Digital implantable loop recorders in the investigation of syncope in children: Benefits and limitations

Darshan S. Kothari, DNB, DCH, FCPS,* Fiona Riddell, NZCS, COP(SCT),† Warren Smith, MB, FRACP,‡ Jamie Voss, MBBS,* Jon R. Skinner, MBChB, FRCPCH, FRACP, MD*

From *Greenlane Pediatric & Congenital Cardiac Services, Starship Children, Auckland, New Zealand, †Cardiac Physiology, Auckland City Hospital, Auckland, New Zealand, ‡Cardiology, Auckland City Hospital, Auckland, New Zealand.

BACKGROUND Conventional diagnostic methods for detecting arrhythmogenic causes of syncope in children are poor. Digital implantable loop recorders are of proven value in adults.

OBJECTIVES The purpose of this study was to evaluate digital implantable loop recorders in the investigation of syncope in children.

METHODS We reviewed the clinical and technical records of 18 consecutive patients (6 female and 12 male; age ≤16 years) who received an implantable loop recorder from 1999 to 2005.

RESULTS Median age at implantation was 11.3 years (range 4.6 – 16.5 years). Median duration of the device in situ was 18 months (range 5–36 months). Median time to diagnosis was 6 months (range 1 day to 17 months). Two patients had a congenital heart defect. Ten children (56%) had an event, 9 (50%) of whom had diagnostic information; 5 (28%) had profound bradycardia or asystole; 2 (11%) had polymorphic ventricular tachycardia (VT); and 1 child had supraventricular tachycardia. One patient died, but the automatically activated recording was recorded over again after death. One child had sinus rhythm during syncope. One child with polymorphic VT had no auto-activation on two occasions, and the third activation was triggered by asystole after VT terminated. Sixteen patients (89%) had false-positive activations as a result of either artifact or sinus tachycardia.

CONCLUSION The digital implantable loop recorder is a useful diagnostic modality in children with unexplained syncope. However, the automatic detection algorithm is imperfect, missing genuine polymorphic VT and frequently interpreting muscle tremors as VT. Because of continuous overwriting by automatic detection, genuine arrhythmias may be over-recorded by artifact.

KEYWORDS Syncope; Loop recorder; Children; Catecholaminergic polymorphic ventricular tachycardia; Neurocardiogenic syncope; Asystole

Introduction

The primary role of the pediatric cardiologist in the evaluation of syncope in children is identifying arrhythmogenic causes. The diagnostic dilemma frequently is challenging, and there may be considerable concerns and anxiety among patients and their parents.

Syncope in the pediatric population accounts for 1% to 6% of all hospital admissions and 3% of emergency room visits every year.1–4 Because syncope can herald a potentially fatal ventricular arrhythmia,5,6 accurate diagnosis is urgent and imperative.

The most common cause of syncope in young patients is neurocardiogenic. This cause often is diagnosed by a detailed history alone, but differentiation from arrhythmogenic causes based on history alone can be difficult. Symptoms may be mimicked using a head-up tilt table test7; however, this test has poor specificity and sensitivity. Twelve-lead ECG is valuable for detecting some cases of long QT syndrome, Brugada syndrome, or Wolff-Parkinson-White syndrome. Other tests, such as ambulatory Holter monitoring, electrophysiologic study, treadmill exercise test, and echocardiography, have low diagnostic yield. Transtelephonic event monitors have increased diagnostic yield when events occur frequently with short intervals between them.

Use of an implantable loop recorder was first reported in 1997.8–10 The implantable loop recorder allows long-term evaluation of infrequent symptoms when a detailed history and baseline investigations are inconclusive. Implantable loop recorders have been shown in adults to be superior to conventional methods in the diagnosis of recurrent syncope.11 Implantable loop recorders may be particularly advantageous in children because many children cannot themselves provide a clear history, may have events witnessed only by other children, and may be less patient or compliant with repeated and often inconclusive investigations.

Because data in the pediatric population are limited, we report here our experience with the use of implantable loop recorders in children.

