Ventricular tachycardia in infants with structurally normal heart: A benign disorder

Mark D. Levin
Washington University School of Medicine in St. Louis

Paul Stephens
The Children's Hospital of Philadelphia

Ronn E. Tanel
University of California - San Francisco

Victoria L. Vetter
The Children's Hospital of Philadelphia

Larry A. Rhodes
The Children's Hospital of Philadelphia

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Original Article

Ventricular tachycardia in infants with structurally normal heart: a benign disorder

Mark D. Levin,1,2 Paul Stephens,1 Ronn E. Tanel,1,3 Victoria L. Vetter,1 Larry A. Rhodes1

1Division of Cardiology, The Children's Hospital of Philadelphia, Pennsylvania; 2Division of Cardiology, Department of Pediatrics, St. Louis Children's Hospital, Washington University School of Medicine, St. Louis, Missouri; 3Children's Hospital and Department of Pediatrics, UCSF School of Medicine, San Francisco, California, United States of America

Abstract We evaluated the presentation, treatment, and outcome of infants who present with ventricular tachycardia in the first year of life. Seventy-six infants were admitted to our institution with a diagnosis of ventricular tachycardia between January, 1987 and May, 2006. Forty-five infants were excluded from the study because of additional confounding diagnoses including accelerated idioventricular rhythm, Wolff–Parkinson–White syndrome, supraventricular tachycardia with aberrancy, long QT syndrome, cardiac rhabdomyoma, myocarditis, congenital lesions, or incomplete data. The remaining 31 included infants who had a median age at presentation of 1 day, with a range from 1 to 255 days, and a mean ventricular tachycardia rate of 213 beats per minute, with a range from 171 to 280, at presentation. The infants were treated chronically with propranolol (38.7%), amiodarone (12.9%), mexiletine (3.2%), propranolol and mexiletine (9.7%), or propranolol and procainamide (6.5%). The median duration of treatment was 13 months, with a range from 3 to 105 months. Ventricular tachycardia resolved spontaneously in all infants. No patient died, or received catheter ablation or device therapy. Median age at last ventricular tachycardia was 59 days, with a range from 1 to 836 days. Mean follow-up was 45 months, with a range from 5 to 164 months, with a mean ventricular tachycardia-free period of 40 months. Infants with asymptomatic ventricular tachycardia, a structurally normal heart, and no additional electrophysiological diagnosis all had spontaneous resolution of tachycardia. Furthermore, log-rank analysis of the time to ventricular tachycardia resolution showed no difference between children who received chronic outpatient anti-arrhythmic treatment and those who had no such therapy. While indications for therapy cannot be determined from this study, lack of symptoms or myocardial dysfunction suggests that therapy may not be necessary.

Keywords: Ventricular tachycardia; accelerated idioventricular rhythm; infant

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IDIOPATHIC VENTRICULAR TACHYCARDIA IN CHILDREN with structurally normal heart was first published in 1942 (Rosenbaum, American journal of Diseases in Children). Since that time, there have been several reports of idiopathic ventricular tachycardia in children with structurally normal heart, which suggest that this disease follows a benign, self-limited course.1–8 However, others have suggested that idiopathic ventricular tachycardia could result in death.9,10 As such, treatment recommendations vary from conservative observation to medical therapy, radiofrequency catheter ablation, or even invasive surgical procedures.1,2,3,8,9,11–13

Correspondence to: L. A. Rhodes, MD, Division of Cardiology, Department of Pediatrics, West Virginia University School of Medicine, 1 Medical Center Drive, Morgantown, West Virginia 26506, United States of America. Tel: 304 293 7036; Fax: 304 293 1409; E-mail: larhodes@hsc.wvu.edu
study was to evaluate the presentation, treatment, and outcome of infants who present with ventricular tachycardia and structurally normal heart in the first year of life. We hypothesised that patient and diagnostic data including demographics, symptomatology, initial electrocardiogram, 24-hour Holter monitor, and echocardiogram data may predict a benign and self-limited process in some infants with ventricular tachycardia. We also sought to identify the relationship between the initial clinical hospital course and the time to ventricular tachycardia resolution. We hypothesised that a more recalcitrant ventricular tachycardia upon initial presentation may portend a more difficult or prolonged long-term clinical course.

