Implantable Cardioverter Defibrillator Therapy in Adults With Congenital Heart Disease
Who Is at Risk of Shocks?

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Background—The value of implantable cardioverter defibrillators (ICDs) in adults with congenital heart disease (CHD) is unknown. We investigated the long-term outcome after ICD implantation and developed a simple risk stratification score for ICD therapy.

Methods and Results—A total of 136 adults with CHD and ICD (mean age ±SD, 41±13 years; 67% male) were identified from 10 tertiary referral centers in the Netherlands and Belgium. The indication for ICD implantation was primary prevention in 50% of patients. Diagnoses included tetralogy of Fallot (51%), septic defects (20%), (congenitally corrected) transposition of the great arteries (13%), and other (16%). Thirty-nine patients (29%) received appropriate ICD shocks during a median follow-up of 4.6 years. Secondary prevention indication (hazard ratio [HR], 3.6; 95% CI, 1.3–9.5; P=0.009), coronary artery disease (HR, 2.7; 95% CI, 1.0–7.2; P=0.042), and symptomatic nonsustained ventricular tachycardia (NSVT; HR, 9.1; 95% CI, 2.8–29.2; P=0.001) were associated with appropriate ICD shocks. A risk score was developed to evaluate the likelihood of appropriate ICD shocks. The 8-year survival curve to first appropriate shocks was 94%, 57%, and 26% for low-, intermediate-, and high-risk patients, respectively. In primary prevention, symptomatic NSVTs (HR, 8.0; 95% CI, 2.3–27.1; P=0.001) and subpulmonary ventricular dysfunction (HR, 3.0; 95% CI, 1.2–12.6; P=0.02) were associated with appropriate shocks in univariable analysis. Inappropriate shocks occurred in 41 patients (30%). In addition, 40 patients (29%) experienced 45 implantation-related complications.

Conclusions—Adults with CHD and ICDs receive high rates of appropriate and effective shocks. Patients with secondary prevention indication, coronary artery disease, and symptomatic NSVT are at highest risk of receiving appropriate ICD shocks. ICD implantation is accompanied by considerable morbidity, including inappropriate shocks and procedure-related complications. (Circ Arrhythm Electrophysiol. 2012;5:101-110.)

Key Words: adult congenital heart disease ■ implantable cardioverter defibrillators ■ sudden cardiac death

Despite the tremendous progress in cardiac surgery, diminished long-term survival remains a major concern in adults with congenital heart disease (CHD). In this population, sudden cardiac death (SCD) is the most common cause of late mortality.1–4 SCD is commonly encountered in patients with repaired aortic stenosis, tetralogy of Fallot (TOF), transposition of great arteries, and aortic coarctation, with an incidence of 0.54%, 0.49%, 0.15%, and 0.13% per year, respectively, in a relatively young population.5 There are criteria for risk stratification in TOF, but these have a low specificity and can likely not be extrapolated to the entire CHD population.6–8 The lack of universal risk criteria makes the contribution of implantable cardioverter defibrillator (ICD) therapy in the reduction of SCD in patients with right ventricular failure unclear. The low incidence of SCD and the heterogeneity within the population of CHD precludes large prospective studies and, indeed, no prospective studies have been published.

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ICD therapy has been proved to be effective in primary and secondary prevention of SCD in adults with ischemic or...
dilated heart disease and impaired left ventricular function. Although the number of patients with CHD who receive an ICD is steadily increasing, risk stratification and the indication for ICD implantation for primary prevention are poorly defined in this group. Moreover, the effects of ICD therapy during long-term follow-up are still unknown. Therefore, we conducted an international retrospective study in adult ICD carriers with CHD. Our primary objectives were as follows: (1) to quantify the outcome of ICD therapy, including appropriate ICD discharges, clinical events, and ICD-related complications; and (2) to develop a simple risk stratification score for ICD therapy. The secondary objectives were inappropriate shocks, any ablation, and mortality.

