
Developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), the American Academy of Pediatrics (AAP), and the Canadian Heart Rhythm Society (CHRS)

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Preamble
The purpose of this consensus statement is to provide up-to-date clinical practice guidelines on the evaluation and management of the asymptomatic young patient with a Wolff-Parkinson-White (WPW) electrocardiographic (ECG) pattern. The terminology WPW was first used to describe a “bundle-branch pattern” with a short PR interval in healthy young people prone to paroxysmal tachycardia and/or atrial fibrillation. Although isolated case reports preceded the 1930 landmark manuscript, history correctly credits its identification of the syndrome to Drs. Wolff, Parkinson, and White. Over the years, the syndrome evolved through observations by anatomists and electrophysiologists to appreciate a reentrant circuit involving both the AV node–His axis as well as the accessory pathway. Isolated ventricular preexcitation refers to the abnormal ECG pattern in the absence of any clinical cardiovascular symptoms. Isolated

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Ablation; HRS/PACES Consensus Statement; Preexcitation; Wolff-Parkinson-White syndrome (Heart Rhythm 2012;9:1006–1024)

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ventricular preexcitation has historically been termed “asymptomatic WPW” or asymptomatic WPW syndrome. This manuscript provides guidelines only for individuals with an abnormal ECG pattern of ventricular preexcitation without symptoms. In response to recently published literature regarding patients with WPW, the Pediatric and Congenital Electrophysiology Society (PACES) in conjunction with the Heart Rhythm Society (HRS) created a writing committee to provide helpful clinical guidelines for asymptomatic patients with WPW. There are at present no specific guidelines addressing risk stratification in the asymptomatic young patient with WPW. Selected members from within PACES and HRS have reviewed and analyzed the published scientific literature, carefully assessing the absolute and relative risks of invasive procedures and therapies so as to provide a practical approach to optimize patient care.

This consensus statement is directed at all health care professionals who treat young patients with WPW. For the specific purpose of this statement, the young patient is defined as being between 8 and 21 years of age, an age span routinely cared for by pediatricians and pediatric cardiologists and generally considered old enough to undergo exercise testing and catheter ablation if indicated. A specific care plan for a particular patient must be made by the health care provider, the patient, and his or her parents after careful consideration and a thorough discussion of patient characteristics that impact on risks and benefits. For the purposes of this document, we defined “consensus” as 75% or greater agreement by the writing members. Writing committee members were selected by PACES or HRS based on their expertise in the field. The 11 pediatric electrophysiologists on the writing committee included representatives from the United States, Canada, Australia, and Europe. The writing committee members were tasked with performing a formal literature review and then weighing the strength of the evidence for or against an observational strategy or a particular procedure in the evaluation and management of asymptomatic patients with a WPW ECG pattern (isolated ventricular preexcitation). Although this document does discuss symptomatic patients with WPW, it does so in the construct of establishing a framework into the historical armamentarium of noninvasive and invasive studies that have been utilized for risk assessment. This document does not address management strategies for symptomatic patients with WPW.

The committee was divided into subgroups to best review key aspects of the evaluation and management of WPW. These sections included detailed reviews and assessments of (1) natural history, (2) noninvasive risk stratification, (3) invasive risk stratification, (4) risks of ablation, (5) WPW and congenital heart disease, and (6) WPW and attention-deficit/hyperactivity disorder. For purposes of this consensus statement the committee defined asymptomatic WPW as individuals without any cardiovascular complaints (chest pain, palpitations, presyncope, and/or syncope) or documented tachycardia.

Methods and evidence
The recommendations listed in this document are, whenever possible, evidence-based. An extensive literature search was performed. The committee also reviewed documents related to the subject matter as previously published by HRS, the American College of Cardiology (ACC), the American Heart Association (AHA), and the European Heart Rhythm Association (EHRA). The committee reviewed and ranked evidence supporting current recommendations based on a standard process as previously described and summarized here (Methodology Manual and Policies from the ACCHF and AHA Task Force on Practice Guidelines June 2010).

A. Classification of Recommendations
- Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment plan is beneficial, useful, and effective
- Class II: Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure or treatment
  - Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy
  - Class IIb: Usefulness/efficacy is less well established by evidence/opinion
- Class III: Conditions for which there is conflicting evidence and/or general agreement that a procedure or treatment is not useful/effective and in some cases may be harmful

B. Level of Evidence
- Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses
- Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies
- Level of Evidence C: Only consensus opinion of experts, case studies, or standard of care
- Level of Evidence D: Expert opinion without studies

Document review and approval
This document was reviewed by the executive committee within PACES, none of whom were on the writing committee, as well as by additional members of HRS. All writing members approved the final version. The writing committee thanks all reviewers for their comments and suggestions, many of which were incorporated into this manuscript. Disclosures for writing members and reviewers are in the Appendix.

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1. Introduction
Since Wolff, Parkinson, and White published their sentinel paper in 1930, much has been learned about the anatomy, electrophysiology, and natural history of accessory connections exhibiting antegrade conduction. Classically, patients with Wolff-Parkinson-White (WPW) syndrome presented with palpitations or presyncope caused by an atroventricular (AV) reciprocating tachycardia or, less commonly, a primary atrial tachycardia. Rapid conduction of atrial fibrillation (AF) over the accessory pathway resulting in ventricular fibrillation (VF) is rare but unfortunately may be the first manifestation of WPW syndrome, even in the young. Refinements in catheter ablation equipment and techniques have rendered ablation a highly effective therapy for WPW in children.

In recent years, the use of electrocardiograms (ECGs) for screening prior to sports participation, medical and surgical procedures, and initiation of some medications has identified increasing numbers of asymptomatic individuals with a WPW ECG pattern. The optimum management of these patients is not known. Although successful catheter ablation is capable of eliminating the risk of sudden death in the asymptomatic child with a WPW ECG pattern, uniform referral of every child for an ablation could also result in serious and potentially life-threatening complications, possibly greater in number than the deaths averted from untreated disease. A PACES position statement for the use of radiofrequency ablation (RFA) in children was published nearly 10 years ago and classified asymptomatic preexcitation in children >5 years to be a Class IIB indication for RFA. No recommendations were given with regard to the evaluation, either noninvasive or invasive, and risk stratification for those young individuals. The arrhythmia task force from the committee forming guidelines for sports recommendations in patients with cardiac disease at the 36th Bethesda Conference recommended consideration of a more in-depth evaluation of individuals with asymptomatic WPW prior to sports participation, including evaluation by an electrophysiologic study before allowing participation in moderate-to-severe high-intensity competitive sports, but there were no recommendations for individuals not participating in sports. Due to the increased awareness of sudden unexpected death in the medical and lay communities, the real but small risk of sudden unexplained death with asymptomatic WPW, and the controversial literature regarding asymptomatic WPW in recent years, PACES working in concert with HRS formed a committee to review the subject and develop guidelines for pediatric and adult electrophysiologists and cardiologists. The purpose of the current paper is to develop updated practice guidelines for the management of the asymptomatic pediatric and young adult patient with a WPW ECG pattern (isolated ventricular preexcitation).

