Perioperative atrial tachycardia is associated with increased mortality in infants undergoing cardiac surgery

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Objective: Few data are available on the frequency or importance of perioperative atrial tachycardia in infants. We hypothesized that atrial tachycardia in infants undergoing cardiac surgery is not rare and is associated with increased morbidity and mortality.

Methods: From 2007 through 2010, 777 infants (median age, 1.8 months; interquartile range, 0.33–5.73) underwent cardiac surgery. Their medical records were reviewed for atrial tachycardia during the perioperative period.

Results: Of the 777 patients, 64 (8.2%) developed atrial tachycardia. The independent risk factors for developing atrial tachycardia included surgical age 6 months or younger (odds ratio, 4.4; 95% confidence interval, 1.1–19.15), use of 3 or more inotropes (odds ratio, 2.9; 95% confidence interval, 1.4–6.2), and heterotaxy syndrome (odds ratio, 2.9; 95% confidence interval, 1.1–7.4). All-cause mortality in the atrial tachycardia group was increased (21.9% vs 7.2%, P < .001) during a median follow-up period of 14.6 months (interquartile range, 6.8–24.6), and atrial tachycardia was independently associated with decreased survival (hazard ratio, 1.9; 95% confidence interval, 1.1–3.8). Infants with perioperative atrial tachycardia had a longer hospital length of stay (32 vs 17 days, P < .001) and duration of inotrope use (10.5 vs 3.0 days, P < .001). A total of 57 patients received antiarrhythmic therapy, with propranolol the most common (n = 31). Among the survivors, 48 patients received outpatient antiarrhythmic therapy, which was successfully discontinued in 23 patients at a median duration of 14 months (interquartile range, 5.7–18.6) without recurrence.

Conclusions: Atrial tachycardia is common in infants undergoing cardiac surgery and is independently associated with decreased survival. Among survivors, antiarrhythmic agents successfully controlled atrial tachycardia in most patients with a low recurrence risk after discontinuation. (J Thorac Cardiovasc Surg 2012;144:396-401)

Among infants undergoing corrective or palliative cardiac surgery, the incidence of perioperative tachyarrhythmias has been reported to be 14% to 60%. Cardiac dysfunction, the postoperative effects of cardiopulmonary bypass, the presence of scar and suture within the myocardium, electrolyte disturbances, and other procedural factors have all been postulated as risk factors for increased rates of postoperative arrhythmia.

Focal atrial tachycardia (AT) is a form of supraventricular arrhythmia that occurs in infants with and without congenital heart disease. Although previous reports have described longer hospital stays, intubation times, and requirement for inotropic support in infants with perioperative cardiac arrhythmias, only limited data have described the risk factors and outcome of perioperative AT in infants undergoing cardiac surgery. Furthermore, the mortality associated with AT has not been reported in this age group. Therefore, the present study aimed to test the hypothesis that AT in infants undergoing cardiac surgery is not a rare occurrence and is associated with increased morbidity and mortality. The risk factors associated with AT were also assessed.

METHODS

A retrospective review of the pediatric cardiovascular surgery database identified all infants who underwent cardiac surgery at Texas Children’s Hospital from July 2007 through July 2010. The medical records of these infants were then reviewed in the pediatric cardiology database to identify those diagnosed with AT within the perioperative period. The Baylor College of Medicine institutional review board approved the study.
Patient Selection

All infants who underwent cardiac surgery during the study period were included. This included all infants with structural heart disease and those who required placement of a ventricular assist device or cardiac transplantation. We excluded infants who underwent pacemaker implantation for congenital atrioventricular block, pericardial window creation for recurrent pericardial effusion, or extracorporeal membrane oxygenation cannulation for cardiopulmonary failure without concomitant cardiac surgery. All infants were admitted to the cardiac intensive care unit postoperatively, received continuous cardiac telemetry during their intensive care unit stay, and had at least 1 electrocardiogram recorded postoperatively. The medical records were reviewed for cases of AT. All cases were confirmed by a pediatric electrophysiologist. Macroreentrant AT such as atrial flutter and fibrillation was not included.