Methods

Study Design and Population

This was a multicenter retrospective study that included adult patients with CHD and an ICD implanted before March 2010. Patients were identified from the databases of 10 tertiary referral centers in the Netherlands and Belgium. Exclusion criteria were patients <18 years at first implantation of ICD and patients with CHD and primary electric disease or inherited cardiomyopathy. Data collection was conducted after approval from the medical ethics committee in the participating centers in the Netherlands and Belgium.

Baseline Characteristics

Details on demographics, cardiac diagnosis, medical history, New York Heart Association functional class, electrocardiographic data, echocardiography, 24-hour Holter monitoring, electrophysiological studies (EPSs), and information on ablations were retrieved from the medical records. Also, coronary angiography, a myocardial perfusion scan, or other diagnostic tools to diagnose coronary artery disease (CAD) were recorded. The complexity of the congenital defect was classified as mild, moderate, and complex. We analyzed the most recent data available before first ICD implants. Rhythm (spontaneous or paced), rate, QRS duration, and QT interval were determined from standard 12-lead ECGs. Data on ventricular function, chamber sizes, and degree of valvular regurgitation and/or stenosis were collected from echocardiography. Ventricular function was classified as normal (ejection fraction [EF], \( \geq 50\% \)) or mildly (EF, 36–49\%) or severely impaired (EF, <30–35\%), and severely (EF, <30\%) impaired. Because the aorta does not always arise from the morphological left ventricle (ie, in transposition of great arteries and double-outlet right ventricle), we classify the ventricles into systemic and subpulmonary ventricles throughout the article, instead of left and right ventricles. We report the function of the systemic ventricle. The presence of ventricular ectopy and nonsustained ventricular tachycardia (NSVT) during Holter monitoring before ICD implantation was documented. EPS was performed according to each institution’s protocol and reviewed for inducibility of sustained monomorphic and polymorphic VT, ventricular fibrillation (VF), and supraventricular arrhythmias. Ablation of arrhythmias and success rate were documented. Nonsustained VTs were classified by electrocardiography and defined as \( \geq 3 \) consecutive beats, terminating spontaneously in <30 s. A clinical subdivision consisted of asymptomatic, hemodynamically stable (eg, palpitations), and hemodynamically unstable (eg, presyncope) NSVTs.

ICD-Related Data

We documented type of ICD (ie, single, dual-chamber ICD, or cardiac resynchronization therapy), type of lead, indication for implant, electric parameters, and defibrillation threshold. Indication for ICD implantation was reviewed in each patient, with emphasis on (pre) syncope, palpitations, impaired ventricular function, clinical NSVT, spontaneous sustained VT, inducible VT during EPS, and VF/resuscitated cardiac arrest. In patients with TOF, QRS duration \( \geq 180 \) ms, severely impaired right ventricular function, and/or dilated right ventricle were also considered an indication for ICD implantation. Secondary prevention was defined as ICD implantation after resuscitated cardiac arrest, VF, or hemodynamically intolerated VT. The absence of a secondary prevention indication defined primary prevention. Use of antiarrhythmic drugs was documented.

Detection rates for ICD therapy were not uniformly programmed. Device programming was performed at the discretion of the patient’s clinical cardiologist. Shocks were classified as appropriate or inappropriate. Number of shocks per episode, number of episodes shocked, time to shock since ICD implanted, and whether the shock was successful in restoring sinus or paced rhythm were documented. The VT cycle length, programmed defibrillator zone (eg, slow VT, fast VT, or VF), and success or failure of therapy were noted. Appropriate ICD therapy was defined as a shock or antitachycardia pacing (ATP) delivered in response to a ventricular tachyarrhythmia (monomorphic VT, polymorphic VT, or VF, with a cycle length within the therapy zone of the device). Electrical storm was defined as the occurrence of \( \geq 3 \) separate episodes of ventricular arrhythmia requiring an ICD shock within 24 hours. Inappropriate ICD therapy was defined as a shock or ATP delivered for reasons other than ventricular arrhythmia and was categorized according to the most probable cause (ie, oversensing, sinus tachycardia, atrial flutter, atrial fibrillation, and other form of supraventricular tachycardia). An experienced electrophysiologist (J.R.d.G. or I.C.V.G.) classified electrograms of ICD therapy as appropriate or inappropriate.

