Late Potentials and Inducible Ventricular Tachycardia in Surgically Repaired Congenital Heart Disease

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We compared signal-averaged electrocardiography with invasive electrophysiological study in patients after surgical repair of congenital heart disease to determine if potentially useful correlations exist between the two methods for assessment of risk for ventricular tachycardia. Thirty-one patients (age, 1–49 years; mean, 10.6 years) with congenital heart disease repaired with right ventriculotomy or postrepair right bundle branch block (77% postoperative tetralogy of Fallot) who had electrophysiological study were studied with signal-averaged electrocardiography. Patients were classified by electrophysiological study results as having no inducible ventricular tachycardia, nonsustained ventricular tachycardia, or sustained ventricular tachycardia. Signal-averaged electrocardiograms were examined for the duration of low-amplitude (≤40 μV) QRS signal, duration of total QRS, and root-mean-square voltage of the terminal 40 msec of the QRS. Low-amplitude terminal root-mean-square voltage of 100 μV or less had 91% sensitivity and 70% specificity for ventricular tachycardia inducible by electrophysiological study. Similar sensitivity but less specificity were seen using the criterion of 20 msec or more total low-amplitude QRS signal (initial plus terminal) or using total QRS duration of 128 msec or more. There was a weaker association between terminal low-amplitude QRS signal of 15 msec or more and inducible ventricular tachycardia. The signal-averaged electrocardiogram did not reliably distinguish sustained from nonsustained inducible ventricular tachycardia. Results of our study suggest that signal-averaged electrocardiography in patients with surgically repaired congenital heart disease correlate with presence or absence of either sustained or nonsustained ventricular tachycardia by electrophysiological study and that 100 μV or less terminal root-mean-square voltage is an appropriate cutoff for interpretation of signal-averaged electrocardiography in this patient group. (Circulation 1990;82:1690–1696)

Ventricular arrhythmias are an important long-term complication in surgically repaired congenital heart disease. Numerous studies have demonstrated a correlation between postoperative ventricular arrhythmias and sudden death in patients who have had surgical repair of tetralogy of Fallot.1–7

Current methods for detecting young patients at risk for episodic ventricular tachyarrhythmias include invasive electrophysiological study, treadmill exercise testing, and 24-hour ambulatory electrocardiography (Holter monitoring). Both exercise testing and Holter monitoring rely on the chance occurrence of ventricular arrhythmia during the time of recording and can be cumbersome and expensive, particularly if serial studies are required. Also, the predictive value of Holter monitoring for long-term clinical response is questionable.7–12 Based primarily on observations in adult patients with ischemic heart disease, electrophysiological testing appears to be a more accurate predictor of clinical response.8–14 However, the invasive nature of an electrophysiological study can be uncomfortable for the patient, involves some risk and radiation exposure, and is expensive. An easy, noninvasive screening test to provide a nonepisodic marker for young people with heart disease who are at risk for ventricular tachycardia (VT) would be valuable.

Signal-averaged electrocardiography (SAECG) has been demonstrated to be a useful noninvasive
technique for detecting patients with coronary artery disease at risk for VT and sudden death by detecting low-amplitude, high-frequency electrical potentials in the terminal portion of their QRS.13–25 Research has just begun on the use of SAECG for detection of patients with episodic VT in the pediatric and young adult age groups.26–29 If SAECG detects pediatric patients at risk for VT, it could help screen patients for electrophysiological studies and/or Holter monitoring.14,30–32 The purpose of this study was to correlate SAECG results with electrophysiological results among a group of patients with surgically repaired congenital heart disease.