Materials and methods

Eighteen patients (6 female and 12 male; age ≤16 years) with a history of syncope received an implantable loop recorder between 1999 and 2005 at our institution, the New Zealand National Centre for Pediatric and Congenital Heart
Disease, which serves a population of 4.2 million people. Of these patients, two were surgically operated cases with a primary congenital diagnosis of L-looped transposition of the great arteries. Detailed and thorough clinical and family histories were taken by a consultant arrhythmia specialist in all cases.

Conventional tests done when indicated are as follows: standard 12-lead surface ECGs (n = 18), treadmill exercise test (n = 13), ambulatory 24-hour Holter monitor (n = 16), head-up tilt table test (n = 4), echocardiography (n = 17), and invasive electrophysiologic study (n = 5).

The implantable loop recorder device used was a Medtronic Reveal Plus (Medtronic Inc., Minneapolis, MN; 61 mm long, 19 mm wide, 8 mm thick; weight 17 g). The device was implanted subcutaneously in all patients by a specialist cardiologist or pediatric cardiac surgeon with the patient under local or general anesthesia. Preimplant mapping was performed to optimize the position and orientation of the device. Four ECG electrodes approximately 4 cm apart, forming four corners of a square, were placed at the upper left sternal border. By pairing two of the electrodes sequentially, the orientation giving the largest QRS complex with a small T wave and visible p wave was sought. For most patients, the best orientation was upper left to lower right (approximating to lead III on the surface ECG).

The number of consecutive beats to trigger activation can be 16 or 32. We generally started with limits at 40 bpm, pause 3 seconds, and heart rate 180 bpm in those younger than 14 years (given the high sinus rates common in children) and >165 bpm in older teenagers, and 16 beats to trigger.

### Table 1: Clinical characteristics, symptom-rhythm correlation, and conventional tests performed

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>No. of syncopal episodes prior to implantable loop recorder placement</th>
<th>Syncope at rest (R) or with exercise (E)</th>
<th>24-hour Holter</th>
<th>Tilt-table test</th>
<th>Electrophysiologic study</th>
<th>Rhythm Type of activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>F</td>
<td>20</td>
<td>R + E</td>
<td>Yes</td>
<td>Yes (Neg)</td>
<td>No</td>
<td>Asystole (18 s) Automatic</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>M</td>
<td>4</td>
<td>R + E</td>
<td>Yes</td>
<td>Yes (Pos)</td>
<td>Yes (Neg)</td>
<td>Polymorphic VT Manual</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>F</td>
<td>5</td>
<td>R + E</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No event</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td>F</td>
<td>1</td>
<td>R + E</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No event</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>M</td>
<td>7</td>
<td>E</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No event</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>M</td>
<td>8</td>
<td>R + E</td>
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<td>No</td>
<td>No</td>
<td>Death Automatic</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>M</td>
<td>11</td>
<td>R + E</td>
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<td>No</td>
<td>No</td>
<td>No event (CHD pacemaker)</td>
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<tr>
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<td>M</td>
<td>21</td>
<td>R + E</td>
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<td>No</td>
<td>No</td>
<td>No event</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
<td>M</td>
<td>6</td>
<td>E</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Asystole (39.4 s) Automatic</td>
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<tr>
<td>10</td>
<td>10</td>
<td>M</td>
<td>4</td>
<td>E</td>
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<td>No</td>
<td>No</td>
<td>No event</td>
</tr>
<tr>
<td>11</td>
<td>15</td>
<td>M</td>
<td>4</td>
<td>R + E</td>
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<td>No</td>
<td>No</td>
<td>No event (borderline long QT interval prior to implantable loop recorder placement) Manual + Automatic</td>
</tr>
<tr>
<td>12</td>
<td>15</td>
<td>M</td>
<td>7</td>
<td>R</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No event (borderline long QT interval prior to implantable loop recorder placement)</td>
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<tr>
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<td>M</td>
<td>9</td>
<td>R + E</td>
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<td>Asystole (8.5 s) Manual</td>
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<tr>
<td>14</td>
<td>9</td>
<td>F</td>
<td>2</td>
<td>R + E</td>
<td>Yes</td>
<td>No</td>
<td>Yes (Neg)</td>
<td>Normal in spite of activation (CHD) Manual</td>
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<tr>
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<td>12</td>
<td>F</td>
<td>9</td>
<td>R + E</td>
<td>Yes</td>
<td>Yes (Neg)</td>
<td>No</td>
<td>No event</td>
</tr>
<tr>
<td>16</td>
<td>10</td>
<td>F</td>
<td>5</td>
<td>R + E</td>
<td>Yes</td>
<td>Yes (Neg)</td>
<td>No</td>
<td>Asystole (15 s) Automatic</td>
</tr>
<tr>
<td>17</td>
<td>15</td>
<td>M</td>
<td>2</td>
<td>R + E</td>
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<td>No</td>
<td>No*</td>
<td>Supraventricular tachycardia (HR 165–180 bpm) Automatic</td>
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<tr>
<td>18</td>
<td>10</td>
<td>M</td>
<td>4</td>
<td>E</td>
<td>Yes</td>
<td>No</td>
<td>Yes (Neg)</td>
<td>Polymorphic VT (auto-activation triggered during subsequent asystole) Automatic</td>
</tr>
</tbody>
</table>