Early and late ICD complications included pocket hematoma, pleural effusion, lead failure, thromboembolic events, pneumothorax, hematotherax, undersensing or oversensing, device malfunction, lead dislodgment, pocket and other infections, pain, erosion, and migration of the device. ICD complications were considered periprocedural if they occurred within 30 days of implantation and late if they occurred after >30 days after the implantation.

Risk Score

Baseline variables associated with the outcome at univariable analysis were included in a multivariable Cox model and tested for their significance and independent association with the incidence of ICD shocks during follow-up. Three clinical variables were identified and included secondary prevention indication, CAD, and symptomatic NSVT. Each variable received 0 to 4 points based on the estimated \( \beta \) coefficients. In the absence of a control group without ICD implantation, these clinical parameters were applied to patients included in the Concor database. Concor (CONgenital CORVita) is a Dutch registry of adults with congenital heart defects. Freedom from appropriate ICD shock was compared with survival in patients without ICD therapy in the Concor database.

Statistical Analysis

Data analyses were performed with SPSS software for Windows (18.0 for Windows, SPSS Inc; Chicago, IL). Two-tailed \( P < 0.05 \) was considered statistically significant. Descriptive statistics for nominal data were expressed in absolute numbers and percentages. Mean values and SDs were calculated for normally distributed continuous variables. When comparing frequencies, the \( \chi^2 \) or \( \text{t} \) test was used where applicable. Kaplan-Meier curves were constructed for time to first (in) appropriate therapy. Comparison between both groups was performed by log-rank statistics. To identify clinical parameters associated with (in) appropriate ICD therapy, univariable and stepwise multivariable Cox proportional hazard models were used after proportional hazard assumptions were verified. Variables with \( P > 0.20 \) in univariable analyses were considered in multivariable models (forward stepwise). The annual event rates for appropriate shocks were calculated by dividing the number of patients with appropriate shocks/sum of follow-up duration of the patients.

Results

Baseline Characteristics

A total of 159 patients with CHD were implanted between November 1990 and February 2010. Twenty-three patients...
were excluded because of age <18 years at the time of first ICD implantation and/or the concomitant presence of Brugada syndrome, long QT syndrome, arrhythmogenic right ventricular cardiomyopathy, and hypertrophic cardiomyopathy. In the remaining 136 patients, ICD implantation was distributed equally in the primary (n=68) and secondary (n=68) prevention group. The underlying cardiac defects are shown in Figure 1. The most common diagnosis was TOF (51%). Baseline characteristics are summarized in Table 1.

Patients with ICDs for primary prevention were predominantly male (76%) and had more often moderately to severely impaired systemic ventricular function. Indications for primary prevention in patients were inducible sustained ventricular arrhythmia in 21 (31%), NSVT and systemic ventricular EF ≤35% in 15 (22%), NSVT in 9 (13%), systemic ventricular EF ≥35% in 9 (13%), syncope without documented ventricular arrhythmia in 6 (9%), presyncope without documented ventricular arrhythmia in 5 (7%), QRS duration ≥180 ms and pulmonary ventricular EF ≤35% in 2 (3%), and palpitations in 1 (2%). Indications for secondary prevention were resuscitated cardiac arrest or VF in 31 (46%) and spontaneous sustained VT in 37 (54%) of patients. Prolonged QTc interval was related to right bundle branch block in 51% of the patients.

