P Wave Signal-Averaged Electrocardiogram as a New Marker for Atrial Tachyarrhythmias in Postoperative Fontan Patients

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OBJECTIVES
This study was undertaken to determine the potential role of P wave signal-averaged electrocardiogram (PSAECG) for risk assessment of atrial tachyarrhythmias (ATs) in patients after Fontan operation.

BACKGROUND
Onset of atrial flutter/fibrillation (AFF) in patients who have undergone Fontan operation for univentricular hearts constitutes an unfavorable clinical event associated with a high risk of cardiovascular complications. There is no data available on PSAECG in postoperative Fontan patients to predict potential susceptibility to ATs.

METHODS
Twenty-four post-Fontan patients and 15 age-matched healthy subjects were prospectively studied with PSAECG, and the following measurements were made: filtered P wave duration (FPWD), P wave vector integrals (PINTs), root-mean-square voltage for the initial 30 ms (RMSi30), and duration of persistent amplitude signals <4 μV from the beginning of the P wave (Di4).

RESULTS
The FPWDs were significantly longer in the study group patients with ATs when compared with the study group patients without ATs (p < 0.01) and compared with the controls (p < 0.001). An FPWD cut point of 135 ms resulted in a sensitivity of 71% and a specificity of 81% in differentiating patients with ATs from patients without ATs among the postoperative Fontan patients. The PINT was significantly greater in Fontan patients with AFF and also without AFF when compared with controls (p < 0.01, p < 0.05, respectively). The RMSi30 and the Di4 were not significantly different between study and control groups.

CONCLUSIONS
Signal-averaged P wave duration is significantly prolonged in postoperative Fontan patients. A prolonged signal-averaged P wave duration may be an effective noninvasive marker to predict risk of development of ATs in this patient group. (J Am Coll Cardiol 2000;36:602–7) © 2000 by the American College of Cardiology

Atrial tachyarrhythmias (ATs) are common complications of surgical correction of certain congenital heart defects. Patients who have had variations of Fontan operation for univentricular heart are at higher risk of AT when compared with other congenital heart problems (1,2). Most of the patients who have undergone Fontan operation demonstrate prolongation of intraatrial conduction time along with abnormalities of sinus node function (3).

P wave signal-averaged electrocardiography (PSAECG) has been used extensively in an attempt to identify patients at risk for developing atrial flutter/fibrillation (AFF) (4,5). Most of these studies have been performed in adults with ischemic heart disease. The issue of AT risk assessment using PSAECG in postoperative Fontan patients is unknown. The purpose of this study was to evaluate the potential beneficial role of PSAECG in assessing the risk of AT in postoperative Fontan patients.

METHODS

Patient selection. The study group consisted of 24 patients who have undergone variations of Fontan operation (age 11.4 ± 7 years). Ten had tricuspid atresia, seven had single ventricle, four had complex double outlet right ventricle, two had hypoplastic right heart syndrome, and one had hypoplastic left heart syndrome. Variations of the Fontan procedure included atrio pulmonary anastomosis in 10 and cavopulmonary anastomosis in 14 patients. Seven patients had a history of AFF, one had atrioventricular (AV) reciprocating tachycardia, and one had frequent premature atrial contractions requiring treatment. Only the patients with a history of AFF were included in the AT subgroup of the study group patients. The patient with a history of frequent PACs was included in the study subgroup with no history of AT, and the patient with a history of AV reciprocating tachycardia was excluded from both subgroups while assessing subgroup differences. Mean duration from time of surgery was 5.9 ± 3.3 years.

The control group consisted of 15 healthy age-matched subjects (age 12.7 ± 7.7 years) with normal 12-lead ECGs.