2. Natural history and presentation of WPW
The natural history of the asymptomatic patient with WPW is extrapolated from data on symptomatic patients and from asymptomatic patients discovered by fortuitous ECG testing. In large-scale general population studies involving children and adults, the prevalence of WPW is estimated to be 1–3 in 1000 individuals. Familial studies have shown an incidence of 5.5 in 1000 among first-degree relatives following an index case of WPW. Identification of the truly asymptomatic patient with WPW is difficult, as these individuals are by definition without palpitations, syncope, or other symptoms secondary to ventricular preexcitation. At present, it is estimated that approximately 65% of adolescents and 40% of individuals over 30 years with a WPW pattern on a resting ECG are asymptomatic. The majority of patients with WPW have normal cardiac anatomy. Accessory pathways are thought to be an embryologic remnant, as substantiated by diagnosis of supraventricular tachycardia (SVT) in utero and by a greater prevalence of WPW in newborns and infants. WPW also occurs in patients with myopathic and structural congenital heart disease (CHD), most notably in patients with Ebstein anomaly. Uncommonly, ventricular preexcitation may coexist with cardiac rhabdomyoma. These accessory pathways are usually discovered in newborns, are associated with tumors located at the AV groove or septum, and likely are due to disruption of the electrical integrity of the AV annulus rather than being true accessory pathways. Hypertrophic cardiomyopathy may be associated with WPW, often in the setting of specific gene mutations.

The presentation of symptomatic WPW in those with a normal heart is age-dependent and may vary with accessory pathway location and properties. In infancy, the diagnosis is typically made following an episode of AV reciprocating tachycardia. Although episodes of SVT often decrease in frequency in the first year of life (>90% of patients), tachycardia recurs in approximately 30% at an average age of 7–8 years. Furthermore, there is evidence that in the first
year of life the accessory pathway loses anterograde conduction in as many as 40% of patients, and SVT becomes noninducible in a similar percentage, suggesting loss of retrograde conduction as well. If WPW and tachycardia coexist in an individual beyond 5 years of age, they continue to be present more than a decade later in more than 75% of individuals. Young adults with WPW typically present with arrhythmia symptoms, but the prevalence of documented SVT is lower. Up to 31% of adults may lose the capacity for ventricular preexcitation and anterograde conduction over a 5-year time period. The loss of preexcitation in children and adolescents over a similar time period is variable (0%–26%). This observation may reflect the loss of preexcitation in younger children compared to a preadolescent or adolescent population.

Rarely patients present with WPW due to the hemodynamic effects of preexcitation alone. This is presumed to be due to dyssynchronous ventricular contraction associated with a highly preexcited rhythm. Tomaske et al found an improvement in ejection fraction after ablation of septal accessory pathways in pediatric patients. The prevalence of septal pathways in the cases reported with dysfunction may relate to the pattern of ventricular activation in these specific pathways, but data are limited.

Most worrisome are the uncommon presentations of syncope or aborted sudden cardiac arrest as the first manifestation of WPW syndrome. The mechanism of sudden death in patients with WPW syndrome is very rapid conduction of atrial flutter and AF, which provokes VF. Although most WPW patients resuscitated from a sudden cardiac death (SCD) event have had prior symptoms, VF or a cardiac arrest may be the sentinel event, particularly in children.

The earliest evidence for higher risk in asymptomatic children was actually somewhat overlooked. In 1979, Klein et al reported on 25 patients with WPW who presented with VF; the only previously asymptomatic patients all were children, ages 8, 9, and 16 years. In 1993, Russell et al reported on life-threatening presentations in a group of 256 children. In 1996, Bromberg et al reported that from a group of 60 children ≤18 years of age with varying risk undergoing WPW surgery, 2 of 10 high-risk patients had a documented VF arrest as their initial presentation. Although none of these retrospective studies followed a cohort of asymptomatic children with WPW to look for events, the data strongly suggest that the incidence of life-threatening symptoms in asymptomatic children with a WPW ECG pattern may be much higher than in adults. This may be because all asymptomatic adults with a WPW ECG pattern by definition have survived childhood without any symptoms, demonstrating a lower risk.

While population studies have yielded variable estimates of the incidence of life-threatening arrhythmias leading to sudden death in WPW, the majority of studies have reported a very low incidence of SCD (Table 1).

An incidence of 4.5 episodes of sudden death, including resuscitated SCD, per 1000 patient-years was recently reported in a prospective study of asymptomatic adults with WPW followed for a mean of 38 months. Furthermore, individuals lacking symptoms are not free of the possibility of developing SVT. In a large community-based combined adult and pediatric WPW population study, none of the 53 asymptomatic individuals (mean age 35 ± 16 years) died suddenly, although approximately one-third of individuals <40 years of age became symptomatic with either documented SVT or palpitations. While the majority of these natural history studies (Table 1) support an excellent prognosis in asymptomatic patients with WPW, the studies have several limitations: variable length of follow-up, variable percentages of asymptomatic and symptomatic patients, and variable percentages of patients <21 years of age.

Intertwined with SCD and developing reentrant SVT is the natural history of WPW patients developing AF. In two separate combined adult and pediatric studies involving 386 patients followed for 10 years, 15% developed spontaneous AF, with 4 having SCD (ages 20, 31, 34, 71 years). In

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Years studied</th>
<th>Age</th>
<th>Follow-up (y)</th>
<th>Died</th>
<th>SCD per patient-year</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berkman (1968)</td>
<td>128</td>
<td>1933–1968</td>
<td>21</td>
<td>20</td>
<td>3</td>
<td>0.0039</td>
<td></td>
</tr>
<tr>
<td>Leitch (1990)</td>
<td>75</td>
<td>1980–1988</td>
<td>34</td>
<td>± 13</td>
<td>4.3</td>
<td>0.0000</td>
<td></td>
</tr>
<tr>
<td>Klein (1989)</td>
<td>27</td>
<td>1981–1989</td>
<td>45</td>
<td></td>
<td>4.5</td>
<td>0.0000</td>
<td></td>
</tr>
<tr>
<td>Munger (1993)</td>
<td>113*</td>
<td>1953–1989</td>
<td>33</td>
<td>± 16</td>
<td>12</td>
<td>0.0015</td>
<td></td>
</tr>
<tr>
<td>Inoue (2000)</td>
<td>57</td>
<td>1985–1993</td>
<td>10.2</td>
<td></td>
<td>8</td>
<td>0.0000</td>
<td></td>
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<td>Goudevenos (2000)</td>
<td>157</td>
<td>1990–1997</td>
<td>20</td>
<td></td>
<td>4.6</td>
<td>0.0000</td>
<td></td>
</tr>
<tr>
<td>Fitzsimmons (2001)</td>
<td>238*</td>
<td>1955–1999</td>
<td>34.3</td>
<td></td>
<td>21.8</td>
<td>0.0002</td>
<td>SCD patient had SVT and atrial fibrillation</td>
</tr>
<tr>
<td>Sarubbi (2003)</td>
<td>98</td>
<td>1985–2001</td>
<td>5.4</td>
<td></td>
<td>4</td>
<td>0.0019</td>
<td></td>
</tr>
<tr>
<td>Pappone (2003)</td>
<td>212</td>
<td>1993–1996</td>
<td>36</td>
<td>± 21</td>
<td>3.2</td>
<td>0.0150</td>
<td>2 patients had VF and were resuscitated</td>
</tr>
<tr>
<td>Santinelli (2009)</td>
<td>184</td>
<td>1995–2005</td>
<td>10</td>
<td></td>
<td>4.6</td>
<td>0.0000</td>
<td>3 patients had VF and were resuscitated</td>
</tr>
</tbody>
</table>

Age is expressed as mean or median (years).
SCD = sudden cardiac death; SVT = supraventricular tachycardia; VF = ventricular fibrillation.
*Combined asymptomatic and symptomatic patients.
a recent study of 709 patients (ages 34 ± 16 years) with WPW undergoing electrophysiologic (EP) testing, AF was the initial presentation in 44 patients. AF was inducible in 17% (42/248) of asymptomatic patients compared to 25.5% (24/94) with a history of syncope. Spontaneous AF was observed in 10% of patients <18 years of age, and the location of the accessory pathway was not predictive of AF. Determining which WPW patients are at highest risk for life-threatening arrhythmia by history alone remains a dilemma, but in the absence of noninvasive and invasive testing the reported warning flags appear to be younger age (<30 years), \( \text{male gender,}^{2,3,28,37} \) history of AF, \( \text{prior syncpe,}^{2} \) associated congenital or other heart disease, \( \text{familial WPW}^{14} \).