The mean age at the time of ICD implantation was 41±13 years. Figure 2 shows the age at first ICD implantation among the various cardiac defects. Single-chamber ICDs were initially implanted in 54 (40%) of patients (more often in secondary prevention: 51% versus 28%), dual-chamber ICDs were implanted in 69 (50%) of patients, and biventricular ICDs were implanted in 13 (10%) of patients. The ICD implantation consisted of an upgrade of a previously implanted pacemaker in 25 patients; in 13 patients, subsequent upgrading to biventricular ICD occurred. Three patients had an epicardial system. There were no implantation-related deaths.

Appropriate ICD Therapy
Thirty-nine patients received appropriate shocks. Appropriate ATP was delivered in 26 of 39 patients with appropriate shocks and was effective in only 5 patients; in the remaining 21 patients, ATP failed and shocks were delivered for conversion. The mean VT cycle length was 280±30 ms. The VT cycle length did not differ among the various cardiac defects. The 3 largest groups of defects, including TOF, (congenitally corrected) transposition of great arteries, and septal defects, had a mean VT cycle length of 296±36, 277±76, and 281±26 ms, respectively. There was no correlation between age and VT cycle length (β=-0.03, P=0.79). It is, therefore, unclear whether age or CHD type can help improve ICD programming. Twenty-six patients received multiple shocks (≥2) anytime during follow-up. Electrical storm occurred in 12 patients (9%). Most of these patients (58%) had TOF as the underlying cardiac defect, and indication for ICD therapy was secondary prevention in 83% of the patients. There was no difference in baseline characteristics and clinical parameters between patients with and without electrical storm. Appropriate shocks were caused by monomorphic VT (92%), polymorphic VT (3%), and VF (5%). All first ICD shocks were successful, albeit the VT recurred in 67% of patients. The median follow-up duration after first appropriate ICD shock was 3.0 (range, 0.1–11.0) years. Patients with primary and secondary prevention indications experienced significant rates of appropriate ICD shocks. Figure 3 shows the distribution of ICD shocks in both groups. The mean numbers of shocks were 2.9 and 5.2 in the primary
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=136)</th>
<th>Primary Prevention (n=68)</th>
<th>Secondary Prevention (n=68)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at ICD implantation, y</td>
<td>40.9±13</td>
<td>40.9±14</td>
<td>40.9±12</td>
<td>0.99</td>
</tr>
<tr>
<td>Median follow-up duration, y</td>
<td>4.6 (0.01–13.9)</td>
<td>3.3 (0.1–11.7)</td>
<td>5.4 (0.1–13.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>91 (67)</td>
<td>52 (76)</td>
<td>39 (57)</td>
<td>0.01</td>
</tr>
<tr>
<td>Severity of CHD, n (%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mild CHD</td>
<td>28 (21)</td>
<td>14 (21)</td>
<td>14 (21)</td>
<td>1.00</td>
</tr>
<tr>
<td>Moderate CHD</td>
<td>78 (57)</td>
<td>41 (60)</td>
<td>37 (54)</td>
<td>0.48</td>
</tr>
<tr>
<td>Severe CHD</td>
<td>30 (22)</td>
<td>13 (19)</td>
<td>17 (25)</td>
<td>0.40</td>
</tr>
<tr>
<td>Coronary artery disease, n (%)</td>
<td>13 (10)</td>
<td>8 (12)</td>
<td>5 (7)</td>
<td>0.38</td>
</tr>
<tr>
<td>NYHA functional class I–II, n (%)</td>
<td>122 (90)</td>
<td>58 (85)</td>
<td>63 (93)</td>
<td>0.17</td>
</tr>
<tr>
<td>History of tachyarrhythmias, n</td>