Definitions

Infancy was defined as patient age younger than 12 months. The perioperative period spanned 10 days preoperatively to 30 days postoperatively. The diagnosis and procedural variables were stratified using the Risk Adjustment for Congenital Heart Surgery scoring system. AT was defined as 3 or more consecutive beats of tachycardia originating from an alternative atrial focus different than sinus. To be included in the present study, the degree of AT was considered to be of enough clinical significance by the attending cardiologist of record to require therapy alteration, including initiation of antiarrhythmic treatment or close electrocardiographic observation. For the purposes of the present study, because single 3-beat runs of tachycardia were typically not treated, they were not included in the present study. Features aiding in the identification of AT included an acute change in P wave morphology during tachycardia at a rate at least 20% faster than sinus. In cases of heterotaxy syndrome, care was taken to accurately identify AT in the presence of more than 1 primary atrial rhythm. A review of inpatient electrocardiographic telemetry or 24-hour Holter monitor data was performed independently by a pediatric cardiac electrophysiologist (J.J.K.) to confirm the diagnosis. A representative 12-lead electrocardiogram and atrial electrocardiogram are displayed.

Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AT</td>
<td>atrial tachycardia</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>ECMO</td>
<td>extracorporeal membrane oxygenation</td>
</tr>
<tr>
<td>IQR</td>
<td>interquartile range</td>
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<tr>
<td>OR</td>
<td>odds ratio</td>
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FIGURE 1. A, Postoperative 12-lead electrocardiogram of an infant with atrial tachycardia. B, Postoperative atrial electrocardiogram (attached to lead V1) of an infant with atrial tachycardia.
Data Collection and Statistical Analysis

The preoperative and postoperative data were obtained by a review of medical records at Texas Children’s Hospital. The intraoperative data were obtained from the pediatric cardiovascular surgery database. Univariate analysis of categorical variables was performed using Pearson’s chi-square or Fisher’s exact test, as appropriate. Continuous variables were analyzed using the Mann-Whitney U test because the data were not normally distributed. Survival analysis was performed using Kaplan-Meier estimation. Factors significantly associated with the development of AT and mortality were subsequently analyzed in multivariable analyses. Multivariable binary logistic regression analysis was used to determine the independent risk factors for mortality. A 2-tailed test of significance was used for all statistical analyses.

RESULTS

Patient Population

A total of 777 infants at a median age of 1.8 months (interquartile range [IQR], 0.33–5.73) who underwent cardiac surgery at Texas Children’s Hospital during the study period were included. Of those, 64 infants (8.2%) were diagnosed with AT. Significant residual cardiac lesions requiring reoperation or catheter-based intervention within the postoperative study period was relatively uncommon and was present in 19 patients (2.4%, 5 in the AT group). The common diagnoses and patient characteristics of both groups are listed in Table 1. AT was more common in Hispanics (P = .02). The median age and weight at surgery were significantly lower for patients with AT than for the control group (P < .001 and P < .001, respectively).

Presence of AT

Of the 777 patients, 64 (8.2%) were diagnosed with AT and were included in the study group. Of these 64 patients, 8 (12.5%) developed AT at a median of 4.0 days (IQR, 0–6.0) preoperatively, and 56 (87.5%) developed AT at a median of 8.5 days (IQR, 3.0–14.0) postoperatively. The mean maximal rate of tachycardia was 241.2 beats/min (range, 160–369) at a median of 7.0 days (IQR, 0.25–12.0) postoperatively. The factors associated with the development of AT on univariable and multivariable analysis are listed in Table 2. On multivariable analysis, heterotaxy syndrome, age at surgery younger than 6 months, the use of 3 or more inotropes, total anomalous pulmonary venous return, and transposition of the great arteries were independent risk factors for the development of AT.