Signal-averaged P wave recording. The Predictor II system (Arrhythmia Research Technology, Inc., Austin, Texas) with three orthogonal bipolar leads, x, y and z, was
Abbreviations and Acronyms

<table>
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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>AFF</td>
<td>atrial flutter/fibrillation</td>
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<tr>
<td>AT</td>
<td>atrial tachyarrhythmia</td>
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<tr>
<td>AV</td>
<td>atrioventricular</td>
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<td>Di4</td>
<td>duration of the persistent amplitude signals &lt; 4 μV from beginning of the P wave</td>
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<td>FPWD</td>
<td>filtered P wave duration</td>
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<td>PINT</td>
<td>P wave vector integral</td>
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<tr>
<td>PSAECG</td>
<td>P wave signal-averaged electrocardiography</td>
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<td>RMSi30</td>
<td>root-mean-square voltage for the initial 30 ms</td>
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used for data acquisition and analysis. Silver/silver chloride electrodes were placed in an orthogonal lead arrangement identical to that used in conventional signal-averaged ECG. A sinus P wave template was selected for averaging. The QRS complex was used as the trigger for the signal-averaging process. The signal was digitized at a frequency of 2,000 samples/s with 16-bit accuracy. P wave complexes that did not match the template with a 99% correlation coefficient were automatically rejected. The P wave complexes were acquired until a noise level <0.7 μV was reached.

The individual x, y and z leads were combined into a vector sum, and a least-squares-fit filter was applied to the averaged output. The least-squares-fit filter was used because it causes less signal distortion and ringing of the P wave (4). The following measurements were made: filtered P wave duration (FPWD), P wave vector integrals (PINT), root-mean-square voltage for the initial 30 ms (RMSi30) and duration of persistent amplitude signals <4 μV from beginning of the P wave (Di4).

Statistical analysis. Data are expressed as mean values ± SD. For multiple comparison, MANOVA test with Bonferroni procedure was used. The relation between pairs of continuous variables was examined with Pearson’s moment correlation method and linear regression analysis. Chi-square test was used for comparison of nominal variables. A p value of <0.05 was considered statistically significant.

RESULTS

Filtered P wave durations were significantly longer in study group patients with AT when compared with study group patients without AT (158 ± 26 ms vs. 120 ± 24 ms, p < 0.01) and with controls (158 ± 26 ms vs. 102 ± 13 ms, p < 0.001) (Fig. 1). Filtered P wave duration was not found to be significantly longer in the study group without AT when compared with controls (120 ± 24 ms vs. 102 ± 13 ms, p = NS). Examples of signal-averaged P waves are shown in Figure 2. Figure 2A is a recording from a control patient, while Figure 2B is from a postoperative Fontan patient with a history of AFF. Note the marked difference in FPWD.

A FPWD cut point of 135 ms resulted in a sensitivity of 71%, a specificity of 81%, a positive predictive value of 63% and a negative predictive value of 87% in differentiating postoperative Fontan patients with atrial tachyarrhythmias (FONTAN [+]) and study group patients without history of atrial tachyarrhythmias (FONTAN [−]) compared with control patients.

A significant correlation was present between the FPWD and the time from surgery (r = 0.77, p < 0.001). A significant correlation was also present between the FPWD and age of the patient (r = 0.76, p < 0.001). However, there was no significant correlation between FPWD and age of the control subject (r = 0.22, p = ns). A linear regression analysis was performed using a stepwise method in order to further analyze the effect of age and time from surgery on the FPWD. Time from surgery had a strong correlation with the FPWD (beta = 0.77, R² = 0.59, p < 0.001). However, age was not found to be significantly associated with the prolongation of the FPWD as an independent factor (Fig. 4).