<td>111 (82)</td>
<td>53 (78)</td>
<td>58 (85)</td>
<td>0.25</td>
</tr>
<tr>
<td>SVT</td>
<td>79 (58)</td>
<td>40 (59)</td>
<td>39 (57)</td>
<td>0.86</td>
</tr>
<tr>
<td>NSVT</td>
<td>35 (26)</td>
<td>31 (46)</td>
<td>4 (6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antiarrhythmic drug therapy, n</td>
<td>68 (50)</td>
<td>34 (50)</td>
<td>34 (49)</td>
<td>0.80</td>
</tr>
<tr>
<td>Class I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>47 (35)</td>
<td>26 (38)</td>
<td>7 (13)</td>
<td>0.36</td>
</tr>
<tr>
<td>Class III</td>
<td>21 (15)</td>
<td>12 (13)</td>
<td>13 (19)</td>
<td>0.23</td>
</tr>
<tr>
<td>Class IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG, n (%)</td>
<td>129 (95)</td>
<td>66 (97)</td>
<td>63 (93)</td>
<td>0.24</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>89 (69)</td>
<td>41 (62)</td>
<td>48 (76)</td>
<td>0.06</td>
</tr>
<tr>
<td>AF/AFL</td>
<td>23 (18)</td>
<td>16 (24)</td>
<td>7 (11)</td>
<td>0.05</td>
</tr>
<tr>
<td>Ventricular paced rhythm</td>
<td>20 (16)</td>
<td>13 (20)</td>
<td>7 (11)</td>
<td>0.17</td>
</tr>
<tr>
<td>Mean QRS duration, ms*</td>
<td>149±37</td>
<td>153±37</td>
<td>145±37</td>
<td>0.25</td>
</tr>
<tr>
<td>QRS duration &gt;180, ms*</td>
<td>27 (21)</td>
<td>17 (26)</td>
<td>10 (16)</td>
<td>0.08</td>
</tr>
<tr>
<td>QT interval*</td>
<td>445±60</td>
<td>445±56</td>
<td>445±65</td>
<td>0.96</td>
</tr>
<tr>
<td>QTc interval*</td>
<td>470±43</td>
<td>467±37</td>
<td>473±48</td>
<td>0.43</td>
</tr>
<tr>
<td>Echocardiography, n (%)</td>
<td>132 (97)</td>
<td>68 (100)</td>
<td>65 (96)</td>
<td>0.31</td>
</tr>
<tr>
<td>Moderate to severe ventricular dysfunction</td>
<td>67 (51)</td>
<td>37 (55)</td>
<td>30 (46)</td>
<td>0.29</td>
</tr>
<tr>
<td>PV</td>
<td>33 (25)</td>
<td>14 (21)</td>
<td>19 (29)</td>
<td>0.31</td>
</tr>
<tr>
<td>SV</td>
<td>47 (36)</td>
<td>31 (46)</td>
<td>17 (26)</td>
<td>0.01</td>
</tr>
<tr>
<td>Combined PFV and SVF dysfunction</td>
<td>15 (11)</td>
<td>9 (13)</td>
<td>6 (9)</td>
<td>0.45</td>
</tr>
<tr>
<td>Holter monitoring performed, n</td>
<td>60 (44)</td>
<td>37 (54)</td>
<td>23 (34)</td>
<td>0.01</td>
</tr>
<tr>
<td>Documented NSVT and/or VT</td>
<td>23 (38)</td>
<td>18 (49)</td>
<td>5 (22)</td>
<td>0.03</td>
</tr>
<tr>
<td>Documented SVT</td>
<td>21 (35)</td>
<td>16 (43)</td>
<td>5 (22)</td>
<td>0.09</td>
</tr>
<tr>
<td>Electrophysiologic study, n (%)</td>
<td>85 (63)</td>
<td>41 (60)</td>
<td>44 (65)</td>
<td>0.59</td>
</tr>
<tr>
<td>Positive for ventricular arrhythmias</td>
<td>67 (78)</td>
<td>28 (68)</td>
<td>39 (87)</td>
<td>0.04</td>
</tr>
<tr>
<td>Sustained ventricular arrhythmias</td>
<td>63 (74)</td>
<td>28 (68)</td>
<td>35 (80)</td>
<td>0.35</td>
</tr>
<tr>
<td>NSVT</td>
<td>7 (8)</td>
<td>2 (5)</td>
<td>5 (11)</td>
<td>0.29</td>
</tr>
<tr>
<td>SVT</td>
<td>21 (24)</td>
<td>11 (27)</td>
<td>10 (22)</td>
<td>0.57</td>
</tr>
<tr>
<td>Ablation, n (%)</td>
<td>36 (26)</td>
<td>13 (19)</td>
<td>23 (33)</td>
<td>0.05</td>
</tr>
<tr>
<td>Any SVT ablation</td>
<td>24 (67)</td>
<td>12 (92)</td>
<td>12 (52)</td>
<td>0.96</td>
</tr>
<tr>
<td>Before ICD implantation</td>
<td>12 (33)</td>
<td>8 (62)</td>
<td>4 (17)</td>
<td>0.22</td>
</tr>
<tr>
<td>Any VT ablation</td>
<td>13 (36)</td>
<td>1 (8)</td>
<td>12 (52)</td>
<td>0.003</td>
</tr>
<tr>
<td>Before ICD implantation</td>
<td>8 (22)</td>
<td>2 (15)</td>
<td>6 (26)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

