Pre-excitation Syndrome: When not to ablate

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Epidemiology

• The incidence of manifest pre-excitation on ECG tracings in the general population is 0.1% to 0.3%.

• SVT is the most common tachyarrhythmia in pre-excitation:
  – 90-95% orthodromic AVRT
  – 5% pre-excited AVRT

• However, not all patients with manifest ventricular pre-excitation develop PSVT

VENTRICULAR FIBRILLATION IN THE WOLFF–PARKINSON–WHITE SYNDROME

George J. Klein, M.D., Thomas M. Bashore, M.D., T. D. Sellers, M.D., Edward L. C. Pritchett, M.D., William M. Smith, Ph.D., and John J. Gallagher, M.D.

INCIDENCE OF SPONTANEOUS ARRHYTHMIAS

LOCATION OF ACCESSORY PATHWAYS
Recommendation for Ongoing Management of Orthodromic AVRT

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-NR</td>
<td>1. Catheter ablation of the accessory pathway is recommended in patients with AVRT and/or pre-excited AF (103,254,276-282).</td>
</tr>
<tr>
<td>Iib</td>
<td>B-R</td>
<td>1. Oral dofetilide or sotalol may be reasonable for ongoing management in patients with AVRT and/or pre-excited AF who are not candidates for, or prefer not to undergo, catheter ablation (99,106).</td>
</tr>
<tr>
<td>Iib</td>
<td>C-LD</td>
<td>2. Oral amiodarone may be considered for ongoing management in patients with AVRT and/or pre-excited AF who are not candidates for, or prefer not to undergo, catheter ablation and in whom beta blockers, diltiazem, flecaïnide, propafenone, and verapamil are ineffective or contraindicated (289,290).</td>
</tr>
<tr>
<td>Iib</td>
<td>C-LD</td>
<td>3. Oral beta blockers, diltiazem, or verapamil may be reasonable for ongoing management of orthodromic AVRT in patients with pre-excitation on their resting ECG who are not candidates for, or prefer not to undergo, catheter ablation (46,287).</td>
</tr>
<tr>
<td>Iib</td>
<td>C-LD</td>
<td>4. Oral digoxin may be reasonable for ongoing management of orthodromic AVRT in patients without pre-excitation on their resting ECG who are not candidates for, or prefer not to undergo, catheter ablation (292).</td>
</tr>
<tr>
<td>Iib</td>
<td></td>
<td>1. Oral digoxin is potentially harmful for ongoing management in patients with AVRT or AF and pre-excitation on their resting ECG (271).</td>
</tr>
</tbody>
</table>

On going Management of Orthodromic AVRT

When not to ablate Pre-excitation?

- Asymptomatic or Isolated pre-excitation?
- The abnormal pre-excitation ECG pattern in the absence of documented SVT or symptoms consistent with SVT.
Recommendations for Long-Term Therapy of Accessory Pathway–Mediated Arrhythmias

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ACC/AHA/ESC PRACTICE GUIDELINES—FULL TEXT

ACC/AHA/ESC Guidelines for the Management of Patients With Supraventricular Arrhythmias*

A Report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular Arrhythmias)

Developed in Collaboration with NASPE-Heart Rhythm Society

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Pre-excitation, asymptomatic

Catheter ablation

IIa

B

(222, 225, 284-290)
Abrupt loss of pre-excitation

Loss of Pre-excitation During Long-term Follow Up of Asymptomatic Pre-excitation

Incidence of AF During Long-term Follow Up of Asymptomatic Pre-Excitation

Risk of SVT among Asymptomatic Pre-excitation Patients

Risk of SCD of Asymptomatic Pre-excitation Patient

Overall Risk of Sudden Cardiac Death

Event rate per 1,000 patient years = 1.25 (95% Confidence Interval 0.57 to 2.19). Heterogeneity p = 0.2, I² = 20%.

Study (reference) | Event rate per 1,000 patient years
--- | ---
Munger (2) | 3.25 (2.00 to 5.00)
Pappone (5) | 2.50 (1.00 to 5.00)
Pappone (6) | 2.75 (1.25 to 5.00)
Santinelli (14) | 2.00 (1.00 to 3.50)
Milstein (15) | 2.25 (1.00 to 5.00)
Klein (16) | 1.50 (0.50 to 3.50)
Satoh (17) | 1.75 (1.00 to 3.00)
Beckman (18) | 2.00 (1.00 to 3.50)
Leitch (19) | 1.25 (0.50 to 2.50)
Brembilla-Perrot (20) | 1.25 (0.50 to 2.50)
Vignati (21) | 1.75 (1.00 to 3.00)
Goudevenos (22) | 1.50 (0.50 to 4.00)
Sarubi (23) | 1.25 (0.50 to 2.50)
Brembilla-Perrot (24) | 1.25 (0.50 to 2.50)
Fazio (25) | 1.00 (0.50 to 2.00)
Santinelli (26) | 1.25 (0.50 to 2.50)
Fitzsimmons (27) | 1.00 (0.50 to 2.00)
Inoue (28) | 1.25 (0.50 to 2.50)
Fukatani (29) | 1.00 (0.50 to 2.00)
Smith (30) | 1.00 (0.50 to 2.00)