This report describes the largest cohort of infants from a single centre in which children with ventricular tachycardia presented in the first year of life. Furthermore, it provides the first data that anti-arrhythmic medications do not hasten the resolution of a discrete population of infants with ventricular tachycardia. Ideally, a randomised trial would be performed to determine the efficacy of medications in the treatment of such a disease. However, given the incidence of this disease process, such a study is not possible at this time. As an alternative, we hope this report provides some evidence that there is a role for withholding anti-arrhythmic medications in a discrete population of infants with ventricular tachycardia and structurally normal heart.

Methods

Study design

We performed a single-centre retrospective analysis of infants and infants with an admission diagnosis of ventricular tachycardia to our institution between January, 1987 and May, 2006. The Institutional Review Board at The Children’s Hospital of Philadelphia approved this study. Patient charts were reviewed for demographic information, presenting symptoms, electrocardiogram, 24-hour Holter monitor, echocardiogram data, birth and family history, pre-hospital and inpatient therapy, and outpatient medications. Length of hospital stay and the number of inpatient medication changes were noted. Follow-up data included duration of follow-up, symptoms, and outpatient medications. Follow-up Holter monitoring was reviewed for the frequency of premature ventricular contractions, ventricular couplets, and runs of ventricular tachycardia. Age at most recent ventricular tachycardia episode, duration of medical therapy, and length of follow-up were also noted. Occurrence of symptoms was assessed at each follow-up visit.

Definitions

Ventricular tachycardia was defined as four or more consecutive wide QRS complexes with atrioventricular dissociation at a rate more than 20% greater the preceding sinus rhythm. The diagnosis was confirmed by electrocardiogram, rhythm strip, or 24-hour Holter monitor recording. Ventricular arrhythmias at a rate less than 20% greater than the sinus rhythm, were termed accelerated idioventricular rhythm and were excluded from analysis. Bundle branch morphology was determined if ventricular tachycardia was recorded on 12-lead electrocardiogram.

Initial ventricular tachycardia rate, length of hospital stay, and the number of drug failures were used as surrogate markers for disease severity. Such markers allowed characterisation of the initial clinical course of the disease. As ventricular tachycardia resolved without significant morbidity in all infants, we chose time to ventricular tachycardia resolution as an indication of the long-term clinical course.

Patient selection

Infants with an admission diagnosis of ventricular tachycardia, who were under the age of 1 year at the time of admission were included following a review of the presenting electrocardiogram or rhythm strip. Infants were excluded if they had a haemodynamically significant congenital cardiac disease, cardiomyopathy, cardiac tumour, or were in overt cardiac failure on admission to the hospital. Furthermore, a diagnosis of long QT syndrome or Wolff–Parkinson–White syndrome was also grounds for exclusion. Finally, infants were excluded if follow-up of at least 6 months was not available.

Statistical analysis

Statistical analysis was performed using SPSS (version 11.5; Chicago, Illinois, United States of America) and GraphPad Prism version 5.0 (GraphPad Software, San Diego, California, United States of America). Significance was set a priori at p less than 0.05. Student’s t-test was used to assess the relationship between continuous variables that were normally distributed, unless indicated. The Mann–Whitney test was used to compare the means of non-normally distributed continuous variables. Such an analysis was performed to determine whether a correlation could be made between the date of clinical presentation and whether the child was prescribed outpatient medication. Using Excel (Microsoft 2008), the dates were converted into a numeric value by calculating the number of days between a reference day (1 January, 1900) and the
date of presentation. These numbers were then entered into Graphpad Prism 5.0, where the Mann–Whitney analysis was performed and the data were graphed. Chi-square analysis was used to determine significance of the categorical data. Linear regression analysis was used to assess the relationship between variables and outcome. Kaplan–Meier survival curves were constructed using the number of days from the first occurrence of ventricular tachycardia to the first subsequent Holter study that showed no evidence of ventricular tachycardia. The log-rank statistic was used to assess the statistical significance between the Kaplan–Meier curves. Bar graphs, linear regression plots, and Kaplan–Meier survival curves were constructed using GraphPad Prism version 5.0 for Windows.

