

## **Results**

Fifty-eight centres, which are members of the EHRA EP research network, responded to the survey and answered the questions. There was a wide geographic distribution of the responding centres (in total, 20 countries: 13 centres from Italy, 7 centres from Spain, 5 centres from Belgium, 4 from Denmark, 3 each from France, Greece, Poland, and Germany, 2 each from Tunisia, Estonia, and Sweden, and one centre from each of 9 other countries; 2 centres did not indicate the country).

More than two-thirds (70.7%) of the responding centres were university hospitals. The majority of responding centres were high-volume ablation centres (32.8% performed between 200 and 299 ablations in 2012 and 29.3% performed 400 or more ablations). Of note, all participating centres performed catheter ablations.

# Ablation procedures for Wolff-Parkinson-White syndrome

Thirty-six per cent of centres have reported that they have observed a definite decline (>25% decrease) in the number of patients ablated for an accessory pathway during the last 10 years (26.8% reported a slight decrease, i.e. a <25% decrease, whereas 17.9% believed that the number of procedures was unchanged).

The majority of centres (39.3%) performed ablation of an accessory pathway in 25-49 patients during the last year (50-74 patients: 21.4%; 75 or more: 8.9%). The distribution between overt WPW (56%) and concealed WPW (44%) during ablation was relatively equal. The majority of centres (41.8%) indicated that re-do ablation procedures corresponded to 2-4.9% of all ablations performed on accessory pathways (<1% of all procedures: 18% of responders; 1-1.9%: 21.8%).

Discontinuation of on-going WPW ablation due to the location of the accessory pathway very close to the atrioventricular (AV) node was reported to happen very rarely in 43.6% of the

responding institutions (never: 16.4%; rarely 16.4%; sometimes: 21.8%; often: 1.8%). If the accessory pathway was found during a catheter ablation to be close to the AV node, the majority (50.9%) would perform a staged energy delivery, 29.1% would switch to cryo-ablation during the same procedure, 3.6% would discontinue the procedure and not perform another later procedure, and 3.6% would refer the patient to another centre.

# Management of patients with atrial fibrillation with pre-excitation

A significant proportion of responders (55.4%) stated that preexcited atrial fibrillation was seen in <5% of patients who were treated with ablation for an accessory pathway (5–10% of patients: 26.8%; 11–20%: 8.9%).

There was a high degree of consent regarding the most likely treatment strategy for a patient seen at the respondent institution with a first episode of pre-excited atrial fibrillation since 80.4% would immediately refer the patient for catheter ablation to be performed within weeks (12.5% would refer for risk stratification; 3.6% would choose a wait and see approach). The majority of responders (50.9%) would use electrical cardioversion as a preferred method to restore sinus rhythm in a patient presenting in the emergency room with pre-excited atrial fibrillation, whereas 34.5% would choose pharmacological cardioversion with a class 1C antiarrhythmic drug; 10.9% would use amiodarone; 1.8% would use a beta-blocker. The preferred choice of an antiarrhythmic medication for a patient presenting with pre-excited AF, while waiting for a catheter ablation, was a class 1C antiarrhytmic drug, in the majority of cases (80.0%); in 25.5%, a beta-blocker was the preferred choice, and amiodarone in 20.0%, whereas none would choose dronedarone (note that several drugs in combination could be chosen).

Similarly, there was a high degree of consent regarding the most likely treatment strategy for a patient seen in the emergency room with a second episode of orthodromic atrioventricular reentry tachycardia (after restoration of sinus rhythm), since 79.2% of responders would refer the patient for immediate ablation in the absence of pre-excitation on the 12-lead ECG, whereas if pre-excitation was present 90.6% would refer for immediate ablation.

#### Risk stratification

With respect to risk stratification of an asymptomatic patient with a delta-wave on the ECG indicating the presence of an overt accessory pathway, there was a large variation in responses. Concerning risk stratification with an invasive electrophysiological study (EPS), the majority (30.2%) would never perform this as an isolated procedure although 17.0% would always do this, 24.5% would often do this, and 28.3% would rarely do it. The majority of responders (57.4%) would never use non-invasive EPS for risk stratification (9.3% would always do this, 13.0% would often do it, 20.4% would rarely). Concerning pharmacological testing as a method for risk stratification, 64.7% of responders would never perform this test (5.9% would often, 29.6% would rarely) do it. With respect to exercise testing for risk stratification, there were a large diversity since 25.0% would never perform this test

**752** J.H. Svendsen et al.

whereas 25.0% would always do it (23.1% would often, 26.9% would rarely).