Summary | 3.00 (1.00 to 5.00)

Event Rate per 1,000 Patient-Years of Follow-up with 95% Confidence Intervals

Conclusions—The prognosis of the Wolff-Parkinson-White syndrome essentially depends on intrinsic electrophysiological properties of AP rather than on symptoms. RFA performed during the same procedure after electrophysiological testing is of benefit in improving the long-term outcomes. (Circulation. 2014;130:811-819.)
Question

What is the usefulness of:

invasive EP study

versus

noninvasive testing or no testing

for predicting arrhythmic events (including SCD) in patients with asymptomatic pre-excitation?
Usefulness of Invasive Electrophysiologic Testing to Stratify the Risk of Arrhythmic Events in Asymptomatic Patients With Wolff-Parkinson-White Pattern

Results From a Large Prospective Long-Term Follow-Up Study

Carlo Pappone, MD, PhD, Vincenzo Santinelli, MD, Salvatore Rosanio, MD, PhD, Gabriele Vicedomini, MD, Stefano Nardi, MD, Alessia Pappone, MD, Valter Tortoriello, MD, Francesco Manguso, MD, PhD, Patrizio Mazzone, MD, Simone Gulletta, MD, Giuseppe Oreo, MD, Ottavio Alfieri, MD

Milan, Italy

OBJECTIVES

The aim of this study was to assess in a large cohort of asymptomatic subjects with Wolff-Parkinson-White (WPW) pattern the usefulness of invasive electrophysiologic testing (EPT) in predicting the occurrence of arrhythmic events over a five-year follow-up.

BACKGROUND

Sudden death may be the first clinical manifestation of the WPW syndrome in previously asymptomatic patients. Serial EPTs have been proposed to identify patients at risk.

METHODS

A total of 212 consecutive asymptomatic WPW patients were enrolled after a baseline EPT; patients were followed for five years, and 162 patients (115 noninducible and 47 inducible) patients underwent a second EPT.

RESULTS

After a mean follow-up of 37.7 months, 33 patients became symptomatic. Of the 115
Asymptomatic Ventricular Preexcitation
A Long-Term Prospective Follow-Up Study of 293 Adult Patients

Vincenzo Santinelli, MD; Andrea Radinovic, MD; Francesco Manguso, MD; Gabriele Vicedomini, MD; Giuseppe Ciconte, MD; Simone Gulletta, MD; Gabriele Paglino, MD; Stefania Sacchi, MD; Simone Sala, MD; Cristiano Ciaccio, MD; Carlo Pappone, MD

Background—Sudden cardiac death can be the first clinical presentation of asymptomatic ventricular preexcitation.

Methods and Results—From 1995 to 2005, we prospectively collected clinical and electrophysiological data among 293 adults with asymptomatic ventricular preexcitation (61.4% males; median age, 36 years; interquartile range [IQR], 28 to 47.5). After electrophysiological testing, patients were prospectively followed, taking no drugs. The primary end point of the study was the occurrence of a first arrhythmic event. Predictors of arrhythmic events were analyzed by univariate and multivariate Cox models. Over a median follow-up of 67 months (minimum to maximum, 8 to 90), after electrophysiological testing, 262 patients (median age, 37 years; IQR, 30 to 48) did not experience arrhythmic events, remaining totally asymptomatic, whereas 31 patients (median age, 25 years; IQR, 22 to 29; median follow-up, 27 months; minimum to maximum, 8 to 55) had a first arrhythmic event, which was potentially life-threatening in 17 of them (median age, 24 years; IQR, 20 to 28.5; median follow-up, 25 months; minimum to maximum, 9 to 55). Potentially life-threatening tachyarrhythmias resulted in resuscitated cardiac arrest (1 patient), presyncope (7 patients) syncope (4 patients), or dizziness (5 patients). In multivariate analysis age \( P = 0.004 \), inducibility \( P = 0.001 \) and anterograde effective refractory period of the accessory pathway \( \leq 250 \text{ ms} \ (P = 0.001) \) predicted potentially life-threatening arrhythmias.

Conclusions—These results indicate that prognosis of adults who present with asymptomatic ventricular preexcitation is good, and the risk of a significant event is small. Short anterograde effective refractory period of the accessory pathway and inducibility at baseline are independent predictors of potentially life-threatening arrhythmic events, and the risk decreases with increasing age. (Circ Arrhythmia Electrophysiol. 2009;2:102-107.)
Question

What are the **efficacy and effectiveness of:**

invasive EP study + catheter ablation of the accessory pathway

versus

noninvasive tests with treatment (including observation) or no testing/ablation

for preventing arrhythmic events (including SCD) and improving outcomes in patients with asymptomatic pre-excitation?
RCT of Prophylactic Ablation in High Risk Asymptomatic Pre-excitation

Freedom from Malignant Arrhythmias and VF in Pre-excitation: RFA vs. No RFA

OBJECTIVE  To review the literature systematically to determine whether noninvasive or invasive risk stratification, such as with an electrophysiological study of patients with asymptomatic pre-excitation, reduces the risk of arrhythmic events and improves patient outcomes.