Results

Patient characteristics

A summary of the baseline patient characteristics is presented in Table 1. Seventy-six infants under the age of 1 year had an admission diagnosis code of ventricular tachycardia. Infants with the following were excluded from further analysis: eight infants with supraventricular tachycardia with aberrancy, four infants with accelerated idioventricular rhythm, four infants with Wolff–Parkinson–White syndrome, three infants with long QT syndrome, three infants with cardiac rhabdomyoma, two infants with cardiomyopathy, 21 infants with haemodynamically significant congenital lesions, and nine infants whose length of follow-up was less than 6 months. Thus, 31 infants were included in the study.

Of the 24 infants with a full 12-lead electrocardiogram available for review, 20 had left bundle branch morphology and four had right bundle branch morphology. Bundle branch morphology could not be assigned to the remaining seven infants for whom the 12-lead electrocardiograms could not be reviewed. Kaplan–Meier survival curves for the time to arrhythmia resolution according to bundle branch morphology of the ventricular tachycardia were drawn. A comparison of these curves by log-rank statistic showed no significant difference (log-rank test $= 4.196$, $p = 0.1227$).

Symptoms

The majority of the infants had no symptoms at the time of presentation. Twelve infants presented during the prenatal period. Often, the diagnosis of ventricular tachycardia was an incidental finding in infants being observed for another condition. Such alternate diagnoses included transient tachypnoea of the newborn, infant of a diabetic mother, and minor genitourinary system abnormalities. No infant had symptoms of cardiovascular compromise, cyanosis, pallor, or seizure. Four infants had non-cardiovascular symptoms at the time of presentation: three infants had fever and mild tachypnoea without evidence of feeding intolerance, gallop, or hepatomegaly; one infant had poor feeding and emesis without evidence of associated respiratory distress.

Viral titres

Viral titres were sent on all four infants with symptoms at presentation with no positive results. The titres were drawn on six additional, asymptomatic infants. All infants were seronegative.

Electrocardiogram results

A baseline electrocardiogram performed when the infants were not in tachycardia showed a mean RR interval of 433 milliseconds, with a standard deviation of 105 milliseconds, mean PR interval of 114 milliseconds, with a standard deviation of 5.2 milliseconds, mean corrected QT interval of 405 milliseconds, with a standard deviation of 26.2 milliseconds, and a mean QRS axis of 109 degrees.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (days)</td>
<td>1</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male: 13</td>
<td>Female: 18</td>
</tr>
<tr>
<td>Median maximum VT rate (bpm)</td>
<td>214</td>
</tr>
<tr>
<td>Range: 158–300*</td>
<td></td>
</tr>
<tr>
<td>Median QRS width in Tachycardia (ms)</td>
<td>100</td>
</tr>
<tr>
<td>Mean corrected QT interval length on baseline ECG (ms)</td>
<td>$405 \pm 26.2$</td>
</tr>
<tr>
<td>VT bundle branch morphology</td>
<td>Left: 20; Right: 4</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>Yes: 4 patients</td>
<td>No: 27</td>
</tr>
<tr>
<td>Shortening Fraction (%; $n = 18$)</td>
<td>37.7 ± 7.8</td>
</tr>
<tr>
<td>Range: 27–56</td>
<td></td>
</tr>
<tr>
<td>Qualitative cardiac function by echocardiogram (number of patients)</td>
<td>Normal: 12</td>
</tr>
<tr>
<td></td>
<td>Mildly decreased: 1</td>
</tr>
</tbody>
</table>

ECG = electrocardiogram; VT = ventricular tachycardia

*Sinus rhythm rate of patient with ventricular tachycardia at a rate of 158 was 122 bpm
with a standard deviation of 39.1 degrees. Ventricular premature contractions were noted in 17 of 31 infants on initial electrocardiogram.