3. Risk stratification in WPW

In current practice the intent of risk stratification in asymptomatic children with a WPW ECG pattern is to identify which individuals are at risk for a lethal cardiac arrhythmia. In its simplest form, risk stratification utilizes noninvasive testing (eg, Holter or exercise stress test) to ascertain true loss of preexcitation at physiological heart rates. Inability to clearly demonstrate absolute loss of manifest preexcitation warrants consideration for more invasive EP testing. The critical obligatory condition for VF is the presence of a short anterograde functional refractory period of the accessory pathway as reflected in the shortest R-R interval between preexcited beats in AF. Invasive EP testing should include measurement of the shortest preexcited R-R interval during induced AF in addition to determination of the number and location of accessory pathways, the anterograde and retrograde characteristics of the accessory pathway(s) and AV node, and the effective refractory period of the accessory pathway(s) (APERP) and of the ventricle at multiple cycle lengths.

4. Noninvasive evaluation of WPW patients

ECG

The ECG during preexcited AF affords a “true” assessment of the anterograde characteristics of the accessory pathway. The measurement of the Shortest Pre-Excited R-R Interval (SPERRI) has been used to determine accessory pathway properties; however, much of the literature is based on invasive studies. A SPERRI of 220–250 ms and especially less than 220 ms is more commonly seen in patients with WPW who have experienced cardiac arrest. Conversely, intermittent loss of preexcitation during sinus rhythm suggests that the risk of cardiac arrest is low. The phenomenon of intermittent preexcitation is poorly understood but is likely related to the refractory period of the accessory pathway as well as the cellular connectivity within the pathway, \( \text{resulting in variable conduction.} \)

The variation can be within a few beats, captured on a single ECG or at disparate points in time, determined on ambulatory monitoring or serial ECGs. The incidence of intermittent preexcitation in one study of WPW using ambulatory monitoring was as high as 67%. \( \text{Although intermittent preexcitation is a predictor of poor anterograde conduction through the accessory pathway,}^{43,44,48} \) it has been observed, on rare occasions, in some patients with cardiac arrest. \( \text{Intermittent preexcitation does not exclude patients from developing SVT. In a large study of primarily military aviators followed over 2 decades, 23% with constant preexcitation developed reentrant SVT in comparison to the 8.3% who only exhibited intermittent preexcitation.}^{49} \)

The presence of multiple accessory pathways has been identified as a risk factor for VF. \( \text{The appearance of different preexcited morphologies on an ECG or ambulatory monitoring confers higher risk and individuals are less likely to be asymptomatic.}^{51} \) Approximately 5%–10% of patients with a WPW pattern may present with preexcited tachycardia, allowing for an understanding of the anterograde conduction properties of the accessory pathway. \( \text{Serial ambulatory ECG monitoring may be used to screen for paroxysmal AF, especially in asymptomatic patients with a WPW ECG pattern who may not be cognizant of brief atrial arrhythmias. The occurrence of paroxysmal AF in asymptomatic patients with WPW may be dependent on the frequency of noninvasive surveillance. In a prospective study of 184 asymptomatic children with WPW followed for 5 years, biannual Holter monitors identified paroxysmal AF in 22 patients (12%),}^{29} \) significantly higher than the spectrum of Holter findings in asymptomatic adults with WPW. \( \text{Medication challenge} \)

Although no longer routinely utilized, sodium channel-blocking agents have been used to determine the properties of an accessory pathway. Gaita et al \( ^{54} \) reported on 65 patients with a WPW pattern, 15 of whom were asymptomatic. Subjects underwent EP study, stress testing, and pharmacologic challenge with procainamide and propafenone. Accessory pathway block with medication challenge was associated with a longer APERP at EP study. \( \text{However, the specificity of loss of preexcitation after administration of sodium-blocking medication was poor compared to the shortest preexcited R-R intervals during inducible AF.}^{54-57} \)

Exercise testing

Disappearance of preexcitation during exercise testing has been proposed as a surrogate method of assessing the accessory pathway refractory period. \( \text{Delta wave behavior during exercise is dependent upon the relative effects of sympathetic stimulation on accessory pathway refractoriness and AV nodal conduction. More rapid AV nodal conduction at higher exertion levels may mask persistent preexcitation through a left-sided accessory pathway, even when subtle clues for WPW are sought.}^{59} \) Daubert et al \( ^{60} \) demonstrated that \text{only abrupt and complete} \text{loss of preexcitation during exercise confirmed a long anterograde APERP. In a predominantly adult prospective study, persistence of preexcitation during exercise stress showed a sensitivity of 96% but a specificity of only 17% in predicting either a SPERRI in AF \( \approx 250 \text{ ms or an APERP of } \approx 250 \)}}
ms. The positive predictive value was 40% and the negative predictive value was 88%. Of note, preexcitation disappeared suddenly in exercise in only 1 of 24 patients with SPERRI/ERP \( \leq 250 \) ms, and this was the patient with the shortest SPERRI (180 ms) in the series.54

Abrupt disappearance of preexcitation during stress testing occurred in only 15% of a predominantly pediatric group of patients.61 Interobserver reliability of loss of delta wave was imperfect, likely related to the difficulties in discerning subtle preexcitation when partially masked by rapid AV nodal conduction. Individuals with abrupt loss of preexcitation on exercise had a statistically longer APERP, though reports of subjects with an APERP of 260 ms were still noted in children who were deemed to have loss of preexcitation on the treadmill. Chimienti et al62 compared exercise testing to an isoproterenol infusion in 20 subjects with a WPW pattern; they found that the APERP did not correlate well with the SPERRI during AF, except under the influence of isoproterenol.

5. Rationale, definition, and techniques for an invasive EP study

In the absence of a clear understanding of the accessory pathway anterograde characteristics by noninvasive testing, invasive testing should be considered. The purpose of such an invasive EP study in asymptomatic patients with a WPW ECG pattern is to identify a potential subgroup of patients who may be at increased risk for lethal cardiac arrhythmias and in whom the risk-to-benefit ratio favors ablation. In adults with asymptomatic preexcitation, 70% of electrophysiologists recently surveyed supported risk stratification and prophylactic ablation.63 In a separate survey of 43 pediatric electrophysiologists, 84% used some form of an EP study to risk-stratify asymptomatic children with WPW,64 with 77% affirming RFA would be indicated when the shortest preexcited R-R interval in AF is \(< 240 \) ms. Utilization of an APERP \(< 240 \) ms or induction of SVT as an indication for RF ablation was only noted in 47% and 26%, respectively.