METHODS  PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials (all January 1, 1970, through August 31, 2014) were searched for randomized controlled trials and cohort studies examining noninvasive or invasive risk stratification in patients with asymptomatic pre-excitation. Studies were rejected for low-quality design or the lack of an outcome, population, intervention, or comparator of interest or if they were written in a language other than English.

RESULTS  Of 778 citations found, 9 studies met all the eligibility criteria and were included in this paper. Of the 9 studies, 1 had a dual design—a randomized controlled trial of ablation versus no ablation in 76 patients and an uncontrolled prospective cohort of 148 additional patients—and 8 were uncontrolled prospective cohort studies (n=1,594). In studies reporting a mean age, the range was 32 to 50 years, and in studies reporting a median age, the range was 19 to 36 years. The majority of patients were male (range, 50% to 74%), and <10% had structural heart disease. In the randomized controlled trial component of the dual-design study, the 5-year Kaplan-Meier estimates of the incidence of arrhythmic events were 7% among patients who underwent ablation and 77% among patients who did not undergo ablation (relative risk reduction: 0.08; 95% confidence interval: 0.02 to 0.33; p<0.001). In the observational cohorts of asymptomatic patients who did not undergo catheter ablation (n=883, with follow-up ranging from 8 to 96 months), regular supraventricular tachycardia or benign atrial fibrillation (shortest RR interval >250 ms) developed in 0% to 16%, malignant atrial fibrillation (shortest RR interval ≤250 ms) in 0% to 9%, and ventricular fibrillation in 0% to 2%, most of whom were children in the last case.

CONCLUSIONS  The existing evidence suggests risk stratification with an electrophysiological study of patients with asymptomatic pre-excitation may be beneficial, along with consideration of accessory-pathway ablation in those deemed to be at high risk of future arrhythmias. Given the limitations of the existing data, well-designed and well-conducted studies are needed.
Sistematic Review on Asymptomatic Pre-excitation Management

- Data from observational studies on 883 patients who did not undergo ablation:
  - up to 9% developed malignant arrhythmias
  - up to 2% developed VF
- Very low risk of complications of EP study
- Risk stratification using an EP study may be beneficial, with consideration of accessory pathway ablation in those deemed to be at high risk of future arrhythmia

Al Khatib et al. JACC. 2016: 67: 1624-38
## Recommendation Management of Asymptomatic Pre-excitation

<table>
<thead>
<tr>
<th>Level</th>
<th>Evidence</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>I</td>
<td>B-NR&lt;sup&gt;SR&lt;/sup&gt;</td>
<td>1. In asymptomatic patients with pre-excitation, the findings of abrupt loss of conduction over a manifest pathway during exercise testing in sinus rhythm (294-297) (Level of Evidence: B-NR)</td>
</tr>
<tr>
<td>I</td>
<td>C-LD&lt;sup&gt;SR&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR&lt;sup&gt;SR&lt;/sup&gt;</td>
<td>1. An EP study is reasonable in asymptomatic patients with pre-excitation to risk-stratify for arrhythmic events (254,256,298-301).</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR&lt;sup&gt;SR&lt;/sup&gt;</td>
<td>2. Catheter ablation of the accessory pathway is reasonable in asymptomatic patients with pre-excitation if an EP study identifies a high risk of arrhythmic events, including rapidly conducting pre-excited AF (254,302,303).</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR&lt;sup&gt;SR&lt;/sup&gt;</td>
<td>3. Catheter ablation of the accessory pathway is reasonable in asymptomatic patients if the presence of pre-excitation precludes specific employment (such as with pilots) (103,254,276-282,302-304).</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR&lt;sup&gt;SR&lt;/sup&gt;</td>
<td>4. Observation, without further evaluation or treatment, is reasonable in asymptomatic patients with pre-excitation (301,306-309).</td>
</tr>
</tbody>
</table>

19 yo Male, rejected to enter Flight School due to Asymptomatic Preexcitation
My Approach

1. Observe/Non-invasive Testing
2. EP Study
   a) High Risk: Ablation
   b) Low Risk:
      i. No Ablation: Delta wave
      ii. Ablation: Normal SR ➔ become a good Pilot.
Conclusion

• All pre-excitation syndrome (incl. asymptomatic patient) warrant EP Study with consideration of accessory-pathway ablation in those deemed to be at high risk of future arrhythmias.

• Asymptomatic patient with low risk arrhythmic events: (may be) no ablation
Thank You