CHD = congenital heart disease; HR = heart rate; Neg = negative; Pos = positive.

*Electrophysiologic study after implantable loop recorder diagnosis was positive for atrioventricular nodal reentrant tachycardia.
Lower rates were used for those who were taking beta blockers or who were paced.

Event analysis and programming were performed at three monthly intervals and after symptomatic events using a standard programmer and software via telemetry. The upper rate detection parameter often needed to be increased to 210 bpm to avoid repeated auto-activation for sinus tachycardia. An event was recorded as a rhythm strip, and this event, stored either manually or by automatic activation, was analyzed. Manual activation was performed with the help of a handheld activator either by the patient or a witness at the time of the symptom. The patient and the parents/guardians were educated with regard to the use of the manual activator. The nature of the clinical events was documented at the time of device interrogation.

The device eventually was explanted either because a definitive diagnosis had been reached or because of end of battery life.

**Results**

The median age at device implantation was 11.3 years (range 4.5–16.5 years). The median duration of the device in situ was 18 months (range 5–36 months). The three patients (no. 5, 8, and 10) who had the device in situ for more than 30 months had shown an end of battery life between 24 and 26 months. The median time to diagnosis was 6 months (range 1 day to 17 months). No complications from the device itself occurred during implantation, while in situ, or after explantation in any of the patients.

The clinical characteristics, symptom–rhythm correlation, and conventional tests performed are summarized in Table 1.

Ten children (55%) had at least one activation with the device in situ. A diagnosis was made in 9 (50%) of these children, excluding the child who died suddenly (patient no. 6). Eight of these 10 children had a diagnosis on auto-activations. Patient no. 14 had a single manual activation.
Patient no. 2 also had a diagnosis on manual activation.

Five (28%) children had asystole, 2 (11%) had polymorphic ventricular tachycardia (VT), 1 had supraventricular tachycardia, and 1 had documented sinus rhythm.

Asystole (Figure 1) ranging from 8.5 to 39.4 seconds was taken as diagnostic for neurocardiogenic syncope. Of the five children with asystole, two had undergone a head-up tilt test, both with negative results.

A 10-year-old boy (patient no. 18) who ultimately was diagnosed with polymorphic VT had no auto-activations with two episodes of syncope while walking. Unfortunately, no manual activations were performed by the patient, family, or witness during these events because the subject repeatedly had left the activator at home. Importantly, the decisive auto-activation in the same patient was triggered by the asystole (18 seconds) and not by the preceding polymorphic VT (Figure 2).

The other child with polymorphic VT (patient no. 2) had a number of false activations. However, when this 12-year-old boy had a syncopal event in front of a large audience to whom he was about to deliver a speech, the mother activated the device, which finally gave the diagnosis (Figure 3). This child was the only patient in the study to have a positive head-up tilt table test (of the four tested).