For this document, EP testing will be defined as “invasive” when it is performed using either intracardiac or esophageal catheters. Protocols for both esophageal and intracardiac studies are well described, and anterograde characteristics of the accessory pathway are well correlated between the two approaches.65,66 However, transesophageal pacing is less effective in its ability to discern multiple accessory pathways, the evaluation of retrograde conduction, and the precise location of the accessory pathway, and would require intracardiac catheter placement if ablation was to be performed during the same procedure. Nonetheless, these two techniques utilize a similar approach to determine the inducibility of AV reciprocating tachycardia, AF, determination of APERP, 1:1 preexcited conduction of atrially paced rhythm, SPERRI in induced AF, and use of isoproterenol. Isoproterenol almost uniformly results in shortening of the anterograde refractory period of the accessory pathway and an increase in ventricular rates during atrial pacing and AF.67 Because of this effect and the fact that the value of isoproterenol in risk stratification has not been clearly determined from a prospective trial, risk profile is generally determined at baseline. Sustained AF or AV reciprocating tachycardia is defined as a tachycardia lasting longer than 1 minute; however, controversy exists as to the duration of induced tachycardia that is considered pathologic, varying between 30 seconds and 5 minutes.68

6. EP risk stratification of WPW

6.1 Symptomatic patients

In clinical studies of adult WPW patients, a SPERRI \( \leq 220–250 \) ms during AF has been shown to be the best discriminator of those at risk of VF.3,4,55 Based on combined pediatric and adult studies (age range 5–68 years; mean 28 years), the APERP is less useful because it (1) is less predictive of life-threatening events (range 180–310 ms) than the SPERRI in AF and (2) is similar between patients with WPW and VF and those with WPW and AV reentrant SVT, but without VF.3,4 In symptomatic patients the presence of multiple accessory pathways and possibly septal bypass tracts may be a separate risk factor for the development of VF.2–4,69 Multiple accessory pathways may also be a determinant of susceptibility to AF independent of degeneration to VF.70

The sensitivity of SPERRI in AF is 88%–100% for identifying symptomatic adults at risk for VF,3,4,55 but because of the low incidence of cardiac arrest in these patients, the positive predictive value of a SPERRI \(< 220 \) ms in adults is only 19%–38%.4,55 This low positive predictive value in adults, especially those over 40 years, has been used to argue against routine use of invasive EP testing to identify the at-risk cohort.3,17,71,72

Bromberg et al37 evaluated symptomatic children with WPW \( \leq 18 \) years of age and grouped patients into those with documented VF, syncpe or spontaneous AF, and isolated reentrant SVT. All patients with clinical VF or asystole in whom AF was inducible at EP testing had a SPERRI \(< 220 \) ms (sensitivity 100%) compared to a SPERRI \(< 220 \) ms in 74% and 35% in the other groups. This study suggested that a SPERRI \(< 220 \) ms carried a threefold increase in the risk of SCD compared to the general WPW population. Paul et al73 performed invasive EP studies in 74 symptomatic children with WPW. Induction of sustained AF was noted in 9 of 14 patients with syncpe but in none of the 60 patients without syncpe. All patients with syncpe and AF had a SPERRI \( \leq 220 \) ms (sensitivity 100%). Of the 34 patients without syncpe but with inducible nonsustained AF, 9 had a SPERRI \( \leq 220 \) ms (specificity 74%). Caution in attributing syncpe to WPW is warranted because vasovagal syncpe is very common and not infrequently the cause of syncpe in these patients.

In children, APERP as an isolated variable was of little prognostic value for risk of syncpe,73 AF,74 or SVT75 and is less well correlated with VF than the SPERRI in AF.4 While the EP properties of the accessory pathway may change over time,28,76 in those patients with a short APERP
(<260 ms) significant lengthening to alter potential risk over time is rare. Finally, Teo reported that the presence of multiple accessory pathways in conjunction with a SPERRI <250 ms achieved a specificity of 92% and a positive predictive value for future arrhythmic events in 22%.

6.2. Asymptomatic patients

The purpose of invasive EP evaluation of the asymptomatic patient with WPW diagnosed by ECG is to identify elevated risk for SCD. Correlation of symptoms with EP indices has varied between studies. Santinelli et al observed that younger age, a shorter refractory period of the accessory pathway, and multiple accessory pathways correlated with clinical symptoms, while Dubin et al found that a short refractory period and presence of multiple accessory pathways were not associated with clinical symptoms. Similarly, symptoms have been shown to be similar in children with WPW and inducible AF and those without atrial vulnerability.

Patients with intermittent preexcitation or accessory pathways with decremental conduction generally have poor anterograde conduction characteristics and possibly carry a lower risk of SCD. However, the conduction properties of septal accessory pathways in particular can be quite variable, with septal pathways exhibiting loss of preexcitation on ambulatory monitoring at a range of heart rates far slower than preexcited R-R intervals during AF. Patients lacking retrograde conduction via the accessory pathway at the time of EP testing similarly appear to be at lower risk for SCD. Leitch et al evaluated 75 asymptomatic adults with WPW and observed lack of a functional retrograde limb in 27%. Approximately 20% of asymptomatic adults may lose their capacity for anterograde conduction, rendering them at negligible risk for SCD. Despite this potentially favorable natural history in adults >35 years of age, some asymptomatic adults with WPW may have EP indices that harbor a concern for the possibility of SCD in the future. A SPERRI <250 ms has been noted in 20%–26% of asymptomatic adults with a WPW pattern.

Confirming these findings, Delise et al compared symptomatic and asymptomatic young adults with WPW by endocardial stimulation and observed that the prevalence of AF and SPERRI <250 ms were not different between the two groups; however, retrograde conduction of the accessory pathway was significantly more prevalent in symptomatic patients (100% vs 22%).

In a prospective study evaluating the prognostic value of a transesophageal evaluation at rest and during effort in young asymptomatic athletes with WPW pattern, Bertaglia et al showed that, although there were no deaths, rapid anterograde conduction of the accessory pathway was observed in 30% of patients. The combination of rapid anterograde conduction, vulnerability to AF, and retrograde conduction of the accessory pathway was found in a significantly higher percentage of patients <25 years of age compared to those >25 years of age.

In a study of 21 asymptomatic adults with a WPW ECG pattern, administration of isoproterenol during invasive EP assessment significantly shortened the SPERRI from 264 to 219 ms, resulting in 67% of patients showing a SPERRI ≤250 ms on isoproterenol compared to 33% at baseline. Use of isoproterenol during EP testing in children has been advocated as a possible surrogate of adrenergic stimulation for testing done under anesthetic conditions. However, there are little natural history data in children and young adults with aborted SCD whose EP studies were performed with isoproterenol. Moore et al recently reported on 151 children with WPW, who underwent invasive EP testing with and without isoproterenol under general anesthesia with propofol, of whom 27 were asymptomatic. They showed that isoproterenol significantly reduced the APERP, minimum cycle length for 1:1 preexcitation during atrial pacing, and the SPERRI in both symptomatic and asymptomatic patients, increasing the percentage of patients with SPERRI ≤250 ms from around 7 to 38. In the asymptomatic group APERP decreased by 74 ± 92 ms, the minimal cycle length for 1:1 preexcitation during atrial pacing decreased by 110 ± 102 ms, and SPERRI decreased by 88 ± 57 ms. Further, there was no correlation between the EP characteristics on isoproterenol and past symptoms, and there were no organized follow-up data.

Three important studies on WPW therapy and the risk of sudden death have recently been published by a single group of investigators in Milan, Italy. The first was a prospective study of 212 asymptomatic adult WPW patients of whom 33 became symptomatic over a 5-year period. Those patients had a shorter APERP at baseline (246 vs 283 ms) and during isoproterenol infusion (203 vs 225 ms). The combination of a short APERP and inducibility of SVT had a positive predictive value of 47% with a negative predictive value of 97% in regard to subsequent arrhythmic events (most commonly, occurrence of SVT). There were three initially asymptomatic patients with an APERP <200 ms and a SPERRI <230 ms who subsequently developed VF.