**Initial Holter monitor results**
Holter monitor recording was performed in all infants. One infant had no ventricular tachycardia on their initial Holter monitor study. The mean maximum heart rate during ventricular tachycardia was 195 beats per minute, with a standard deviation of 57.7 beats per minute, whereas the median sinus heart rates during the entire recording period was 136 beats per minute, with a standard deviation of 20.9 beats per minute. The median number of ventricular tachycardia episodes per patient was 717, with a range from 0 to 77,449, whereas the median longest run of ventricular tachycardia was 28.5 beats per minute, with a range from 4 to 12,786.

**Echocardiogram results**
All infants underwent complete echocardiographic evaluation. Three infants had haemodynamically insignificant patent ductus arteriosus. No child had significant atrioventricular or semilunar valve insufficiency. A mean shortening fraction of 37.7%, with a standard deviation of 7.8%, was found in the 18 infants who had a quantitative assessment of cardiac function. Of the remaining 13 infants, qualitative assessment revealed one infant with mildly decreased shortening fraction, whereas the remaining 12 had normal ventricular shortening.

**Medications and interventions**
Fifteen infants received intravenous anti-arrhythmic medications while in the hospital: 13 received lidocaine, one received amiodarone and one received esmolol. The oral medications administered to infants while in the hospital are summarised in Fig 1a.

During the initial hospitalisation, 19 infants had no anti-arrhythmic drug failures, seven infants had one failure, three infants had two failures, one infant had three failures, and one infant had four failures. Linear regression showed no correlation between the number of inpatient medications and the time to freedom from arrhythmia ($r = 0.0003985$, $p = 0.9166$).

In addition to medication administration, other potential interventions included cardioversion, transoesophageal electrophysiology study, invasive electrophysiology study, radiofrequency catheter ablation, or surgery. In our cohort, one infant underwent direct current cardioversion. No infant underwent radiofrequency catheter ablation or surgical intervention.

**Length of stay**
The median length of stay was 7 days, with a range from 1 to 38 days.

**Discharge medication**
Outpatient oral anti-arrhythmic medication usage is summarised in Fig 1b. Nine infants were discharged home on no anti-arrhythmic drugs. Twenty-two infants received outpatient medications. Outpatient oral anti-arrhythmic drugs used included propranolol, procainamide, mexiletine, and amiodarone. Seven infants were treated with a combination of medications; five infants were given mexiletine and propranolol, whereas two infants were treated with procainamide and propranolol.
An analysis to assess the differences between the group that received outpatient anti-arrhythmic drugs and those who received no outpatient anti-arrhythmic drugs failed to detect any statistically significant association. The results of this analysis are summarised in Table 2. The variables that were assessed included gender, bundle branch morphology, maximum tachycardia rate at presentation, duration of initial tachycardia episode, number of ventricular tachycardia episodes on initial 24-hour ambulatory electrocardiogram recording, and date on which the patient presented. No significant difference was found between these two groups.

**Outpatient clinical course**

The outpatient clinical course is summarised in Table 3. There were 115.5 patient-years of follow-up entailed in this study. Mean total follow-up was 6.8 years with a range from 7 months to 10.7 years. The mean number of patient visits was 7.7 with a range from 3 to 20 visits.

Ventricular tachycardia resolved spontaneously in all infants. The median age at the last ventricular tachycardia episode was 60 days, with a range from 1 day to 2.29 years. The mean follow-up period after ventricular tachycardia resolution was 41.1 months, with a range from 2.3 to 127 months. The infant whose last ventricular tachycardia episode was at 2.29 years had no ventricular tachycardia episodes captured on 24-hour Holter monitor studies performed between the ages of 9 months and 2.29 years. No symptoms were reported in any infants at follow-up.