On univariable analysis, the specific inotropes used during the perioperative period were associated with an increased risk of postoperative AT. The preoperative use of dopamine (odds ratio [OR], 2.97; 95% confidence interval [CI], 1.17–7.56) or calcium chloride (OR, 3.38; 95% CI, 1.4–8.15) was significantly associated with an increased risk of AT. Postoperatively, epinephrine (OR, 5.59; 95% CI, 2.98–10.12), vasopressin (OR, 3.37; 95% CI, 2.01–5.67), and calcium chloride (OR, 4.36; 95% CI, 2.51–7.57) use were significant. Milrinone did not significantly contribute any additive risk to the development of AT. Although no individual inotrope was significantly associated with the development of AT on multivariable

<table>
<thead>
<tr>
<th>TABLE 1. Patient demographics</th>
<th>No AT</th>
<th>AT</th>
<th>P value</th>
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<tbody>
<tr>
<td>Age (mo)</td>
<td>Median</td>
<td>IQR</td>
<td></td>
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<tr>
<td>2.37</td>
<td>0.27</td>
<td></td>
<td>.001</td>
</tr>
<tr>
<td>Male gender (n)</td>
<td>391 (54.8)</td>
<td>42 (65.6)</td>
<td>.06</td>
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<td>Ethnicity (n)</td>
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<td></td>
<td></td>
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<tr>
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<td>99 (13.9)</td>
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<td>Hispanic</td>
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<td>33 (51.6)</td>
<td>.02</td>
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<td>White</td>
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<td>.03</td>
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<tr>
<td>Prematurity (n)</td>
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<td>15 (23.4)</td>
<td>NS</td>
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<td>Birth weight (kg)</td>
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<td>3.0</td>
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</tr>
<tr>
<td>IQR</td>
<td></td>
<td>2.79–3.72</td>
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</tr>
<tr>
<td>Weight at surgery (kg)</td>
<td>2.59–3.35</td>
<td>2.71–3.39</td>
<td>.001</td>
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<td>Diagnosis (n)</td>
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<td></td>
<td></td>
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<td>Ventricular septal defect</td>
<td>105 (14.7)</td>
<td>2 (3.1)</td>
<td>&lt;.001</td>
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<tr>
<td>Tetralogy of Fallot</td>
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<td>2 (3.1)</td>
<td>.02</td>
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<td>73 (10.2)</td>
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<td>55 (7.7)</td>
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<td>Coarctation of aorta</td>
<td>49 (6.9)</td>
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<td>Transposition of great arteries</td>
<td>38 (5.3)</td>
<td>9 (14.1)</td>
<td>.01</td>
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<td>Heterotaxy syndrome</td>
<td>33 (4.6)</td>
<td>11 (17.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total anomalous pulmonary venous return</td>
<td>29 (4.1)</td>
<td>7 (10.9)</td>
<td>.02</td>
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<td>Cardiopulmonary bypass time (min)</td>
<td>n = 530</td>
<td>n = 53</td>
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<td>Median</td>
<td>168.5</td>
<td>182</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>121–216</td>
<td>135.5–231</td>
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<tr>
<td>Aortic crossclamp time (min)</td>
<td>n = 508</td>
<td>n = 51</td>
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<tr>
<td>Median</td>
<td>96</td>
<td>94</td>
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<tr>
<td>IQR</td>
<td>69.3–129</td>
<td>67–139</td>
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<tr>
<td>Antegrade cerebral perfusion time (min)</td>
<td>n = 113</td>
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<td>NS</td>
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<td>Median</td>
<td>56</td>
<td>66</td>
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<tr>
<td>IQR</td>
<td>25–84</td>
<td>37.8–79.8</td>
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<td>Deep hypothermic circulatory arrest time (min)</td>
<td>n = 115</td>
<td>n = 16</td>
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<tr>
<td>Median</td>
<td>13</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>8–23</td>
<td>8–39</td>
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</table>

Data in parentheses are percentages. AT, Atrial tachycardia; IQR, interquartile range; RACHS-I, Risk Adjustment for Congenital Heart Surgery.

analysis, the use of 3 or more inotropes was significant (OR, 2.91; 95% CI, 1.37–6.19; Table 2).