# Ablation of for Wolff-Parkinson-White syndrome in young children

The volume of paediatric catheter ablations performed in children younger than 12 years was low (46.4% had none; while 46.4% had 1-9 patients per year). In this survey, we asked what the anticipated treatment strategy would be for a child presenting in the emergency room with symptomatic orthodromic AV reentry tachycardia and delta-waves on the 12-lead ECG during sinus rhythm and we asked for a score describing the agreement of the responder with a specific statement (score 1 indicates full disagreement whereas 5 indicates full agreement with the statement). Data are shown in Table 1. The majority (53.0%) would only perform ablation if the child was severely symptomatic (score 4 or 5). The majority (54.0%) would only perform ablation if the child was severely symptomatic despite medical treatment (score 4 or 5). The largest part of responders (62.0%) would only perform ablation if the child had a weight of >15 kg (score 4 or 5). Fourty-six per cent of the responders would only perform ablation if the parents expressed a strong wish for cure (score 4 or 5). However, the majority of responders would disagree with the statement 'I will wait with ablation until the child can make its own decision - preferably older than 18 years'; 33.3% answered score 1; and 21.6% answered score 2. A majority of responders (64.2%) fully disagreed with the sentence: 'I will refer the child to another centre and let them decide'.

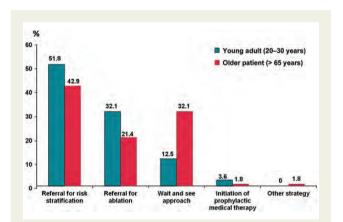
## Lack of guidelines

The majority of responding centres (61–69%) reported that their country lack national guidelines, which could potentially describe which patients would be candidates for ablation or give treatment advice for conversion of pre-excited atrial fibrillation, termination of AV reentry tachycardia and prophylactic antiarrhythmic therapy.

Figure 1 shows the differences in the preferred strategy for a young vs. an older individual with identical presentation including delta waves on the 12-lead ECG and without symptoms. It is clear that the younger person would have a higher likelihood of being risk-stratified or receiving ablation therapy.

## **Discussion**

The major finding from this EHRA EP network survey is that ablation in children with WPW is still performed in low numbers even in European high volume ablation centres, and the majority of centres will only perform ablation in children with overt WPW syndrome and recurrent episodes of AV reentry tachycardia if the patient is severely symptomatic and the child weights >15 kg. Patients with the potentially life-threatening pre-excited atrial fibrillation will have a very high likelihood of being referred for immediate ablation. However, older patients with asymptomatic ventricular pre-excitation have a lower likelihood of receiving catheter ablation or risk stratification testing compared with younger individuals with similar presentation, despite the fact that the older individual has a per se much higher risk of developing atrial fibrillation. Apparently, discontinuation of a WPW ablation due to proximity of the accessory pathway to the AV node occurs only rarely. There is still an unmet need for national



**Figure I** Response to the question: How do you anticipate a patient with accidentally diagnosed WPW pattern on electrocardiogram (without symptoms and without occupational risk) would be treated at your institution as preferred strategy? Results are given as per cent of responders. Columns indicated results for a young adult (20–30 years old) and an older person (>65 years of age).

Table I Anticipated treatment strategy for a child presenting at your emergency department with overt WPW (pre-excitation) and symptomatic orthodromic AV-reentry tachycardia

	Score 1 (fully disagree)	Score 2	Score 3	Score 4	Score 5 (fully agree)
Only ablation if severely symptomatic (%)	15.7	13.7	17.6	27.5	25.5
Only ablation if severely symptomatic despite medical therapy (%)	18.0	20.0	8.0	22.0	32.0
Only ablation if patient weighs >15 kg (%)	14.0	10.0	14.0	38.0	24.0
Only ablation if parents have a strong wish for cure (%)	16.0	14.0	24.0	32.0	14.0
I will wait with ablation until the child can make its own decision (ideally >18 years) (%)	37.4	17.6	13.7	13.7	17.6

In their answer to the question the responders should indicate to what degree they would agree with a statement. Score 1 indicates that the responder fully disagree with the statement, whereas score 5 indicates that the responder fully agrees with the statement.

guidelines dealing with the various clinical challenges related to WPW syndrome.

The majority of responding centres have observed a decline in ablation activity for WPW syndrome. Among patients treated by ablation of an accessory pathway, previous preexcited atrial fibrillation is a rarely occurring arrhythmia.

A previous Italian prospective study, which followed 293 asymptomatic patients with ventricular preexcitation (older than 18 years) after electrophysiological testing, found that during 67 months of follow-up, 17 patients had a potentially life-threatening arrhythmia. Predictors of these arrhythmias were age, inducibility during EPS, and anterograde effective refractory period of the accessory pathway shorter than 250 ms.<sup>4</sup> One small randomized study including a total of 72 asymptomatic patients with preexcitation has shown that 37 individuals who were randomized to prophylactic ablation had a lower event rate of arrhythmias compared with the group without ablation.<sup>5</sup> However, a large meta-analysis including 1869 patients with asymptomatic ventricular pre-excitation harvested from 20 studies with 11722 patient years of follow-up found a total of 10 cases of sudden cardiac death and a total of 156 supraventricular tachycardia events thereby questioning the need for aggressive therapy of asymptomatic individuals.<sup>6</sup> In general, children seem to have higher event rate than adults.<sup>6</sup> A small-scale randomized trial involving 47 children with asymptomatic pre-excitation showed that prophylactic ablation reduced the frequency of potentially life-threatening arrhythmia.<sup>7</sup> A long-term follow-up study in 184 children with an average age of 10 years with asymptomatic ventricular pre-excitation and an initial electrophysiological study showed that during a median follow-up of 57 months, 51 children had a first-time arrhythmic event, which was potentially life-threatening in 19.8 In their multivariate analysis, an anterograde refractory period of the accessory pathway <240 ms or multiple accessory pathways were independent predictors of potentially life-threatening arrhythmias.8 In a large series of 807 patients who underwent EPS for WPW syndrome, the incidence of induced antidromic tachycardia was relatively rare at 8%.9