The median duration of outpatient anti-arrhythmic drug treatment was 223 days, with a range from 0 day to 8.5 years, following hospital discharge. One infant who had no initial outpatient oral anti-arrhythmic treatment was re-hospitalised at 4 months of age to initiate propranolol treatment due to the presence of ventricular tachycardia on 24-hour Holter monitor.

No patient underwent radiofrequency catheter ablation, received device therapy, underwent surgery, or died. One infant had a transoesophageal electrophysiology study during which ventricular tachycardia was induced following the administration of isoproterenol.

There was one adverse event that was attributed to a medication side effect. A 27-month-old female child received propranolol during an acute illness during which the child had poor oral intake. She subsequently suffered a hypoglycaemic seizure, which was treated with parenteral glucose. The child had no subsequent seizures.

<table>
<thead>
<tr>
<th>Received outpatient medication (n = 22)</th>
<th>No outpatient medication (n = 9)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation (days)</td>
<td>24.4 ± 63</td>
<td>28 ± 79</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>VT bundle branch morphology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>Right</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Maximum VT rate at presentation (bpm)</td>
<td>217 ± 26.9</td>
<td>201 ± 40.8</td>
</tr>
<tr>
<td>Length of initial hospitalisation (days)</td>
<td>14.4 ± 10.4</td>
<td>8.4 ± 8.4</td>
</tr>
<tr>
<td>Longest VT episode (bpm)</td>
<td>1371 ± 3389</td>
<td>21.2 ± 29.2</td>
</tr>
<tr>
<td>Number of VT episodes on initial Holter study</td>
<td>7245 ± 20,302</td>
<td>1168 ± 1937</td>
</tr>
<tr>
<td>Age at last VT (days)</td>
<td>163 ± 234</td>
<td>68.4 ± 78.7</td>
</tr>
<tr>
<td>Number of premature ventricular contractions on initial Holter study</td>
<td>8990 ± 33,005</td>
<td>37.3 ± 25.3</td>
</tr>
</tbody>
</table>

NS = not significant; VT = ventricular tachycardia
Student’s t-test used, unless indicated
*Fisher’s exact test
**Statistics calculated by Mann–Whitney test
Survival analysis

To assess the effect of outpatient oral anti-arrhythmic administration on the course of idiopathic ventricular tachycardia, we constructed the Kaplan–Meier survival curves for children who received outpatient oral medication as well as a similar curve for those children who received no outpatient medication. Again, there were no complications or deaths in those infants who received no outpatient medication. We compared the survival curves of these two groups using the log-rank statistic. Figure 2 shows the result of this analysis. The log-rank statistic was 1.94, yielding a p-value of 0.167. Thus, there was no statistically significant difference between the survival plots of those taking oral anti-arrhythmics and those taking no anti-arrhythmic drugs.

Discussion

Idiopathic ventricular tachycardia in infants with structurally normal heart is a rare disorder. We performed a retrospective analysis of all cases of idiopathic ventricular tachycardia in children under the age of 1 year who presented to our institution since 1987. We found that a distinct cohort of infants without structural cardiac disease, prolonged QT interval, or overt signs of cardiomyopathy had a benign course with spontaneous resolution of their tachycardia.

Previously, published series of idiopathic ventricular tachycardia in children show findings similar to ours.1–5,7,8,14 In general, the reports to date suggest a favourable prognosis for idiopathic ventricular tachycardia infants. Most recently, Pfammatter and Paul concluded that idiopathic ventricular tachycardia carries a favourable prognosis.6 Furthermore, these authors suggested children with normal left ventricular function by echocardiogram, who were asymptomatic, could be followed without drug treatment.6 This study, however, included heterogeneous populations of children, ranging in age from the neonatal period to 16 years old.