### Patient Outcomes

Patients with AT had longer hospital stays and inotrope durations compared with the non-AT group (Table 3). A total of 15 patients (1.9%), 10 control patients and 5 study patients (P < .01), required extracorporeal membrane oxygenation (ECMO) support during the postoperative period owing to hemodynamic instability of differing etiologies. Incessant AT was the indication for ECMO in only 1 neonate, who initially required 72 hours of support, but went on to an uneventful discharge home. Although the remaining 4 study patients developed AT sometime during the perioperative period after ECMO decannulation, the indication for ECMO postoperatively was an acute, nonarrhythmic cause of hemodynamic compromise.

The overall mortality of the study group was 21.9% versus 7.2% in the control group (P < .001) during the follow-up period. The median follow-up was 12.3 months (IQR, 4.5–24.5) in the AT group and 14.7 months (IQR, 7.0–24.7) in the non-AT group (P = 0.21). On multivariable analysis, perioperative AT was independently associated with a greater risk of mortality (Table 4). Within the study group, 8 patients died before discharge home; however, the mortality during the immediate 30-day postoperative period was similar between the 2 groups. No statistically significant difference was seen in the risk of mortality between patients who developed AT preoperatively versus postoperatively (P = 0.25). The Kaplan-Meier survival curves for both groups and the log-rank test of significance are displayed in Figure 2.

### Antiarrhythmic Therapy

A total of 57 patients (89.1%) received inpatient antiarrhythmic therapy at the onset of AT. Propranolol was the most commonly used agent in 31 (54.4%) patients, procainamide in 11 (18.9%), esmolol in 7 (12.1%), amiodarone in 5 (8.8%), propranolol with digoxin in 2 (3.5%), and metoprolol in 1 (1.7%). Treatment failure occurred in 13 patients. The initial therapy with propranolol failed in 10 patients and required transition to sotalol in 6 patients and amiodarone in 4 patients. Esmolol therapy failed in 2

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**TABLE 2. Risk factors for developing AT**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
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<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
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<tr>
<td>Age ≤ 6 mo at surgery</td>
<td>10.47</td>
<td>2.54–43.23</td>
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<td>Total anomalous pulmonary venous return</td>
<td>2.90</td>
<td>1.22–6.90</td>
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<tr>
<td>Use of ≥ 3 inotropes</td>
<td>5.92</td>
<td>3.33–10.54</td>
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<td>Heterotaxy syndrome</td>
<td>4.28</td>
<td>2.05–8.94</td>
</tr>
<tr>
<td>Transposition of great arteries</td>
<td>2.91</td>
<td>1.34–6.32</td>
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<tr>
<td>Single ventricle physiology</td>
<td>2.41</td>
<td>1.41–4.10</td>
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<td>Hispanic</td>
<td>1.83</td>
<td>1.10–3.06</td>
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<td>RACHS-1 score ≥ 4</td>
<td>3.76</td>
<td>2.21–6.41</td>
</tr>
<tr>
<td>Use of preoperative inotropes</td>
<td>2.17</td>
<td>1.13–4.17</td>
</tr>
<tr>
<td>Hypoplastic left heart syndrome</td>
<td>2.22</td>
<td>1.07–4.59</td>
</tr>
<tr>
<td>Use of postoperative inotropes</td>
<td>2.55</td>
<td>1.12–5.69</td>
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**TABLE 4. Risk factors for mortality**