The 15-year-old boy (patient no. 17) found to have sudden-onset supraventricular tachycardia had three appropriate auto-activations. Two of these events occurred at night (Figure 4) and one during the day.

A 9-year-old girl found to have sinus rhythm (patient no. 14) had a manual activation after “excessive laughter” that caused her to blackout for a few seconds. This girl was one of the two patients with a congenital heart defect (L-looped transposition of great arteries and pulmonary atresia) who previously had undergone a Senning-Rastelli procedure.

Patient no. 6 (a 15-year-old boy) who died suddenly had no previous activations during the 5 months the device was implanted. A 24-hour Holter recording had been unremarkable. An exercise test done performed prior to device implantation had shown some multiform ventricular ectopic beats during stage two of the Bruce protocol. The boy was quietly watching television in his own room when he died, and he was found some time later. The device was activated during the final moments; however, because of prolonged over-recording even after the boy’s death, multiple artifacts and electrical activity confused the device, so a diagnosis
could not be reached. A postmortem examination also was inconclusive.

Eight patients had no syncope with the implantable loop recorder in situ.

In addition to the false-negative results described, false positive auto-detections occurred in 16 patients (89%). Figure 5 shows auto-activation in a child who was exercising in school. The recording shows sinus rhythm when the heart rate exceeded 180 bpm (set upper limit). This auto-activation could have been avoided had the upper limit been set higher. Certain patients also recorded “noise” artifact, presumably as a result of pectoral muscle activity (Figure 6). In addition, a typical artifact followed by a straight line that was picked up as asystole was noted (Figure 6). We speculate that this loss of signal results from saturation of ECG amplifier inputs, with the apparent asystole representing the recovery time of the amplifier.

**Outcome**

Once VT was excluded, we were able to reassure the five patients with asystole. Standard advice regarding early recognition of presyncope was given. Three of these patients (no. 1, 13, and 17) have taken beta-blockers, and one patient (no. 11) has a rate-responsive dual-chamber device. None of these patients have experienced complete syncope since, although presyncope is common. A 9-year-old boy (patient no. 9), now 13 years old, still suffers from occasional syncope with painful stimuli, sometimes while playing rugby, which he will not give up.

The two patients with polymorphic VT underwent subsequent implantable cardioverter-defibrillator (ICD) insertion and beta-blocker therapy. Patient no. 2, who collapsed prior to delivering his speech, subsequently was found to have a pathologic mutation within the cardiac ryanodine gene RyR2.

The child with supraventricular tachycardia underwent successful radiofrequency ablation of an atrioventricular nodal reentrant tachycardia with no further syncopal episodes since.

Among the children who had no activations, six had no further investigations or treatment, and syncope has not
recurred. Patient no. 4 who required cardiopulmonary re-suscitation during the first syncopal episode with a normal ECG was subsequently found to have a mutation in the SCN5A gene associated with Brugada syndrome in another kindred. As yet we have been unable to obtain the family’s consent for an ICD insertion. Patient no. 12 had borderline long QT interval and was taking beta-blockers before the implantable loop recorder insertion. Genetic screening has been negative. The diagnosis remains uncertain.

Discussion

The use of implantable loop recorders in the diagnosis of recurrent syncope in adults is well established. Its role in pediatric practice remains to be defined. Syncope in most children can be diagnosed by simple detailed history, physical examination, and conventional tests. However, conventional testing such as 24-Holter monitoring has a low diagnostic yield, providing a symptom–rhythm correlation. We did not use these devices in the subset of patients presented in the present study primarily because of the long time between events. Had a device been used and in place for 2 weeks, a recorded event would have been obtained in only one patient (no. 16). Gooch et al showed that symptoms are not reproduced during the exercise test in >50% of patients with exercise-related events.

