Prophylactic Radiofrequency Ablation in Asymptomatic Patients With Wolff–Parkinson–White Is Not Yet a Good Strategy
A Decision Analysis

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Background—Therapeutic management of asymptomatic patients with a Wolff–Parkinson–White (WPW) pattern is controversial. We compared the risk:benefit ratios between prophylactic radiofrequency ablation and no treatment in asymptomatic patients with WPW.

Methods and Results—Decision analysis software was used to construct a risk–benefit decision tree. The target population consisted of 20- to 40-year-old asymptomatic patients with WPW without structural fatal heart disease or a family history of sudden cardiac death. Baseline estimates of sudden death and radiofrequency ablation complication rates were obtained from the literature, an empirical data survey, and expert opinion. The outcome measure was death within 10 years. Sensitivity analyses determined the variables that significantly impacted the decision to ablate or not. Threshold analyses evaluated the effects of key variables and the optimum policy. At baseline, the decision to ablate resulted in a reduction of mortality risk of 8.8 patients for 1000 patients compared with abstention. It is necessary to treat 112 asymptomatic patients with WPW to save one life over 10 years. Sensitivity analysis showed that 3 variables significantly impacted the decision to ablate: (1) complication of radiofrequency ablation, (2) success of radiofrequency ablation, and (3) sudden death in asymptomatic patients with WPW.

Conclusions—This study provides a decision aid for treating asymptomatic patients with the WPW ECG pattern. Using the model and the population we tested, prophylactic catheter ablation is not yet ready for widespread clinical use. (Circ Arrhythm Electrophysiol. 2013;6:185-190.)

Key Words: arrhythmia (heart rhythm disorders) ■ catheter ablation ■ decision analysis ■ sudden death ■ Wolff–Parkinson–White syndrome

Wolff–Parkinson–White syndrome (WPW) syndrome has a prevalence of 0.9% to 3% in the general population. Most patients remain asymptomatic throughout their lives; however, in ≈0.6% of WPW patients, there is a risk of sudden death. This risk of sudden death is attributed to the development of atrioventricular reciprocating tachycardia (AVRT) that deteriorates to atrial fibrillation and finally to ventricular fibrillation. Short refractory periods of the accessory pathway (AP) could increase the risk of this fatal outcome.

Clinical Perspective on p 190

According to the current American College of Cardiology and European Society of Cardiology guidelines, the use of the radiofrequency (RF) catheter ablation to manage asymptomatic patients with WPW should be restricted to those with high-risk occupations, including professional athletes. Previously, a reduced risk of a patient becoming symptomatic after RF catheter ablation was reported in high-risk children and adults. Despite the high success rate (≈90%) of RF catheter ablation, some problems are associated with its implementation. RF catheter ablation is an invasive technique that could lead to several technical complications, such as thromboembolism, infection, bleeding, cardiac perforation with or without cardiac tamponade, and new arrhythmias. In some cases, the position of the AP affects the risk of complications. Hence, the use of this technique may not be always advisable. Consensual risk stratification is best analyzed by electrophysiological testing; however, the screening process of an entire population
itself is not economically feasible. Furthermore, RF catheter ablation is a complicated technique, and the ability of electrophysiologists, in general, to perform this technique safely is highly questionable.

We conducted a survey in France in 2004 using responses from 282 cardiac rhythm specialists. It was concluded that no consensus has been reached on the management of asymptomatic patients. Only 43% of clinicians performed invasive tests and only 50% of them systemically ablated the AP. The information currently available does not indicate the best strategy to adopt for managing asymptomatic WPW patients (unpublished results). Because the risk:benefit ratio of ablation to abstention has never been quantified, we decided to use a decision analysis model to resolve this question. This model is a useful tool for determining the validity of certain clinical outcomes. It also allows for sensitivity analysis with combinations of different variables for the condition that can be analyzed over a range of plausible values. In our study, the outcome of the decision analysis model was measured as a reduction in the risk of death using 2 management strategies: RF catheter ablation and abstention. With this analysis, we hope to address some compelling issues that could provide better judgment about the use of RF catheter ablation in asymptomatic patients with WPW.

Methods
Decision-tree sensitivity analysis was performed to compare 2 management strategies in patients with permanent pre-excitation: abstention (ie, receiving no treatment) and RF ablation of the AP. The decision analysis was performed using TreeAge DATA pro decision analysis software (TreeAge Software, Inc., Williamstown, MA).