In the second Milanese study, clinical and invasive EP data were collected on 184 asymptomatic children with WPW with a median follow-up of 5 years. In comparison with those who remained asymptomatic, the 51 patients who later became clinically symptomatic were observed to have significantly different EP indices, including an APERP ≤240 ms (89% vs 17%), multiple accessory pathways (47% vs 6.0%), and an intact AV reentrant SVT circuit (84% vs 23%). Three patients experienced VF, but all three were successfully resuscitated without neurologic sequelae. Interestingly, all three children had documented preexcited AF with rapid ventricular response that degenerated to VF just prior (1 patient) or at hospital admission (2 patients). All 3 had high-risk accessory pathway characteristics at the initial EP study (APERP <220 ms and SPERRI <200 ms), and all subsequently underwent successful ablations. In evaluating an anterograde APERP ≤240 ms for assessment of risk for VF there was excellent sensitivity (100%) and...
negative predictive value, but low specificity (25%) and positive predictive value in affirming its role for identifying patients at low risk for VF. This study population is remarkable for the high rate of major clinical events compared to other studies of larger WPW populations in adults.

In a separate prospective clinical trial, 47 asymptomatic children with a WPW pattern at high risk for arrhythmias (inducible AF or SVT) were randomized to ablation or observation.\textsuperscript{50} During 3 years of follow-up, 7 children developed symptoms, 2 having AF with rapid ventricular response. Five others were observed to have silent AF on ambulatory monitors and 1 died suddenly, a potentially important observation. Multiple accessory pathways conferred increased risk for developing arrhythmias.\textsuperscript{50} It is worth noting that in each of these studies, the life-threatening event rate was substantially higher than a meta-analysis that followed 749 adults for a total of 6726 years without any cases of SCD.\textsuperscript{83}

Using invasive evaluation of the accessory pathway in asymptomatic children with WPW whose preexcitation persists beyond the elementary school year and exhibit persistent preexcitation at higher heart rates, 25% may have short refractory periods of the pathway even in the absence of an inducible reciprocating tachycardia during the EP study.\textsuperscript{67} Sarubbi et al.\textsuperscript{50} followed 98 asymptomatic children with a WPW pattern over 4 years. SVT was inducible in 48% of patients at the initial EP study, but during follow-up only 5 patients developed SVT (4 SVT, 1 AF). The minimal atrial paced cycle length with sustained preexcitation was shorter in children who subsequently became symptomatic (236 ms) than in those who did not (276 ms), a finding consistent with previously mentioned adult studies. One previously asymptomatic patient whose parents refused therapy recommended for rapid anterograde EP conduction indices died suddenly at 8 years of age. Inability to induce SVT conferred a good prognosis regardless of the anterograde accessory pathway properties.

To summarize the data for the value of invasive EP testing to identify risk in patients with symptomatic WPW, the sensitivity and negative predictive value of a SPERRI ≤250 ms is high, but the specificity and positive predictive value are appreciably lower. Further, in asymptomatic adults and children, the specificity and positive predictive value are even lower because the incidence of subsequent sudden death is so low (Table 2). Although isoproterenol clearly raises the sensitivity for events in symptomatic patients by placing many more patients in a high-risk category, it markedly reduces the specificity of invasive EP testing. These observations apply to both adults and children; however, there is far less natural history data in children, and the prognostic value of the addition of isoproterenol for risk stratification has not been adequately studied in any group.

### 6.3. Risks of invasive EP study

The results of EP testing using programmed atrial and/or ventricular stimulation assist in risk stratification of asymptomatic patients with WPW and elucidate the mechanism of SVT in those with palpitations. While complications of an invasive EP study are infrequent, patients exposed to such invasive testing undergo a procedure to assess risk for potentially life-threatening arrhythmias but may receive no direct benefit from ablative therapy. The risk of femoral

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**Table 2  Invasive electrophysiologic parameters in asymptomatic children and young adults with WPW pattern**

<table>
<thead>
<tr>
<th>Author</th>
<th>Pts</th>
<th>Age (y)</th>
<th>F/U</th>
<th>APERP</th>
<th>SPERRI ≤240</th>
<th>SPERRI ≤250</th>
<th>Inducible SVT</th>
<th>PPV of SCD (SPERRI ≤250)</th>
<th>NPV of SCD (SPERRI ≤250)</th>
<th>VF arrest</th>
<th>Actual death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pappone</td>
<td>212</td>
<td>36</td>
<td>3</td>
<td>275 ± 34</td>
<td>47 (22%)</td>
<td>12 (9%)</td>
<td>77 (42%)</td>
<td>3/48**</td>
<td>136/136**</td>
<td>3*</td>
<td></td>
</tr>
<tr>
<td>Santinelli</td>
<td>184</td>
<td>10</td>
<td>4.7</td>
<td>270 (240–290)</td>
<td>48 (26%)</td>
<td>23 (31%)</td>
<td>22 (29%)</td>
<td>0/23</td>
<td>49/49</td>
<td>0 0</td>
<td></td>
</tr>
<tr>
<td>Dubin</td>
<td>23</td>
<td>12</td>
<td>2.5</td>
<td>12</td>
<td>2 (9%)</td>
<td>14 (61%)</td>
<td>16 (38%)</td>
<td>0/7</td>
<td>35/35</td>
<td>0 0</td>
<td></td>
</tr>
<tr>
<td>Leitch</td>
<td>72</td>
<td>34</td>
<td>4.3</td>
<td>293 (280–310)</td>
<td>274 (240–325)</td>
<td>23 (31%)</td>
<td>22 (29%)</td>
<td>0/23</td>
<td>49/49</td>
<td>0 0</td>
<td></td>
</tr>
<tr>
<td>Beckman</td>
<td>15</td>
<td>33</td>
<td>7.5</td>
<td>356 ± 194</td>
<td>438 ± 106</td>
<td>2 (13%)</td>
<td>3 (20%)</td>
<td>0/2</td>
<td>13/13</td>
<td>0 0</td>
<td></td>
</tr>
<tr>
<td>Milstein</td>
<td>42</td>
<td>36</td>
<td>2.4</td>
<td>333 ± 106</td>
<td>277 ± 48</td>
<td>7 (17%)</td>
<td>16 (38%)</td>
<td>0/7</td>
<td>35/35</td>
<td>0 0</td>
<td></td>
</tr>
<tr>
<td>Satoh</td>
<td>34</td>
<td>36</td>
<td>1.3</td>
<td>252 ± 23</td>
<td>3 (9%)</td>
<td>12 (55%)</td>
<td>0/3</td>
<td>31/31</td>
<td>0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brembilla</td>
<td>40</td>
<td>35</td>
<td>1.8</td>
<td>240 (230–270)</td>
<td>234 (150–650)</td>
<td>7 (18%)</td>
<td>7 (18%)</td>
<td>0/7</td>
<td>33/33</td>
<td>0 0</td>
<td></td>
</tr>
<tr>
<td>Pappone</td>
<td>27</td>
<td>10</td>
<td>1.6</td>
<td>240 (230–270)</td>
<td>230 (215–230)</td>
<td>10 (44%)</td>
<td>14 (40%)</td>
<td>1*</td>
<td>3*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pappone</td>
<td>35</td>
<td>22</td>
<td>5</td>
<td>240 (230–260)</td>
<td>240 (225–250)</td>
<td>14 (40%)</td>
<td>14 (40%)</td>
<td>1*</td>
<td>3*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bertaggia</td>
<td>88</td>
<td>20</td>
<td>3.8</td>
<td>27 (30%)</td>
<td>0/27</td>
<td>61/61</td>
<td>1 0</td>
<td>0 0</td>
<td>0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fazio</td>
<td>8</td>
<td>7.8</td>
<td>4.2</td>
<td>2 (25%)</td>
<td>2 (25%)</td>
<td>0 (0%)</td>
<td>0/2</td>
<td>1</td>
<td>0 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarubbi</td>
<td>35</td>
<td>10</td>
<td>7.4</td>
<td>276 ± 39</td>
<td>238 ± 9</td>
<td>5 (14%)</td>
<td>17 (48%)</td>
<td>1/5</td>
<td>30/30</td>
<td>1 1</td>
<td></td>
</tr>
</tbody>
</table>

\*AF = atrial fibrillation; APERP = accessory pathway effective refractory period; EP = electrophysiologic; NPV = negative predictive value; PPV = positive predictive value; SPERRI = shortest pre-excited RR in atrial fibrillation; WPW = Wolff-Parkinson-White; Other abbreviations as in Table 1.