The possible influence of certain cardiovascular medications on FPWDs was also evaluated. Four postoperative Fontan patients were on medications (atenolol, procainamide and quinidine) either alone or in combination that might have affected the intraatrial conduction time (Table 1). Filtered P wave duration of patients who were on any one of these antiarrhythmic medications was significantly longer than FPWD of patients who were not on any of these medications (161 ± 29 ms vs. 123 ± 25 ms, p < 0.01). However, the patients who were on antiarrhythmic medications had a longer time since surgery (10.3 ± 4 years vs. 5.1 ± 2.7 years, p < 0.01) and were also significantly older when compared with the patients who are not on antiarrhythmic medications (22.2 ± 0.8 years vs. 9.2 ± 5.2 years, p < 0.001). The estimated FPWD at 9.8 years after...
surgery was calculated to be 159 ms (using linear regression formula obtained earlier: FPWD = 91.5 + 6.9 × time from surgery).

Ten patients in the study group had atriopulmonary connection, and 14 patients had total cavopulmonary connection. In the atriopulmonary connection group, 60% of patients (6 out of 10) had a history of AT, whereas, in the total cavopulmonary connection group, only one out of 14 patients had AT. The one patient in the cavopulmonary connection group was the oldest patient (22 years) in that group and had a FPWD of 150 ms. Filtered P wave duration of atriopulmonary connection patients was significantly longer than it was in total cavopulmonary connection patients (149.5 ± 24.9 ms vs. 117.2 ± 23.7 ms, p < 0.001) (Fig. 5). However, the atriopulmonary connection group patients were significantly older than the total cavopulmonary connection group patients (15.9 ± 5.6 years vs. 7.6 ± 4.9 years, p < 0.01). The atriopulmonary connection group patients also had a significantly longer time since surgery compared with the total cavopulmonary connection group patients (8.9 ± 2.8 years vs. 3.8 ± 1.6 years, p < 0.001). Even though the control group subjects were significantly older than the patients who had total cavopulmonary connection (12.7 ± 7.7 years vs. 7.6 ± 4.9 years, p < 0.05),
the FPWD of the total cavopulmonary connection group was not significantly different than the FPWD of the control group (117.2 ± 23.7 ms vs. 102 ± 13 ms, p = NS). Therefore, the finding of prolonged FPWD in the atrio-pulmonary connection group compared with the total cavopulmonary connection group appears to be more related to the time elapsed since surgery rather than age of the patient.

Root-mean-square voltage for the initial 30 ms and Di4 were not significantly different between the study and the control groups.

**DISCUSSION**

Patients who have undergone variations of the Fontan operation have been known to be at high risk of AT. However, so far there have been no studies to find a noninvasive method of analysis for assessing the risk of development of ATs in this patient group. Although PSAECG has been widely examined in adult patients who are at risk of paroxysmal atrial fibrillation, to date no study has been done to investigate the potential utility of PSAECG in the arrhythmia risk assessment of patients who have undergone Fontan operation. Findings of this study

**Table 1.** Characteristics of Postoperative Fontan Patients on Medications

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Dtsx (yr)</th>
<th>Surgery</th>
<th>Arrhythmia</th>
<th>FPWD (ms)</th>
<th>Medication</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>11</td>
<td>Atriopul</td>
<td>AFF</td>
<td>192</td>
<td>Dig, Quin</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>6</td>
<td>Cavopul</td>
<td>AFF</td>
<td>150</td>
<td>Atn</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>8</td>
<td>Atriopul</td>
<td>AFF</td>
<td>126</td>
<td>Pro</td>
</tr>
<tr>
<td>4</td>
<td>21.5</td>
<td>14</td>
<td>Atriopul</td>
<td>AFF</td>
<td>175</td>
<td>Dig, Quin</td>
</tr>
</tbody>
</table>

AFF = atrial flutter/fibrillation; Atn = atenolol; Atriopul = atrio-pulmonary connection; Cavopul = total cavopulmonary connection; Dig = digoxin; Dtsx = time from surgery; FPWD = filtered P wave duration; Pro = procainamide; Quin = quinidine.
showed that FPWD was significantly prolonged in patients who have had Fontan operation for various forms of univentricular heart. A cut point of 135 ms duration discriminated the postoperative Fontan patients with AT from the ones without tachyarrhythmias with good sensitivity, specificity, positive predictive value and negative predictive value. Measurements of P wave durations from conventional ECG were not found to be helpful in making a distinction between patients with AT and patients without AT in the Fontan patient group.