Study Population and Data Source
The study population consisted of patients, aged between 20 and 40 years, who had permanent ventricular pre-excitation on a standard resting ECG, were asymptomatic, did not experience structural heart disease, and had no familial history of sudden death. To estimate the probabilities for our model, we used data obtained from a literature review and expert opinions. Fifty articles were selected through electronic databases, such as MEDLINE, EMBASE, Current Contents, and PubMed, and another 40 articles were selected through a manual search. We contacted 4 national experts known for their work in WPW syndrome and who had more than 10 years of experience in ablation techniques. The data obtained from these experts included the number of RF catheter ablations performed each year during the past 10 years at their respective centers, success and recurrence rates of RF catheter ablations, the rates and types of complications of RF catheter ablation, and an assessment of the risk of death at the time of the procedure. The mean values obtained from the experts were calculated and weighed according to the sample size of each.

Structural Components of the Decision Tree
For the purpose of setting up the decision tree, an arbitrary efficacy scale was used. The study population did not undergo an initial stratification for the risk of arrhythmic events, and the study did not account for the risk of recurrence after the initial success of RF catheter ablation. The study did not take cryotherapy into consideration, although it was used to treat ventricular pre-excitation during the study period. The study was scheduled to last for 10 years. The rationale for choosing a 10-year duration was that severe complications due to RF ablation jeopardize the vital prognosis, especially in the short and medium terms. The criterion of efficacy used was the outcome for the final health status and was scored as survival=1 or death=0. For the safety analysis, the following serious complications were included: lesional complete AV block, tamponade requiring emergency surgical drainage, massive cerebrovascular attack, and massive pulmonary embolism. Each serious complication could lead to the death of the patient.

Decision Tree
The decision-tree consisted of 3 nodes linked by branches (Figure I in online-only Data Supplement). The decision tree always started with a decision node. This represented the choice between the 2 options: abstention or RF catheter ablation. The random nodes consisted of exhaustive and mutually exclusive events, and each random node had the same number of branches. Probabilities (Table) were linked to the random nodes, using objective data from the literature or from expert opinion. The terminal nodes correspond to the consequences of each decisional route. Each terminal node had a numeric value called the utility (survival=1; death=0).

The choice of the probabilities of each event occurring was a fundamental stage in producing the model. We tried to use the closest value for each probability for each event from the literature. We adopted the expert opinion value when there was no data available.

The final stage was to weigh the efficacy using the probability of random events that occurred for each strategy. For the values of experts, we calculated the average rate by the weighted sample size of patients followed by the experts. The expected efficacy of a strategy was the sum of the products of the probabilities for the efficacy measurements of each branch. The difference observed between the efficacies expected for each strategy helped in making a decision.

Sensitivity Analysis
After analyzing all the probabilities from P1 to P20, a Tornado diagram identified the probabilities that were most likely to influence the results of the decision analysis. Sensitivity analysis was performed by examining the relative influence of these probabilities on the expected results. The sensitivity analysis assessed the effect of inaccuracy or alteration in the key variables and determined the optimal treatment strategy under diverse conditions.

Results
Expected Efficacy
Using the decision analysis, the expected efficacy of the 2 strategies was calculated. The expected efficacy of RF catheter ablation was 0.9989261, whereas that of abstention was 0.9900449. The RF catheter ablation strategy resulted in a 8.88 of 1000 patients reduction in mortality in comparison with the abstention strategy. Thus, the results suggest that 1 of 112 (8.88/1000) patients treated would have a reduction in the risk of death within 10 years.

Tornado Diagram
The variation interval of all the probabilities was calculated using sensitivity analysis (Table). The Tornado diagram (Figure II in online-only Data Supplement) identified 3 probabilities that were likely to influence the results of the decision analysis; namely, the rate of serious complications produced by RF ablation (P5), the rate of success for RF ablation (P2), and the rate of sudden death owing to the presence of ventricular pre-excitation per patient per year (P1).

Sensitivity Analysis
Results of the sensitivity analysis conducted on the 3 variables influencing the decision model are shown in Figure 1A through 1C. The analysis revealed that RF catheter ablation was more
suitable than abstention if the success rate of RF ($P_2$) was at least 0.1 (10%), the rate of serious complications was no more than 5% (0.05), and if there was an increased risk of sudden death due to the presence of ventricular pre-excitation.

**Trivariate Sensitivity Analysis**

Trivariate sensitivity analysis was conducted by varying all 3 variables simultaneously (Figures 2A and 2B). When $P_1$ and $P_2$ varied simultaneously and the value of $P_5$ was defined as zero, RF catheter ablation was preferred. When the probability interval between $P_1$ and $P_2$ was varied simultaneously, and the value of $P_5$ was defined as 0.003 (value used in the decision tree), the results were similar to those obtained from bivariate analysis of $P_1$ and $P_2$. Thus, the sensitivity analysis still favored RF catheter ablation, indicating that $P_5$ did not influence our decision analysis. When the probability interval between $P_1$ and $P_2$ was varied simultaneously, and the risk of serious complications was equal to that given by the Multicenter European Radiofrequency Survey Study (0.33) (0.5, 0.5), the results showed that if the risk of sudden death was equal to that defined in the decision tree (1/1000 patients/y), abstention was the best strategy, irrespective of the success rate of RF catheter ablation.