*Data are from 2 controls at EP study.
†Data are from 21 controls at EP study.
‡Data based on esophageal EP study.
\#Data are from 18 patients without SVT and/or AF.
\$Data are from 17 patients with SVT and/or AF.
\^Data are from 22 patients on Isuprel.

A portion of this table was previously published (Copyright Permission: Journal of Cardiovascular Medicine 2007;8:668–674).
venous occlusion and/or formation of an arteriovenous fistula is 2% and is more frequent in children weighing <10 kg. In two large studies focusing on >1300 adult patients, complications related to EP procedures included venous thrombosis (1%), pulmonary emboli (0.3%–1.6%), thrombophlebitis (0.6%), infection (0.8%), and catheter-induced permanent complete AV block (0.1%). All EP studies, transesophageal or intracardiac, may result in induction of VF, even in those who are asymptomatic. The amount of radiation exposure for a diagnostic EP catheterization is relatively small but needs to be taken into context in patients who have other sources of radiation exposure. Radiation exposure generally is avoided by the use of transesophageal pacing.

7. Catheter ablation: success rates, risks, and other considerations
Since it was first introduced for WPW in the pediatric population in 1990, RFA has offered a potential definitive cure for arrhythmias that could previously be treated only with medications, DC ablation, or surgery. RFA is now widely accepted as a therapy for WPW and is frequently considered to be first-line therapy. This is due to high success rates and a low-risk profile, particularly when the use of cryoablation is included for septal accessory pathways and those near small coronary arteries. The success rates, risks, and other lifestyle considerations, including the potential cure for a chronic illness, are important issues when deciding whether a particular patient is a candidate for catheter ablation therapy. A thorough understanding of the current state of catheter ablation therapy is critical to the recommendation of this procedure to the family of an asymptomatic pediatric patient with WPW syndrome.

7.1. Efficacy of catheter ablation
Shortly after the first pediatric RFA procedure, members of the Pediatric Electrophysiology Society established the Pediatric Radiofrequency Ablation Registry. The Registry provided valuable insight into the progress of catheter ablation therapy and prompted the Prospective Assessment of Pediatric Cardiac Ablation study (PAPCA).

Registry data through the mid-1990s demonstrated a success rate for RFA of accessory AV pathways of 91% in pediatric patients. Similar to that observed in studies involving adult patients, success rates varied by arrhythmia substrate location. The recurrence rate following a successful accessory pathway ablation during this era was a remarkably high 23% at 3-year follow-up. The presence of structural heart disease has been shown to be a predictor of lower success rates. Institutional experience strongly affects procedural success rates, with pediatric procedural experience conferring success rates >90%. To further evaluate the issue of operator experience, the Registry data were divided into an early era (1991–1995) and a later era (1996–1999) for RFA of SVT. Overall, there was a significant increase in ablation success rates from 90% in the early era to 95.2% in the later era. Compared with all substrates during these two periods, success rates for procedures involving an accessory pathway were evaluated, the success rate increased from 89% to 94%. A decrease in the complication rate from 4.3% to 2.9% in patients who underwent catheter ablation for an accessory pathway was observed in this study, and fluoroscopy times were shortened by 21% but were still remarkably high with a mean of 40.1 minutes.

In the subsequent PAPCA study, the overall success rate of ablated substrates study was 95.7%, with a success rate of 93% for manifest accessory pathways. The overall recurrence rate at 1-year follow-up reported in the prospective study was 10.7%, more favorable than previously reported. Most of the recurrences occurred during the first 2 months following the ablation procedure. The recurrence rate for manifest accessory pathways was 11.3%, with the lowest recurrence rate for left lateral and left septal accessory pathways and the highest recurrence rate for right lateral and septal accessory pathways. Similar results with RFA were more recently published (2007) in a combined pediatric and adult publication of 508 patients with accessory pathways. Acute success rates were 94.9% across all locations (highest for left free wall, midseptal, and right free wall locations). Right anteroseptal accessory pathways were successfully ablated 78.5% of the time. Despite, reasonable RFA success across all locations, recurrent accessory pathway conduction was observed in 24.2%, 16.7%, 14.3%, 13%, and 5% for right free wall, midseptal, right anteroseptal, posteroseptal, and left free wall accessory pathways.

Several studies from individual pediatric centers reported success rates for ablation of WPW. Acute success rates of 92%–100% and recurrence rates of 0%–13% were reported in these smaller studies. Factors identified as contributing to a lack of long-term success included the presence of underlying structural heart disease and the presence of more than one accessory pathway. Similar results with RFA in pediatric patients with WPW have never been differentiated between patients with and without symptoms.

Ablation outcomes in the very young child
SVT due to WPW in infancy can usually be managed medically and tends to become less frequent after the first few months of life. However, there exists a subset of young patients with medically refractory arrhythmias, complex substrates (multiple accessory pathways and/or CHD), and severe symptoms who could potentially benefit from catheter ablation therapy. Studies from the Registry have suggested that the rates of successful ablation are probably similar to that seen in older children, but the rates of adverse events may be higher. However, Blaufox et al. did not find any significant differences between patients less than 18 months when analyzing registry data. As experience is still limited and varied, indications for ablation are more conservative in infants and young children, and an asymptomatic WPW ECG pattern is generally not considered to be an indication for risk stratification or ablation.
7.2. Cryoablation

Cryoablation has been widely applied in pediatric practice in an attempt to further enhance the safety of the procedure, especially in those with septal accessory pathways or in close proximity to the coronary sinus. In 2006, the first study to evaluate outcomes in pediatric patients with manifest septal accessory pathways alone reported a similar acute success rate to RFA (88%), but with higher rates of recurrence. Although not statistically significant, success rates increased from 74% to 83% and recurrence rates decreased modestly from 57% to 33% over the course of the institution’s experience, suggesting that operator experience and modifications to the procedure may lend to improved outcomes. Similar results were reported by the investigators of a multicenter study involving patients who underwent cryoablation for both manifest and concealed accessory pathways located within the coronary sinus. Sequentially, other centers have shown promising results with cryoablation in pediatric patients with accessory pathways at all AV valve annuli locations, especially with increased institutional experience and modifications to the procedure. Based on the reported recurrence rates following an acutely successful cryoablation, data suggest that a greater number and longer cryoablation applications may lead to improved efficacy and fewer recurrences of accessory AV pathway conduction. In fact in a recent study 24 left-sided accessory pathways were successfully ablated with cryo-application with only 1 recurrence. In 2010, Sacher et al reported a 7-year multicenter study of 89 patients with WPW who failed a prior ablation. Although 91% were successfully ablated using multiple approaches (steerable sheaths, irrigated-tip catheters, cautious RF titration), parahisian and midseptal accessory pathways continued to pose a significant challenge. Cryoablation was used in 7 patients with an acute success in 6; however, recurrences within 30 days were appreciated in 3 patients. Follow-up cryoablation data in children will need to be tracked to assess true efficacy and risk compared to both diagnostic EP testing without ablation as well as RF application.