Methods

Patient Population

Candidates for inclusion in this study were selected from the pediatric or adult cardiology clinic population at the University of Nebraska Medical Center if they fulfilled the requirements of diagnosis of congenital heart disease repaired with ventriculotomy or with postoperative right bundle branch block, sinus rhythm, and a current invasive electrophysiological study with ventricular stimulation protocol. Thirty-one patients were studied (age range, 1–49 years; mean age, 10.6 years). A total of 22 males and 9 females were included. Twenty-four of the patients had surgically repaired tetralogy of Fallot (77%); two had repaired subpulmonary stenosis with intact ventricular septum (6%); one had repaired truncus arteriosus (3%); two had repaired ventricular septal defect and obstructive right ventricular muscle bundle, including one with ventricular inversion (6%); one had repaired complex transposition of the great arteries (3%); and one had repaired perimembranous ventricular septal defect (3%). The time interval from surgery to SAECG ranged from 4 months to 28 years (mean, 6.7 years). All SAECGs were performed within 3 months of electrophysiological study. The study population was subdivided based on the results of invasive electrophysiological study. Five patients (16%) had inducible sustained ventricular tachycardia (VT-S), six patients (19%) had inducible nonsustained ventricular tachycardia (VT-NS), and 20 patients (65%) had no inducible ventricular tachycardia (No VT) by electrophysiological study.

Signal-Averaged Electrocardiography

SAECG recordings were recorded using the Arrhythmia Research Technology (ART) Model 1200 EPX or the Predictor Signal Averaging Electrocardiograph (Corazonix Corporation) programmed with the Predictor 40 protocol. At least 200 beats were averaged during each recording, and in all cases the noise levels were less than 0.8 \( \mu V \). The SAECGs were recorded during sinus rhythm from standard bipolar X, Y, and Z leads. After passing through a template recognition program to reject ectopic beats and grossly noisy signals, the signals were averaged, amplified, and filtered with a bidirectional filter at a frequency between 25 and 250 Hz. A vector magnitude was calculated as \( V=\sqrt{X^2+Y^2+Z^2} \) by combining the filtered signals from the three leads. The onset and termination of the QRS were determined electronically, and measured intervals were: QRS duration (QRS); duration of initial, terminal, and total low-amplitude signals of less than 40 \( \mu V \) (LAS\(_{i}, \) LAS\(_{t}, \) and LAS, respectively); and root-mean-square voltage of the signals in the last 40 msec of the filtered QRS complex (RMS) (see Figure 1). Measurement of duration of initial low-amplitude QRS signal was included because of previous observations of abnormal low-amplitude signal in the initial QRS in patients with VT\(^{33}\) and in those with rejection of a transplanted heart.\(^{34}\)

Ventricular Stimulation Protocol During Intracardiac Electrophysiological Study

Single (S\(_{2}\)), double (S\(_{2}-S_{3}\)), and triple (S\(_{2}-S_{4}\)) programmed ventricular premature stimuli were introduced into ventricular (drive) paced rhythm as previously described.\(^7\) At least two drive cycle lengths (most often, 500 and 400 msec) were used, and at least two areas were stimulated within the right ventricle (apex and outflow tract) unless reproducible sustained VT was induced before the completion of the stimulation protocol. Sustained VT was present when reproducible tachycardia was more than 30 seconds in duration or shorter-duration VT was terminated by DC cardioversion or overdrive ventricular pacing because of symptomatic hypotension. Nonsustained VT was defined when reproducible tachycardia was more than 3 beats but less than 30 seconds before spontaneous termination. In patients in whom the electrophysiological study was repeated to evaluate the effectiveness of a specific antiarrhythmic medication in controlling an identified VT, only the original electrophysiological study that identified the type of VT was used to classify the patient.

Statistics

Values for LAS\(_{i}, \) LAS\(_{t}, \) LAS, RMS, and QRS as well as age at operation and age at SAECG were compared among the groups of patients with VT-S, VT-NS, and No VT, using analysis of variance. When analysis of variance showed differences among these groups (\( p<0.05 \)), individual two-tailed \( t \) tests were performed using the Bonferroni correction for multiple \( t \) tests.\(^{35}\) A \( p \) value less than or equal to 0.05 was considered statistically significant.