**Discussion**

The main result of our study is that the expected efficacy of RF ablation in asymptomatic patients with WPW is weak. We found that 112 patients had to be treated for 1 patient to have a reduced risk of death at 3 years. This in contrast with the findings of Pappone et al who found that prophylactic AP ablation markedly reduced the frequency of arrhythmic events in asymptomatic patients with WPW syndrome.

Sudden death in patients with WPW is the primary rationale for using RF catheter ablation in the management of asymptomatic patients with WPW, RF catheter ablation is used with great success in reducing the risk of arrhythmias by ≈92%, and increases event-free survival in asymptomatic patients. However, the decision to ablate is not simple due to multiple factors that include the cost of the screening process and the complications of invasive techniques. Prospective complications that may arise due to the procedure can often outweigh the benefits.

A combination of inducible AV reciprocating tachycardia and short refractory interval in atrial fibrillation, as observed via electrophysiological testing, provides the best indication for ablation. However, in many patients with WPW such characterization is not evident. In fact, the predictive value of invasive electrophysiological testing is too low to justify its use in the risk analysis of asymptomatic patients with WPW. Hence, the use of prophylactic RF catheter ablation in low-risk patients is not warranted. In light of these opposing findings, it is difficult to make a strong recommendation for the best treatment approach. The decision analysis model is intended to shed light on the risk:benefit ratio of the RF catheter ablation technique. This will aid clinicians in making better judgments for asymptomatic WPW cases.

### Table: Probabilities of Random Events Occurring in the Model

<table>
<thead>
<tr>
<th>Events</th>
<th>Probability of the Event</th>
<th>Literature (Reference)</th>
<th>Experts</th>
<th>Used in the Flow Diagram</th>
<th>Variation Interval (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS/WPW</td>
<td>$P_1$</td>
<td>0.00113</td>
<td>0.001</td>
<td>0.001</td>
<td>0–0.01</td>
</tr>
<tr>
<td>RF success</td>
<td>$P_2$</td>
<td>0.9514</td>
<td>0.95</td>
<td>0.95</td>
<td>0–1</td>
</tr>
<tr>
<td>No complications</td>
<td>$P_3$</td>
<td>0.95613</td>
<td>0.996</td>
<td>0.996</td>
<td>0.7–0.997</td>
</tr>
<tr>
<td>Non-serious complications</td>
<td>$P_4$</td>
<td>0.021613</td>
<td>0.001</td>
<td>0.001</td>
<td>0–0.005</td>
</tr>
<tr>
<td>Serious complications</td>
<td>$P_5$</td>
<td>0.02213</td>
<td>0.003</td>
<td>0.003</td>
<td>0–0.1</td>
</tr>
<tr>
<td>Complete AV block</td>
<td>$P_6$</td>
<td>0.2813</td>
<td>0.5</td>
<td>0.5</td>
<td>0.28–0.6</td>
</tr>
<tr>
<td>Tamponade</td>
<td>$P_7$</td>
<td>0.3213</td>
<td>0.3</td>
<td>0.3</td>
<td>0–0.4</td>
</tr>
<tr>
<td>CVA</td>
<td>$P_8$</td>
<td>0.0613</td>
<td>0.0002</td>
<td>0.0002</td>
<td>0–0.06</td>
</tr>
<tr>
<td>PE</td>
<td>$P_9$</td>
<td>0.0413</td>
<td>0.0002</td>
<td>0.0002</td>
<td>0–0.04</td>
</tr>
<tr>
<td>Other complications</td>
<td>$P_{10}$</td>
<td>0.2613</td>
<td>0.203</td>
<td>0.203</td>
<td>0–0.26</td>
</tr>
<tr>
<td>ST death/cAVB</td>
<td>$P_{11}$</td>
<td>013</td>
<td>0.0002</td>
<td>0.0002</td>
<td>0–0.001</td>
</tr>
<tr>
<td>ST death/tamponade</td>
<td>$P_{12}$</td>
<td>0.058813</td>
<td>0.3</td>
<td>0.3</td>
<td>0–1</td>
</tr>
<tr>
<td>ST death/CVA</td>
<td>$P_{13}$</td>
<td>0.33313</td>
<td>0.3</td>
<td>0.3</td>
<td>0–1</td>
</tr>
<tr>
<td>ST death/PE</td>
<td>$P_{14}$</td>
<td>0.31513</td>
<td>0.3</td>
<td>0.3</td>
<td>0–1</td>
</tr>
<tr>
<td>ST death/other</td>
<td>$P_{15}$</td>
<td>0.07713</td>
<td>0.3</td>
<td>0.3</td>
<td>0–1</td>
</tr>
<tr>
<td>LT death/cAVB</td>
<td>$P_{16}$</td>
<td>0.000115</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0–0.001</td>
</tr>
<tr>
<td>LT death/tamponade</td>
<td>$P_{17}$</td>
<td>0</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0–1</td>
</tr>
<tr>
<td>LT death/CVA</td>
<td>$P_{18}$</td>
<td>0.291516</td>
<td>...</td>
<td>0.29</td>
<td>0–0.5</td>
</tr>
<tr>
<td>LT death/PE</td>
<td>$P_{19}$</td>
<td>0.211716</td>
<td>...</td>
<td>0.21</td>
<td>0–0.5</td>
</tr>
<tr>
<td>LT death/other</td>
<td>$P_{20}$</td>
<td>...</td>
<td>...</td>
<td>0.3</td>
<td>0–1</td>
</tr>
</tbody>
</table>