Prolongation of FPWD had a strong correlation with the time from surgery. Age was not significantly associated with prolongation of FPWD as an independent factor. These findings suggest that there is a time dependent increase in the incidence of ATs in patients after Fontan operation (6).

Atriopulmonary connection group patients had a significantly longer FPWD compared with the cavopulmonary connection group patients. We also observed the presence of a time-dependent prolongation of FPWD after surgical repair, and this prolongation seemed to be more related to the time from surgery rather than the age of the patient. Since atriopulmonary group patients had a significantly longer time from surgery compared with the cavopulmonary group patients, the longer FPWD in the atriopulmonary group was speculated to be due to time-dependent prolongation of FPWD.

Four of the patients in this study were on antiarrhythmic medications that might have potentially affected the FPWD to some extent. However, time from surgery seemed to be a more significant factor among the variables that could have affected the FPWD.

A recent study reported by Durongpisitkul, et al. (7), which included 499 patients with a mean follow-up of five years, failed to demonstrate any significant difference in the frequency of early or late onset clinically significant ATs among patients undergoing various modifications of the Fontan operation. In that study, the incidence of ATs after various types of atrio-pulmonary connection was not higher than 21%, and the incidence of ATs was 22% in the total cavopulmonary connection group. However, in our study, patients who had atriopulmonary connection had a much higher incidence of ATs compared with patients who have undergone total cavopulmonary connection. This might be explained by the fact that the mean follow-up period for our atriopulmonary connection group was significantly longer than the total cavopulmonary connection group. Overall incidence of ATs was also higher in our patient group who had atriopulmonary connection (7 out of 10 patients, 70%). However, the mean follow-up period after surgery was longer (8.8 years). Since the FPWD was prolonged in association with time from surgery, one could hypothesize that, with longer follow-ups, we might see a significant increase in the incidence of ATs in postoperative Fontan patients.

Yamada, et al. (8) have used RMSi30 and Di4 to determine the presence of low amplitude potentials early in the filtered P wave. In that study they found that these low amplitude early potentials were characteristic of sick sinus syndrome. This study demonstrated the absence of low amplitude signals early in the filtered P wave in our patient group. These findings might be a reflection of having a different patient population when compared with most of the PSAECG studies, which deal with adult patients with paroxysmal atrial fibrillation. The presence of congenital heart disease and younger age are probably some of the factors that might have affected this study’s findings.

P wave vector integral is a measurement of the area under the P wave curve and, therefore, it involves analysis of both amplitude and duration of the P wave. This study has shown that PINT was significantly greater in the postoperative Fontan patients when compared with the healthy controls. However, there was no significant correlation between the PINT and the time from surgery or age of the patient.

Study limitations. Studying larger populations would be necessary for comparison of patients who had different types of Fontan operation in a more objective manner. Although our study did not seem to be significantly affected by the usage of some medications, it would be more ideal to have a population with ATs before initiation of antiarrhythmic medications. P wave signal-averaged electrocardiography was performed using a QRS triggered SAECG acquisition system. Even though previous investigators have used the same method, it would be more ideal to use a P wave triggered system in order to control for potential beat to beat variations of the PR interval.

Conclusions. The results of this study suggest that the signal-averaged P wave duration is significantly prolonged in the postoperative Fontan patients in association with time elapsed after surgery. A prolonged signal-averaged P wave duration may be an effective noninvasive marker to predict risk for development of ATs in this patient group.
As a new tool, P wave integral needs more investigation for its potential future benefit in assessment of patients at risk for AFF. Further prospective studies in large patient groups are needed in order to determine the potential clinical benefit of PSAECG in identifying patients at risk for ATs after Fontan operation.

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REFERENCES