7.3. Risks and complications

Serious adverse events attributed to catheter ablation are AV block, cardiac perforation, coronary artery involvement, and thromboembolic events. Early registry studies reported an overall complication rate of 3.2% using a very inclusive definition of adverse events, which lumped major and minor events. Second- or third-degree AV block occurred in 0.7% and thrombus formation or thromboembolic event occurred in 0.3%. The PAPCA study reported a complication rate of 4.0% (based on the EP study and the RF ablation) and included no deaths. Right bundle branch block was reported in 0.5%, left bundle branch block in 0.1% of patients, and valvular regurgitation in 0.3% of patients. Hematoma at the catheter entry site was the most common complication reported (1.4%). AV block occurred in 0.9% of patients with manifest accessory pathways, but only in patients with a right or left septal pathway.

Some investigators have demonstrated that RFA and prolonged intravascular catheterization may be thrombogenic. Factors involved with thrombus formation during RFA include hyperthermia-induced coagulation and tissue necrosis, and endothelial injury. Thromboembolic events have been reported to occur in 0.6%–0.8% of procedures. The consequences of systemic embolization are greater when ablation is performed within the left-sided heart chambers and for ventricular tachycardia. In a multicenter study that included children and only reported events during ablation of SVT due to accessory pathway-mediated tachycardia or AV nodal reentrant tachycardia, the incidence of embolic complications with temperature-controlled RFA was 0.7%. The risk of thromboembolic events was not eliminated by anticoagulation protocols or number of RF lesions or mode of temperature-controlled ablation.

Patient weight of <15 kg was identified as a risk factor for a higher complication rate, but later studies no longer reported a statistically significant higher incidence of complications in smaller patients. The complications that occurred in the infant group did not appear to be related to age, weight, the presence of structural heart disease, or operator experience. A subsequent report of complications during RFA procedures in small children suggested that the incidence was related to RF energy dose, lesion number, and total application time, indexed for body size. As might be expected, infants with an accessory pathway had a higher complication rate when the substrate was at a septal location, primarily due to the incidence of AV block, than at other sites.

Coronary artery injury has been reported after RF ablation for accessory pathway-mediated tachycardias in children, adults, and various animal studies secondary to thermal injury to the coronary artery wall. These cases have involved both left- and right-sided coronary arteries as well as posterior descending branch of the right coronary artery during ablation of a posterior septal AP. The exact clinical incidence and significance are not known since the occurrence has mostly been described anecdotally and no large-scale studies assessing the risk by serial selective coronary angiography are available. In a large retrospective study of 250 patients with WPW in which there were no coordinated attempts to investigate coronary artery injury after RF ablation, the reported incidence of injury was 0.8%. However, in a study in which coronary angiography was performed before and after RF ablation for accessory pathway-mediated tachycardias, Solomon et al reported a 1.3% incidence of coronary artery injury in 70 patients.

There may be a time-dependent factor with regard to the clinical detection of coronary arterial narrowing following RF ablation. Animal studies have shown coronary artery effects both early and late after RFA. The inflammatory component of tissue injury caused by RF energy has been shown to invade layers of the right coronary artery, leading to acute narrowing when RF energy is applied to the atrial side of the lateral tricuspid annulus in pigs. Further maturation of this injury can result in significant late steno-
The highest incidence of coronary artery damage has been reported in patients with CHD, specifically Ebstein anomaly of the tricuspid valve. One center reported a prospectively identified incidence of coronary artery injury of 1.7% (2/117) in patients with a structurally normal heart and a posteroseptal accessory pathway. Reports of coronary artery stenosis have been identified by post-RFA angiography. Unless coronary artery injury is actively sought, it may be undiagnosed and underreported. Smaller children may be at particular risk for coronary artery injury, because the distance between the ablation catheter and the coronary arteries is significantly less than in adults. Coronary artery distance from endocardial ablation sites also varies in young patients and is correlated to accessory pathway location.

Death has been reported as a complication of pediatric RFA due to cardiac perforation, myocardial trauma, coronary or cerebral thromboembolism, and ventricular arrhythmia. The overall incidence reported in the largest cohort (7600 procedures) of pediatric patients by the Registry was 0.22%. The incidence was 0.12% in children between the ages of 0.1 to 13.3 years with a structurally normal heart and 0.89% in those with structural heart disease. Of the patients with a structurally normal heart, 4 of the 5 patients in whom mortality occurred were undergoing catheter ablation of an accessory pathway mechanism. In the Registry report, mortality was more frequent in patients with structural heart disease, smaller patients, those who received a greater number of RF energy applications, and those undergoing left-sided procedures.

Radiation exposure during fluoroscopy is important to consider when recommending catheter ablation therapy. Fluoroscopy times can be particularly lengthy during technically challenging procedures, such as those involving a right lateral free wall accessory pathway. The recent incorporation of nonfluoroscopic imaging techniques, such as three-dimensional electroanatomic mapping, has contributed to decreased radiation exposure during fluoroscopy but has not at present replaced the use of fluoroscopy for all WPW substrates.

8. Special issues
8.1. WPW and CHD
The association of ventricular preexcitation and WPW with CHD is well known. In a study of infants with WPW, 20% had CHD. Ventricular preexcitation is most often associated with Ebstein anomaly, seen in as many as 44%, but has also been described in patients with D-TGA, pulmonary atresia/intact ventricular septum, patent ductus arteriosus, parachute mitral valve, tetralogy of Fallot, total anomalous pulmonary venous return, and a ventricular septal defect. As one might suspect, AV reentrant tachycardia in the presence of CHD is more likely to be hemodynamically unstable, prompting early antiarrhythmic therapy or ablation. However, in a study of adult and pediatric WPW patients, comparing those with and without Ebstein anomaly, no significant difference was seen concerning preablation arrhythmias, antiarrhythmic drugs, cardiac arrest, documented AV reentrant tachycardia, or AF. There is also a higher risk of atrial arrhythmias in patients with Ebstein anomaly of the tricuspid valve, which, in the presence of ventricular preexcitation, places the patient at a potentially higher risk of lethal ventricular arrhythmias. Finally, in patients who undergo staged palliation for CHD having single ventricle physiology, intracardiac access is limited after the bidirectional Glenn stage. Due to the concerns of poorly tolerated SVT in patients with WPW and CHD, several authors have proposed preoperative invasive testing and ablation to prevent perioperative or postoperative compromise.

The small amount of invasive data available on WPW and CHD are primarily from patients with Ebstein anomaly. Most accessory pathways in this disease are right-sided, and many patients have multiple pathways. In a retrospective study comparing WPW patients with and without Ebstein anomaly, those with Ebstein anomaly had significantly longer AV reentrant cycle lengths (359 vs 310 ms), but no difference was seen in the shortest preexcited complexes during AF (215 vs 218 ms). Early data (1998) from the Pediatric RF Ablation Registry of 65 patients with Ebstein anomaly undergoing RFA reported acute success rates and recurrence rates for right free wall, right septal, and other locations of 79%/32%, 89%/29%, and 75%/27%. Multiple pathways were observed in 49% of patients, and a relatively large percentage (22%) were ablated for life-threatening arrhythmias.

In addition to structural congenital heart defects, ventricular preexcitation has also been described in cardiomyopathy patients. Several gene mutations have been associated with ventricular preexcitation, including PRKAG2 and AMPK. Most of these cardiomyopathies appear to be hypertrophic and progressive but, as opposed to the traditional myocardiopathy disarray seen in sarcomeric protein hypertrophic cardiomyopathy abnormalities, the hypertrophy associated with ventricular preexcitation appears to be secondary to intracellular accumulation of glycogen, as in the case of AMPK, amylopectin. It is not entirely clear whether the ventricular preexcitation seen in the PRKAG2 and AMPK mutations is mediated by an accessory pathway, but arrhythmias are common and include sinus node dysfunction, AF, accelerated AV nodal conduction, and AV block. SCD is well described in this patient population, but the correlation of sudden death with ventricular preexcitation is similarly unclear.