AV indicates atrioventricular; cAVB, complete atrioventricular block; CVA, cerebral vascular accident; LT, long term; PE, pulmonary embolism; RF, radiofrequency; ST, short term; and WPW, Wolff–Parkinson–White.
Serious complications caused by ablation procedures that could cause death occur immediately or within the first 3 years. Hence, the study was scheduled to last for 3 years to increase its clinical validity. We considered the risk of sudden death as the primary outcome. A homogeneous population of patients aged 20 to 40 years was considered to minimize bias in the risk of sudden death.

Sensitivity analysis conducted using 3 variables concluded that ablation was advantageous compared with abstention at certain thresholds. A success rate superior to 20% (currently estimated at 95%), a rate of serious complications inferior to 1% (currently estimated at 3/1000), and a risk of sudden death of nearly zero are sufficient to justify the ablation option. Indeed, ablation had superior benefits when there was an increased risk of sudden death due to ventricular pre-excitation. Notably, the clinical reality is often far from the decision.

Figure 1. Results of the one-way sensitivity analysis conducted on the 3 variables influencing the decision model. A, The effectiveness of the ablation therapy decreases as the probability of serious complication increases. The dashed line indicates the threshold value at which ablation strategy yields a better outcome than abstention. Above this threshold, ablation is the optimal strategy, below this threshold, the standard therapy becomes the preferred option. B, The effectiveness of the ablation therapy increases as the probability of successful ablation increases. The dashed line indicates the threshold value at which ablation strategy yields a better outcome than abstention. C, The effectiveness of the ablation therapy improves as soon as the estimation of sudden death rate increases. EV indicates expected value; and RF, radiofrequency.

Figure 2. Trivariate sensitivity analyses of the 3 variables influencing the decision model with a probability of serious complications of (A) 0.003 or (B) 0.022. RF indicates radiofrequency.

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thresholds. The possible imprecise estimate of $P_1$, therefore, has no repercussions because a risk of nearly zero is enough to favor the RF ablation strategy. The decision tree was built to help the physician in the decision-making process. With the formulation in number of the differences between strategies, the information transmitted to the patient can be improved. Finally, only patients can judge whether they prefer one or the other of the following situations: (1) accepting a risk of sudden death at 1 of 1000 patient-years and an $\approx 30\%$ risk of becoming symptomatic without risking the need for a cardiac stimulator, (2) accepting a risk of 1.5 of 1000 of needing a cardiac stimulator with a 95% chance of the risk of sudden death and of becoming symptomatic disappearing.

Our findings remain robust over a wide range of assumptions for clinical inputs in sensitivity analysis. As determined by trivariate sensitivity analysis, when the probability of serious complications was 0.022 (as determined by the Multicenter European Radiofrequency Survey study), the risk of sudden death was 1 of 1000 patients per year. In this case, abstinence was the best strategy. RF catheter ablation with a success rate of 0.95 can be considered superior only when the risk of sudden death is at least 1.5 of 1000 patients per year. On the basis of these results, we conclude that patient risk evaluation is a greater determinant of the benefits of RF ablation. RF catheter ablation is not the best alternative for clinical use in the overall population.