Receiver operating characteristic curves\(^{36}\) were plotted for each SAECG measurement as an indicator for inducible VT and inspected for the cutoff point, which maximized the true-positive ratio while maintaining the false-positive ratio at less than 50% (see Figure 2). These high-sensitivity, moderate-specificity points were chosen because it would be desirable to have a screening-type test that would not produce many false-negative results. For each measurement, a \( 2 \times 2 \) table was generated using cutoff points determined by the above method and analyzed.
for sensitivity, specificity, and positive and negative predictive values.

Results

Clinical Characteristics of Patient Groups

Among the five patients with VT-S, all had Holter monitoring and three had exercise testing. One of the five had syncope without clinical evidence of paroxysmal atrioventricular block and had documented nonsustained monomorphic VT by Holter monitor. Another patient had symptomatic sustained spontaneous monomorphic VT requiring cardioversion. None of the remaining patients had symptoms or VT by Holter, but one had ventricular couplets on Holter and premature ventricular contractions (PVCs) that increased with exercise testing. The other two in this group were asymptomatic, had no complex ventricular ectopy by Holter, and had no PVCs with exercise. None was receiving antiarrhythmia drugs at the time of electrophysiological study or SAEcg. Sustained induced ventricular tachycardia was monomorphic in all patients. One had central right bundle branch block (ventricle to right ventricular apex interval, ≥30 msec).

Among the six patients with VT-NS, all had Holter monitoring and exercise testing. One of the six had syncope without evidence of paroxysmal atrioventricular block but no complex ventricular ectopy by Holter and only one PVC with exercise. Two others had increasing PVCs with exercise but were asymptomatic (one had nonsustained VT by Holter, and the other had single PVCs). Another two of the six were asymptomatic and had multiform single PVCs on Holter but none on exercise testing. The last of the six had no symptoms and no clinically documented arrhythmias. None of these patients was receiving antiarrhythmia drugs at the time of SAEcg or electrophysiological study. Nonsustained induced ventricular tachycardia was monomorphic in five and polymorphic in one. Five patients had central right bundle branch block.

Among the 20 patients in whom VT could not be induced, there were two infants who had normal Holters with a history compatible with apnea or syncope. One older patient with occasional dizziness and palpitations had single uniform PVCs on Holter and exercise test. None of the three symptomatic patients had evidence of paroxysmal atrioventricular block. The remaining 17 patients were asymptomatic. Among these, 14 had no PVCs or rare uniform single PVCs by Holter. One of the 14 had exercise-induced ventricular ectopy (multiform couplets). Three of the 17 asymptomatic patients had multiform PVCs or couplets by Holter; none had VT. Two of these three

FIGURE 1. Two signal-averaged electrocardiograms are shown with measurements indicated. LASi is duration of low-amplitude signals (<40 μV) in initial QRS (msec). LAS, is duration of low-amplitude signals (<40 μV) in terminal QRS. LAS = LASi + LAS, . QRS is total duration of QRS complex. Last 40 msec of QRS complex are shaded. RMS is root-mean-square voltage of shaded section (μV). Tracing A: Patient without inducible ventricular tachycardia. Tracing B: Patient with inducible sustained ventricular tachycardia. Values in parentheses are actual measurements for these tracings (intervals in msec and RMS in μV). Note longer LASi, LAS, and QRS and smaller RMS in tracing B.
had exercise testing, and both had persistent PVCs with exercise. Thirteen of the 20 had central right bundle branch block.

Age at operation and SAECG were different among the three groups (Table 1). The mean age at operation of patients with VT-S was higher \((p<0.05)\) than for the No VT group. The mean age at SAECG was also higher for the VT-S and VT-NS groups compared with the No VT group.

**Signal-Averaged Electrocardiographic Data**

Table 2 gives values of \(\text{LAS}_i\), \(\text{LAS}_s\), \(\text{LAS}\), \(\text{QRS}\), and \(\text{RMS}\) for each of the three electrophysiological groups—VT-S, VT-NS, and No VT. Analysis of variance showed differences among the three groups for \(\text{LAS} (p<0.01)\), \(\text{LAS}_i, (p<0.05)\), \(\text{QRS} (p<0.05)\), and \(\text{RMS} (p<0.05)\) but not \(\text{LAS}_s\). Subsequent \(t\) testing showed no significant difference between the VT-S and VT-NS groups for any of the SAECG measurements.