<table>
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<th>Factor</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
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<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
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<tr>
<td>Use of preoperative inotropes</td>
<td>3.59</td>
<td>2.09–6.17</td>
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<tr>
<td>Perioperative AT</td>
<td>3.49</td>
<td>1.92–6.33</td>
</tr>
<tr>
<td>Use of postoperative inotropes</td>
<td>2.37</td>
<td>1.07–5.22</td>
</tr>
<tr>
<td>Heterotaxy syndrome</td>
<td>2.84</td>
<td>1.4–5.75</td>
</tr>
<tr>
<td>Single ventricle physiology</td>
<td>2.62</td>
<td>1.59–4.33</td>
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<tr>
<td>Age ≤ 6 mo at surgery</td>
<td>2.73</td>
<td>1.18–6.35</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.73</td>
<td>1.05–2.85</td>
</tr>
<tr>
<td>RACHS-1 score ≥ 4</td>
<td>3.15</td>
<td>1.84–5.41</td>
</tr>
</tbody>
</table>

**FIGURE 2.** Kaplan-Meier survival curve of infants with perioperative atrial tachycardia compared with those without atrial tachycardia.

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Data in parentheses are percentages. AT, atrial tachycardia; ECMO, extracorporeal membrane oxygenation.
patients, who were transitioned to procainamide, and pro-
cainamide therapy failed in 1 patient, who was transitioned
to amiodarone. Treatment failure was not significantly asso-
ciated with death ($P = 0.26$). The decision to not treat AT in
7 patients was predominantly because of the identification
of reversible iatrogenic causes such as the presence of a
deep central venous catheter or electrolyte derangement.
One untreated patient died before discharge and the remain-
ing 6 were successfully discharged with no antiarrhythmic
therapy and no recurrence of AT to date.

Of the 56 survivors at hospital discharge, 48 (85.7%) re-
ceived outpatient antiarrhythmic therapy. Propranolol was
again the most commonly used agent in 32 patients
(66.7%). Sotalol was used in 7 (14.6%), amiodarone in 5
(10.4%), propranolol with amiodarone in 2 (4.2%), pro-
pranolol with digoxin in 1 (2.1%), and metoprolol in 1
(2.1%). Antiarrhythmic therapy was successfully discontin-
ued in 23 patients (41.0%) at a median follow-up of
14.1 months (IQR, 5.7–18.6) without recurrence.

**DISCUSSION**

In the present retrospective study of 777 infants undergo-
ing cardiac surgery, perioperative AT developed in 8% of
the infants and was independently associated with increased
mortality, a finding not previously reported in the current lit-
erature. In the AT group, all-cause mortality was 21.9%
compared with 7.2% in the control group during a median
follow-up period of 16 months. Similar to a recent study by
Trivedi and colleagues describing arrhythmias in children
with hypoplastic left heart syndrome, we did not find a sig-
nificant difference in 30-day mortality between the AT and
control groups. This is in contrast to a previous investigation
examining all arrhythmias. However, no study to date,
including the aforementioned reports, has examined AT
and its associated mortality. An analysis of inpatient mortal-
duty did not reveal the cause of death to be directly attribut-
able to AT. It would be difficult to ascertain whether AT
directly led to death in patients with out-of-hospital events
because their heart rhythm was not recorded at the event;
however, it is unlikely that AT was the direct cause of death
in these patients. We hypothesized that the association of
AT with mortality is likely a surrogate marker of overall
poor cardiovascular health and not a direct result of the
arrhythmia.