In the 2009 EHRA survey on ventricular pre-excitaion, 69% centres would have referred patients with asymptomatic pre-excitation for risk stratification.<sup>2</sup> Today, a young asymptomatic patient would be risk-stratified or ablated in 84% of centres whereas an older similar subject would be risk-stratified or ablated in 64% of centres (*Figure 1*). The lower rate of intervention in older patients may raise some concerns when considering the higher risk of atrial fibrillation in elderly.

In the recent PACES/HRS expert consensus document on treatment of asymptomatic young WPW subjects, it is recommended that ablation should be considered in subjects between 8 and 21 years with asymptomatic WPW pattern if they have RR intervals shorter than 250 ms during atrial fibrillation due to increased risk of sudden cardiac death.<sup>3</sup> Apparently, based on this survey the treating physicians do not have problems with choosing

ablation therapy despite that the patient (a child) may not have been involved in the decision, and the majority do not consider it necessary to wait until the child is 18 years and has full legal responsibility.

### **Conclusion**

This survey revealed that electrophysiologists do not sufficiently take risk of atrial fibrillation into account when evaluating patients with asymptomatic ventricular pre-excitation as older patients have a lower likelyhood of being risk-stratified or receiving ablation compared with younger individuals. Pre-excited atrial fibrillation is uniformly treated across Europe with immediate ablation. There is an unmet need for national (and international) guidelines for management of patients with WPW syndrome.

## **Acknowledgements**

The production of this EP Wire document is under the responsibility of the Scientific Initiatives Committee of the European Heart Rhythm Association: Carina Blomström-Lundqvist (chairman), Maria Grazia Bongiorni, Nikolaos Dagres, Dan Dobreanu, Thorsten Lewalter, Gregory YH Lip, Philippe Mabo, Antonio Madrid, Germanas Marinskis, Laurent Pison, Alessandro Proclemer, and Jesper Hastrup Svendsen.

The authors acknowledge the EHRA Research Network centres participating in this EP Wire. A list of the Research Network centres can be found on the EHRA website.

Conflict of interest: none declared.

#### References

- Scheinman MM. History of Wolff–Parkinson–White syndrome. Pacing Clin Electrophysiol 2005;28:152–6.
- Cantú F, Goette A. EHRA Scientific Initiatives Committee. Sudden cardiac death stratification in asymptomatic ventricular preexcitation. Europace 2009;11:1536–7.
- 3. Cohen MI, Triedman JK, Cannon BC, Davis AM, Drago F, Janousek J et al. PACE/ HRS Expert Consensus statement on the management of the asymptomatic young patient with a Wolff-Parkinson-White (WPW, preexitation) electrocardiogram pattern. Heart Rhytm 2012;9:1007-24.
- Santinelli V, Radinovic A, Manguso F, Vicedomini G, Ciconte G, Gulletta S et al. Asymptomatic ventricular preexcitation: a long-term prospective follow-up study of 293 adult patients. Circ Arrhythmia Electrophysiol 2009;2:102–7.
- Pappone C, Santinelli V, Manguso F, Augello G, Santinelli O, Vicedomini G et al.
   A randomized study of prophylactic catheter ablation in asymptomatic patients with the Wolff–Parkinson–White syndrome. N Engl J Med 2003;349:1803–11.
- Obeyesekere MN, Leong-Sit P, Massel D, Manlucu J, Modi S, Krahn AD et al. Risk of arrhythmia and sudden death in patients with asymptomatic preexcitation: a meta-analysis. Circulation 2012;125:2308–15.
- Pappone C, Manguso F, Santinelli R, Vicedomini G, Sala S, Paglino G et al. Radiofrequency ablation in children with asymptomatic Wolff–Parkinson–White syndrome. N Engl J Med 2004;351:1197–205.
- Santinelli V, Radinovic A, Manguso F, Vicedomini G, Gulletta S, Paglino G et al. The natural history of asymptomatic ventricular pre-excitation a long-term prospective follow-up study of 184 asymptomatic children. J Am Coll Cardiol 2009;53:275–80.
- 9. Brembilla-Perrot B, Pauriah M, Sellal JM, Zinzius PY, Schwartz J et al. Incidence and prognostic significance of spontaneous and inducible antidromic tachycardia. *Europace* 2013;doi:10.1093/europace/eus354. Published online ahead of print 12 November 2012.