**Contingency Table Analysis**

Because of the failure to document differences in SAECG data between groups VT-S and VT-NS, these groups were combined for further comparison with the No VT group. Receiver operating characteristic curve analysis identified high-sensitivity cutoff criteria for RMS equal to or less than 100 \(\mu\)V, \(\text{LAS}\) equal to or more than 20 msec, \(\text{QRS}\) equal to or more than 128 msec, \(\text{LAS}_i\) equal to or more than 15 msec,
and LAS, equal to or more than 8 msec (Figure 2). We generated 2x2 contingency tables using these cutoffs as indicators for VT inducible at electrophysiology study (Table 3). Using RMS equal to or less than 100 μV as the criterion of a positive test, sensitivity is 91% and specificity is 70%. The criteria of LAS equal to or more than 20 msec or QRS equal to or more than 128 msec were as sensitive but somewhat less specific. LAS, and LAS, were neither highly sensitive nor highly specific indicators of VT by electrophysiology study.

Discussion

The data in this study show a relation between signal-averaged electrocardiographic results and the results of programmed ventricular stimulation after right ventriculotomy. The clinical relevance of this relation is dependent on the importance of inducible nonsustained or sustained VT in this patient group. Widely disparate opinions about the implications of inducible ventricular arrhythmias have been published. A number of electrophysiologists who care for adult patients assert that induced VT is important only when it is sustained and identical to a clinically documented rhythm that produces symptoms.37 Others emphasize the importance of any sustained inducible monomorphic VT.38,39 However, sustained polymorphic VT is induced in some patients with clinically important spontaneous VT.40,41 Still others contend that even nonsustained inducible VT in patients without clinical VT may place them at higher risk for sudden death.42 One of the major concerns of pediatric cardiologists is that sudden death often is the first symptom of the fast VT typically found in this group of patients.4,7,39-42 Although commonly accepted, there is no conclusive proof that inducible VT at electrophysiological study is a poor prognostic sign in these patients.

The results of this study relate only to children and young adults after surgical repair of congenital heart disease, primarily tetralogy of Fallot. The conclusions, therefore, cannot be generalized to other groups at risk for VT. No normal values for SAECG measurements are established in childhood; however, this does not impair the interpretation of SAECGs in patients after right ventriculotomy for congenital heart disease because identifiable differences were detected between patients with inducible VT and a control group without inducible VT. The wide range in ages of patients evaluated in this study is a potential problem. The sample size did not permit meaningful subdivision by age; however, the effects of age on the signal-averaged electrocardiogram after heart surgery is an area for ongoing investigation.

Our results differ from those of Zimmermann et al,28 who found no relation between the abnormal SAECG and the occurrence of ventricular arrhythmias in postoperative tetralogy of Fallot. There are several possible explanations for this. First, their data did not include a ventricular stimulation protocol and relied on information obtained by 24-hour ambulatory electrocardiography (only one electrocardiogram per patient). The limited value of 24-hour ambulatory electrocardiography in predicting VT and its discordance with the electrophysiological results have been demonstrated in recent studies of adult patients with ischemic heart disease.6-12 Second, their patient population had a very low incidence of complex ventricular arrhythmias for evalu-

| TABLE 1. Study Population Features by Electrophysiological Study Classification |
|--------------------------------------|----------------|----------------|----------------|----------------|------------------|
| Group 1, VT-S (n=5) | Group 2, VT-NS (n=6) | Group 3, No VT (n=20) | p | t tests |
| Age at repair (yr) | 10.80±12.36 | 5.33±3.61 | 2.35±2.89 | NS | <0.05 | NS |
| Age at SAECG (yr) | 24.80±18.01 | 14.83±3.76 | 5.85±5.42 | NS | <0.005 | <0.005 |
| VT-S, inducible sustained ventricular tachycardia; VT-NS, inducible nonsustained ventricular tachycardia; No VT, no inducible ventricular tachycardia; SAECG, signal-averaged electrocardiography. |