8.2. Asymptomatic WPW and attention-deficit/hyperactivity disorder
Attention-deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral disorder in childhood. Stimulant medications are an important component of the treatment plan for patients with ADHD. With the high prevalence of ADHD within the pediatric population, a significant number of patients with WPW will likely be candidates for treatment with ADHD medications. Although this writing committee does not advocate electrocardiographically screening patients starting treatment with stimulants, if patients starting treatment with stimulants are screened electrocardiographically, it will increase identification of asymptomatic patients with a WPW ECG pattern.
ADHD medications increase the heart rate on average 1 to 2 bpm and the systolic blood pressure 3–4 mm Hg. Although statistically significant, the clinical implications of these changes in heart rate and blood pressure are minimal in most patients, while some will have larger changes that may need to be addressed. In a study of 584 children on Adderall XR, no clinically significant changes in mean ECG parameters were observed over the duration of the study. Further, in all cases where abnormalities occurred, the findings were deemed harmless, clinically insignificant, or normal by pediatric cardiologists. Although a number of case reports of sudden death in patients taking ADHD medications and structural cardiac abnormalities or a family history of ventricular arrhythmias were identified by the Food and Drug Administration (FDA), there are currently no specific reports of SCD in patients with WPW receiving ADHD medications [http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4210b-index.htm].

Further, the FDA Adverse Event Reporting System reported rates of sudden deaths from 1992–2004 less than the background rates of sudden death reported in the literature for both adults and children. Although the FDA concluded there was no evidence that adverse cardiac events in patients on methylphenidate-based stimulants were causally related to the treatment, the recommendation was made to label all ADHD medications with the following warning: “children with structural heart defects, cardiomyopathy, or heart rhythm disturbances may be at risk for adverse cardiac events including sudden death.” In a recent population–based cohort multicenter study of young and middle-aged adults during 806,182 person-years of follow-up, the use of ADHD medications was not associated with an increased risk of serious cardiovascular events. Although there are theoretical concerns about using ADHD medications in the presence of WPW, there is no definitive evidence to support an increased risk of cardiac events, and ADHD medications may be administered to patients with a WPW ECG pattern with close observation for the development of symptoms.

8.3. WPW and sports participation
Preparticipation assessment of athletes at various levels, including high school, can include an ECG and a diagnosis of WPW is sometimes made in this context. The use of the screening ECG for a variety of potentially life-threatening conditions varies between 80% and 100% among the four major professional U.S. sports teams, a strategy that is similar to the routinely used national Italian preparticipation screening program for competitive athletes. Standardization and understanding as to how national and major league affiliates address specific ECG abnormalities are unclear. In a survey of >4000 professional athletes, less than 20 individuals (mostly patients who had hypertrophic cardiomyopathy with WPW) were disqualified over a 15-year period.

WPW syndrome accounted for approximately 1% of deaths in a long-term registry of sudden death in athletes. However, it is not known whether these were asymptomatic individuals by definition. While many of the cases of SCD with WPW have an association with exercise, training does not alter the EP properties in WPW. Based on the 36th Bethesda Conference, risk stratification with an EP study is advisable in asymptomatic athletes engaged in moderate- to high-level competitive sports. This is in contrast to a slightly more aggressive statement from the European Society of Cardiology, which mandates that all athletes with WPW undergo a comprehensive risk assessment including an EP study. Assessment of the risk profile in these athletes include the SPERRI <240 ms in AF or <220 ms during stress or isoproterenol, presence of multiple accessory pathways, or easily inducible AF. While ablation has generally been recommended in asymptomatic athletes with WPW, for those individuals refusing ablation or those with a parahisian location, competitive sports may be allowed if none of the aforementioned EP risk factors are present. While there are currently differences between the European and American Cardiology Societies recommendations in the management of asymptomatic athletes with a WPW ECG pattern, the discovery of ventricular preexcitation in an adolescent, regardless of athletic status, should prompt referral to a specialist with expertise in pediatric electrophysiology to initiate the process of risk stratification, as detailed in this document.

9. Recommendations for young asymptomatic patients (8–21 years) with WPW ECG pattern
1. An exercise stress test, when the child is old enough to comply, is a reasonable component of the evaluation if the ambulatory ECG exhibits persistent preexcitation (Class IIA, Levels of Evidence B/C). In patients with clear and abrupt loss of preexcitation at physiological heart rates, the accessory pathway properties pose a lower risk of sudden death. In children with subtle preexcitation the ECG and exercise test may be difficult to interpret.

2. Utilization of invasive risk stratification (transesophageal or intracardiac) to assess the shortest preexcited R-R interval in atrial fibrillation is reasonable in individuals whose noninvasive testing does not demonstrate clear and abrupt loss of preexcitation (Class IIA, Levels of Evidence B/C).

3. Young patients with a SPERRI ≤250 ms in atrial fibrillation are at increased risk for SCD. It is reasonable to consider catheter ablation in this group, taking into account the procedural risk factors based on the anatomical location of the pathway (Class IIA, Levels of Evidence B/C).

4. Young patients with a SPERRI >250 ms in atrial fibrillation are at lower risk for SCD, and it is reasonable to

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*Children ages 5–8 years may be placed in the “younger-observe” or “older-assess risk” categories based on provider preference and the specifics of the individual patient and his/her family.

*In the absence of inducible atrial fibrillation, the shortest pre-excited RR interval determined by rapid atrial pacing is a reasonable surrogate.
defer ablation (Class IIA, Level of Evidence C). Ablation may be considered in these patients at the time of diagnostic study if the location of the pathway and/or patient characteristics do not suggest that ablation may incur an increased risk of adverse events, such as AV block or coronary artery injury (Class IIB, Level of Evidence C).

5. Young patients deemed to be at low risk might subsequently develop cardiovascular symptoms such as syncope or palpitations. These patients should then be considered symptomatic and may be eligible for catheter ablation procedures regardless of the prior assessment.

6. Asymptomatic patients with a WPW ECG pattern and structural heart disease are at risk for both atrial tachycardia and AV reciprocating tachycardia, which may result in unfavorable hemodynamics. Ablation may be considered regardless of the anterograde characteristics of the accessory pathway (Class IIB, Level of Evidence C).

7. Asymptomatic patients with a WPW ECG pattern and ventricular dysfunction secondary to dyssynchronous contractions may be considered for ablation, regardless of anterograde characteristics of the bypass tract (Class IIB, Level of Evidence C).

8. Asymptomatic patients with a WPW ECG pattern may be prescribed ADHD medications. This recommendation follows the American Heart Association Guidelines, which state that ADHD medications may be used in this setting after cardiac evaluation and with intermittent monitoring and supervision of a pediatric cardiologist.

9.1. Management algorithm

*patients unable to perform an exercise stress test should undergo risk-stratification with an EP study

Δprior to invasive testing, patients and the parents/guardians should be counseled to discuss the risks and benefits of proceeding with invasive studies, risks of observation only, and risks of medication strategy.

†patients participating at moderate-high level competitive sports should be counseled with regards to risk-benefit of ablation (Class IIA) and follow the 36th Bethesda Conference Guidelines.

¶in the absence of inducible atrial fibrillation, the shortest pre-excited RR interval determined by rapid atrial pacing is a reasonable surrogate.
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### Appendix

#### 11. Author Disclosures

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<th>Writing Group</th>
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