Although the majority of the reports shows a benign prognosis, deaths have been reported in children with ventricular tachycardia without structural cardiac disease. This discrepancy likely results from discrepant patient populations. Fulton et al,3 report no deaths in their cohort, but cite reports of nine deaths in previously reported cases of ventricular tachycardia among children without structural cardiac disease. Included in this latter group were infants with myocarditis. Deal et al2 reported a 13% mortality in their cohort. The infants in this study ranged from 6 to 21 years of age.2,7 Garson et al9,13 reported cases of incessant ventricular tachycardia in infants arising from hamartomas or Purkinje cell tumours. None of our infants had such incessant tachycardia. Gillette10

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Outpatient treatment</th>
<th>No outpatient treatment</th>
<th>p-value</th>
<th>Mean (s.d.)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Anti-arrhythmic therapy (days)</td>
<td>Median 382</td>
<td>–</td>
<td>–</td>
<td>364 ± 102</td>
<td>0–3135</td>
</tr>
<tr>
<td>Length of follow-up (months)</td>
<td>101.2 ± 266</td>
<td>36.42 ± 26.5</td>
<td>NS (0.476)</td>
<td>82.6 ± 225</td>
<td>7–1284</td>
</tr>
<tr>
<td>Number of visits</td>
<td>8.3 ± 3.6</td>
<td>6.1 ± 3.5</td>
<td>NS (0.129)</td>
<td>7.7 ± 3.6</td>
<td>3–20</td>
</tr>
<tr>
<td>Median age at last VT episode (days)</td>
<td>157.2 ± 230.0</td>
<td>72.3 ± 82.5</td>
<td>NS (0.293)</td>
<td>60</td>
<td>1–836</td>
</tr>
<tr>
<td>Days observed VT free</td>
<td>1298.2 ± 923.6</td>
<td>1055.9 ± 777.9</td>
<td>NS (0.495)</td>
<td>1233 ± 875</td>
<td>70–3810</td>
</tr>
</tbody>
</table>

VT = ventricular tachycardia; NS = not significant
Student’s $t$-test is used to determine significance

Figure 2.
Kaplan–Meier survival-type plot showing the number of days to ventricular tachycardia resolution stratified by those receiving outpatient anti-arrhythmic medications and those receiving no outpatient anti-arrhythmic medication. Log-rank statistic shows no statistical difference between survival plots (log-rank test = 1.735, $p = 0.1877$).
suggested that there was an infrequent progression from neonatal ventricular tachycardia to such incessant ventricular tachycardia caused by hamartomas. None of the infants in our cohort showed such a progression. This finding is consistent with those reported by Van Hare and Stanger.8

The limitations of this study rest on its retrospective nature. Although we describe the largest cohort of infants with ventricular tachycardia and structurally normal heart, the number of cases remains relatively small. Finally, the diagnosis of ventricular tachycardia was based on non-invasive tracings, instead of directly recording ventricular electrograms within a laboratory setting.

We have shown that ventricular tachycardia in an infant who has a structurally normal heart, without symptoms of haemodynamic compromise or alternate electrophysiologic diagnosis follows a benign course. Ventricular tachycardia resolved in all infants without the occurrence of life-threatening events or death. We have further shown that there was no difference in the clinical outcome or clinical course between those infants who received outpatient medication and those who received no outpatient anti-arrhythmic therapy. All infants had a resolution of their ventricular tachycardia, regardless of whether or not they received outpatient anti-arrhythmic drugs. This conclusion was drawn after constructing the Kaplan–Meier survival curves for the infants who received outpatient anti-arrhythmic agents with those who received no such outpatient medication. Statistical analysis showed no significant differences between these groups that might have led to a selection bias to one of the two groups. Interestingly, the only infant with significant morbidity was the one who suffered hypoglycaemic seizures associated with propranolol administration. Although indications for therapy cannot be determined from this study, the lack of symptoms or myocardial dysfunction suggests that therapy may not be necessary in this narrowly defined group of infants.

References