A number of independent risk factors for developing AT
were identified including age 6 months or younger at sur-
gery, the use of 3 or more inotropes, transposition of the great
arteries, total anomalous pulmonary venous return, and het-
 erotaxy syndrome. Although Rosales and colleagues re-
ported univariable associations between postoperative AT
and both inotrope use and transposition of the great arteries,
the present study is the first to report independent risk fac-
tors. Similar to previous studies, younger age continued to
be a risk factor for ectopic automatic arrhythmias in infants
from unknown mechanisms. The arrhythmogenic nature
of inotropic agents and increased catecholamine levels
might enhance atrial automaticity and thus providing the
substrate to develop AT. Although the patient receiving 3
or more inotropes likely has morbidities beyond AT alone,
those who develop AT with significant inotropic support
likely represent an at-risk population of patients with com-
parably worse cardiovascular health. It is important to note
that AT was associated with mortality, independent of all
studied variables, including inotropic support. Thus, the pa-
tient receiving 3 or more inotropes who did not develop AT
was at a decreased risk of death compared with those who
did develop AT, suggesting that inotropes alone do not ex-
plain the increased risk of mortality in these patients.
Although the use of epinephrine, calcium chloride, dopa-
mine, and vasopressin in the perioperative period was asso-
ciated with AT, the use of milrinone was not, in contrast to
a recent report by Smith and colleagues. Thus, the combi-
nation of inotropes and the failing heart might manifest itself
as AT, representing a marker of overall poor cardiovascular
health and prognosis.

Specific diagnoses, including heterotaxy syndrome, were
associated with AT. Heterotaxy syndrome is often associ-
ated with complex congenital heart disease and atrial isom-
erism. Previous studies have reported the prevalence of
arrhythmias in both right and left atrial isomerism. Al-
though the development of AT in these patients is likely
multifactorial owing to the presence of associated anatomic
cardiac lesions, the present study was not designed to ex-
plor e the mechanistic etiologies of AT. Furthermore, the in-
fants in the present study who developed AT did so at
a median of 8.5 days postoperatively, which might be later
than expected if the inciting factor responsible for the onset
of AT was simply surgical trauma. This later time of onset
might speak to an etiology and natural history different
from trauma, such as inflammatory mechanisms, anatomic
substrates, or a failing myocardium. Potential additional in-
vestigation might help to better elucidate the possible mech-
anic etiologies for the development of AT, as well as possible
therapeutic strategies to minimize untoward out-
comes. The recognition and diagnosis of AT in this sub-
group is difficult owing to the abnormal, multiform P
waves. Therefore, vigilant observation of abnormal heart
rates that acutely change, the “warm up and cool down”
characteristics of the tachycardia, P wave morphology anal-
ysis, and atrioventricular conduction is needed to properly
make the diagnosis.

AT was associated with significantly increased morbidity,
including increased hospital length of stay and total ino-
trope duration. This is likely a factor of the infant’s overall
cardiovascular state and not directly attributable to AT
alone. The 30-day readmission rate was not significantly
different statistically between the 2 groups. Although the
use of postoperative ECMO was more likely in the study
group, AT was not the primary indication for ECMO in 4 of 5 patients.

In our cohort, AT was successfully treated with antiarrhythmic agents, as determined by follow-up Holter monitoring demonstrating no recurrent AT. Inpatient therapy with β-blockade, using propranolol and esmolol, was most commonly used, followed by procainamide and amiodarone. Treatment failure or the lack of treatment was not associated with death. Outpatient therapy was equally effective in the outpatient setting and can be successfully discontinued in most patients with a low risk of recurrence.

**Study Limitations**

Although this was the largest study of infants with perioperative AT to date, the study was limited by its single-center, retrospective design of a moderate number of patients. This sample size made it difficult to exclude the possibility of a type II error for other factors associated with mortality. Although overall mortality was worse in the AT group, the small sample size of the AT group was of limited statistical power to show a statistically significant difference in 30-day mortality between the 2 groups. In the subgroup analyses, considerations regarding the predictive risk factors were also of limited statistical power. The potential for selection bias also exists because sicker infants with closer monitoring might have had more frequent detection of AT than their healthier counterparts.

In conclusion, AT is an independent risk factor for mortality among infants undergoing cardiac surgery. It was observed during the perioperative period in 8% of infants undergoing cardiac surgery and was more common among infants aged 6 months or younger at surgery, those receiving 3 or more inotropes, and those with heterotaxy syndrome. Among the survivors, antiarrhythmic agents successfully controlled AT in most patients with a low recurrence risk after discontinuation. Additional study is needed to understand the influence of AT on outcome in this population.

**References**