| TABLE 2. Signal-Averaged Electrocardiographic Results by Electrophysiological Study |
|--------------------------------------|----------------|----------------|----------------|----------------|------------------|
| Group 1, VT-S (n=5) | Group 2, VT-NS (n=6) | Group 3, No VT (n=20) | p | t tests |
| LAS (msec) | 11.6±5.9 | 14.3±13.2 | 7.0±4.4 | NS | NS |
| LAS (msec) | 23.2±5.7 | 20.7±12.7 | 13.8±6.7 | NS | <0.05 |
| LAS (msec) | 35.0±10.8 | 35.0±15.1 | 20.8±8.3 | NS | <0.01 |
| RMS (μV) | 35.1±11.8 | 122.8±134.3 | 146.9±79.0 | NS | <0.05 |
| QRS (msec) | 160.6±27.1 | 144.1±23.4 | 125.5±26.2 | NS | <0.05 |
| VT-S, inducible sustained ventricular tachycardia; VT-NS, inducible nonsustained ventricular tachycardia; No VT, no inducible ventricular tachycardia; LAS, duration of low-amplitude signal ≤40 μV in initial QRS; LAS, duration of low-amplitude signal ≤40 μV in terminal QRS (LAS=LAS+LAS); RMS, root-mean-square of voltage during last 40 msec of QRS complex; QRS, duration of QRS complex from beginning to termination. |

Values are given as mean±SD.
TABLE 3. 2×2 Contingency Tables

<table>
<thead>
<tr>
<th>LAS, ≥8 msec</th>
<th>Inducible VT</th>
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<tr>
<td>+</td>
<td>7</td>
</tr>
<tr>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Sensitivity, 64% Specificity, 60%</td>
</tr>
<tr>
<td></td>
<td>+Predictive value, 46% -Predictive value, 77%</td>
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<tr>
<td>LAS ≥20 msec</td>
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<tr>
<td>+</td>
<td>10</td>
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<td>-</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sensitivity, 91% Specificity, 55%</td>
</tr>
<tr>
<td></td>
<td>+Predictive value, 53% -Predictive value, 92%</td>
</tr>
<tr>
<td>RMS ≤100 µV</td>
<td></td>
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<tr>
<td>+</td>
<td>10</td>
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<td>-</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sensitivity, 91% Specificity, 70%</td>
</tr>
<tr>
<td></td>
<td>+Predictive value, 62% -Predictive value, 93%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>LAS, ≥15 msec</th>
<th>Inducible VT</th>
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<tbody>
<tr>
<td>+</td>
<td>8</td>
</tr>
<tr>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Sensitivity, 73% Specificity, 50%</td>
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<tr>
<td></td>
<td>+Predictive value, 44% -Predictive value, 77%</td>
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<table>
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<tr>
<th>QRS ≥128 msec</th>
<th>Inducible VT</th>
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<tr>
<td>+</td>
<td>10</td>
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<td>-</td>
<td>1</td>
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<tr>
<td></td>
<td>Sensitivity, 91% Specificity, 60%</td>
</tr>
<tr>
<td></td>
<td>+Predictive value, 56% -Predictive value, 92%</td>
</tr>
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Significant by SAECG. Finally, differing recording methods for SAECG make comparisons difficult. In our study, the SAECG was recorded in a fashion much more in accordance with standard methods established in many previous studies.16,22,24,30,31,43 bundle presence of those from previous studies.16,22,24,30,31,43 Subdivision of our patient population into those with and those with peripheral right bundle branch block did not permit meaningful interpretation of the data because of small sample size.

Signal-averaged electrocardiography can be applied in this patient population with high sensitivity and high negative predictive value for inducible VT. This is ideal in this clinical circumstance because it identifies a large group of patients who have very low probability of inducible VT by electrophysiologically testing. Also identified is a second group with higher probability of inducible VT who can be evaluated more fully with ventricular stimulation in the hope of selecting those who would benefit from antiarrhythmia treatment.

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