Neurocardiogenic syncope usually can be diagnosed with reasonable confidence based on the history alone. However, the patients in this study had atypical presentations, such as absence of the typical prodrome, association of syncope with exercise, or a QT interval in the upper normal range. Furthermore, patient no. 9 was a 9-year-old boy who collapsed with painful stimuli while participating in rugby matches. The patient with laugh syncope had a form of congenital heart disease with high risk for both atrioventricular nodal disease (L-looped transposition) and for ventricular and atrial arrhythmias (Rastelli-Senning procedure). The implantable loop recorder findings were reassuring in both cases.

The tilt-table test has been reported by others to have a high degree of specificity in the diagnosis of asystolic syncope. However, of the four tilt-table tests performed in this small cohort, the only positive result was obtained in patient no. 2, who subsequently was diagnosed with catecholaminergic polymorphic VT. Furthermore, two other negative tests occurred in patients (no. 1 and 9) now known to have prolonged asystolic syncope. These results are consistent with those in 81 adults with suspected arrhythmic syncope reported by García-Civera et al, who found no statistical association between tilt-table test results and the mechanism of syncope found with the implantable loop recorder.

Our study showed that by placing the implantable loop recorder in the pediatric population, the diagnosis of syncope was possible in half of the patients. A study performed by Rossano et al produced a 67% yield; however, those authors also included palpitations, acute life-threatening events, and near-syncope in their inclusion criteria. Two adult studies by Krah et al and Ashby et al provided symptom–rhythm correlation in 52% to 94% of patients with implantable loop recorder placement in undiagnosed syncope. More recent series in adult patients dealing only with syncope have reported lower diagnostic yields: 33% by Farwell et al, 55% by Brunchhorst et al, and 53% by Lombardi et al. Thus, our results in children are broadly consistent with those reported for the adult population.

Preventing sudden death remains a primary goal in these children. We have shown that although there is a definite increase in the number of children diagnosed, the implantable loop recorder has certain crucial limitations. Failure of the auto-activation on three occasions in a patient with polymorphic VT is a major concern. Of note are the frequent false-positive activations usually related to muscle tremors and what we suspect to be amplifier saturation.

Failure of auto-activation by the Reveal Plus device is not unique to children. Ng et al found that of 682 auto-activations in 50 patients, 83% were inappropriate, due to both undersensing and oversensing. Chrysostomakis et al found that alternative placement of the implantable loop recorder (near the cardiac apex) made no difference to the problem of undersensing. Together, the results of these studies suggest strongly that modifications to the QRS detection algorithms are needed.

Given that auto-activation seems unreliable in our pediatric series, high-quality patient and family education is an integral component associated with device implantation in order to ensure manual activation during syncope. Our best and frequently repeated efforts clearly were not sufficient in the family of the child with failed auto-detection of polymorphic VT. If the family member had manually activated the device when the auto-activation failed, then a diagnosis could have been made earlier.

Consideration must be given to the invasive nature of this procedure on two separate occasions (implantation and explantation). This could have a potential psychological effect on the child, especially with regard to scar formation, more so in adolescent girls. Alternative placements that would move the scar from a prominent position are being explored. However, in our experience, the children and their parents were generally accepting of the need for the procedure. This may be partly attributed to the frustration and anxiety associated with the children having undergone multiple tests/procedures with no definitive diagnosis, but also the desire shared by most parents and children with their cardiologist to exclude a sinister cause of the syncope.

Conclusion

In our cohort of children 16 years and younger with undiagnosed syncope, the implantable loop recorder was successful in making a diagnosis in half of the patients. This
has allowed more confident and definitive reassurance of children with neurocardiogenic syncope and opens the door to pacemaker therapy. The two children with polymorphic VT may ultimately owe their lives to the fact that this arrhythmia was detected, and screening of family members will be equally valuable. However, the limitations of this device in the pediatric population must be acknowledged. The failure of auto-activation in distinguishing from among polymorphic VT, noise, and sinus rhythm indicates that the diagnostic utility of the implantable loop recorder depends pivotally on the compliance of the patient and family to activate the device. Furthermore, artifactual activations may over write genuine, even terminal arrhythmias.

References