**Limitations**

Our model does not take the risk of complete AV block into account well, which is the most frequent serious complication ($P_{12}=0.5$). This difficulty can be explained by the low mortality rate due to short- and long-term complete AV block ($P_{11}=0.0002$ and $P_{16}=0.0001$, respectively). To improve our model, it would be of interest to choose a usefulness scale that takes quality of life into account. However, available data seem insufficient to perform an analysis solely focused on quality of life after AP ablation. Consequently, we preferred to focus on survival, which is an unquestionable end point. The greatest difficulty concerns the estimate of short- and long-term death rates for each complication. The retained values influenced our model because we used an arbitrary scale that assigns 0 to death and 1 to survival. For this reason, the most frequent but seldom deadly serious complication, complete AV block, is poorly taken into account by this model. To avoid underestimating the risks linked with complications, it is likely that we were slightly pessimistic vis-à-vis the outcomes of our patients by using, in particular, the figures reported in the literature for pulmonary embolism and cerebral vascular accidents. However, it is probable that the risks of dying of pulmonary embolism, a cerebral vascular accident, or even a tamponade in the short term are lower if the patient is hospitalized than if the patient is at home.

Our decision analysis model used data from asymptomatic adult patients only. Further decision analysis models that could provide valuable results include the use of cryotherapy as an alternative to RF ablation, medico-economic evaluations, and the benefits/risks of ablation in children. An arbitrary scale for efficacy that provides a better understanding of the quality of life instead of overall mortality data could be more useful.

We mainly used French experts opinion and unpublished data to estimate sudden death and complication of RF ablation rates. This national expertise could provide different data than the worldwide experience. In addition, because the centers’ data were not anonymous, we can presume that the experts had a conflict of interest. As the complication percentage is a judgment criterion for the quality of care of centers performing catheter ablation, the experts might have underestimated it. However, it would have been virtually impossible to rely solely on published data.

**Conclusions**

We found that the expected benefit of RF ablation in asymptomatic patients with WPW is limited. A more comprehensive approach would be a multicenter, prospective, randomized study with long-term follow-up. This study will enable a better stratification of patients with the risk of sudden death, as well as the significant benefits of ablation. However, such a randomized trial would be very difficult to perform. Considering all the currently available information, we propose stratification of patients based on the risk of sudden death. Furthermore, the 1995 guidelines for the management of asymptomatic patients with WPW could be revised to indicate use of ablation in patients categorized as high risk after electrophysiological analysis.

**Disclosures**

None.

**References**

10. ACC/AHA/ESC, ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias: executive summary: a
Wolff–Parkinson–White (WPW) syndrome has a prevalence of 0.9% to 2% in the general population. Many patients remain asymptomatic throughout their lives; however, there is a small risk of sudden death, occurring in ≈0.6% of patients with WPW. Therapeutic management of asymptomatic patients with a WPW pattern is controversial. We compared the risk:benefit ratios between prophylactic radiofrequency ablation and no treatment in asymptomatic patients with WPW. Decision analysis software was used to construct a risk–benefit decision tree for a target population of 20- to 40-year-old asymptomatic patients with WPW without structural heart disease or a family history of sudden cardiac death. The outcome measure was death within 10 years. Sensitivity analyses determined the variables that significantly impacted the decision to ablate. Threshold analyses evaluated the effects of key variables and the optimum policy. At baseline, the decision to ablate resulted in a reduction of mortality risk of 8.8 patients for 1000 patients. We found that it is necessary to treat 112 asymptomatic patients with WPW to save one life over 10 years. Sensitivity analysis showed that 3 variables significantly impacted the decision to ablate (1) complication of radiofrequency ablation, (2) success of radiofrequency ablation, and (3) sudden death rate in asymptomatic patients with WPW. This study provides a decision aid for treating asymptomatic patients with the WPW ECG pattern. Using the model and the population we tested, prophylactic catheter ablation is not yet ready for widespread clinical use.
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Two references were erroneously switched: reference 19 should have been reference 13, and reference 13 should have been reference 19.

The authors apologize for the error.

The online version of the article has been corrected.
Figure 2

Tornado Diagram

- p5: 0 to 0.1
- p2: 0 to 1
- p1: 0 to 0.01
- p12: 0 to 1
- p17: 0 to 1
- p6: 0.28 to 0.6
- p20: 0 to 1
- p15: 0 to 1
- p7: 0.2 to 0.4
- p9: 0 to 0.04
- p11: 0 to 0.001
- p16: 0 to 0.001
- p8: 0 to 0.06
- p14: 0 to 1
- p13: 0 to 1
- p19: 0 to 0.5
- p18: 0 to 0.5
- p4: 0 to 0.005

Expected efficacy of the chosen strategy