ICD indicates implantable cardioverter defibrillator; CHD, congenital heart disease; NYHA class, New York Heart Association; SVT, supraventricular tachycardia; NSVT, nonsustained ventricular tachycardia; AF/AFL, atrial fibrillation/atrial flutter; PV, subpulmonary ventricle; SV, systemic ventricle; SMVT, sustained monomorphic ventricular tachycardia; SPVT, sustained polymorphic ventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia.

*Excluding patients with ventricular paced rhythm.
significant relation. Seventeen patients (13%) had symptom-
atic NSVTs, with complaints of palpitations in 11 and
dizziness/presyncope in 6. Even when patients with NSVTs and
dizziness or presyncope were considered as having a
secondary prevention indication in the analysis, the presence of
symptomatic NSVTs was still associated with appropriate
ICD shocks. CAD was present in 13 patients, of whom 10 had
a previous myocardial infarction and moderately to severely
impaired systemic ventricular function. The localization of
the myocardial infarctions was anteroseptal (n=7), inferior
(n=2), and posterior (n=1). However, the indication for ICD
therapy was the congenital condition in all of these patients.
Sixty-eight patients (50%) used class II and/or III antiarrhyth-
ic drugs before or during ICD implantation. However,
neither class II (HR, 1.1; 95% CI, 0.5–2.2; P=0.706) nor class III
(HR, 1.0; 95% CI, 0.4–2.4; P=0.900) antiarrhythmic
drugs reduced the risk of appropriate shocks.

The clinical parameters associated with appropriate ICD
shocks in the primary and secondary prevention indication
groups were analyzed separately. Herein, no multivariable
analysis was performed because of the few cases in each
subgroup (Table 2). In patients with primary prevention,
clinical variables associated with appropriate shocks in univari-
variable analyses were symptomatic NSVTs (HR, 8.0; 95%
CI, 2.3–27.1; P=0.001) and moderate-to-severe subpulmo-
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P=0.02).

In patients with secondary prevention, the presence of mild
CHD was associated with occurrence of appropriate shocks
(HR, 2.6; 95% CI, 1.1–5.9; P=0.02). However, compared
with patients with moderate-to-severe CHD, patients with
mild CHD were older (52±14.6 versus 38±11.4 years;
P=0.001), more often had CAD (36% versus 12%;
P=0.001), and had a moderately to severely impaired sys-
temic ventricle (63% versus 28%; P=0.001).

**Clinical Parameters Associated With Appropriate
ICD Therapy**

Clinical parameters associated with appropriate shocks are
summarized in Table 2. Overall, secondary prevention indi-
cation (hazard ratio [HR], 3.6; 95% CI, 1.3–9.5; P=0.009),
documented CAD (HR, 2.7; 95% CI, 1.0–7.2; P=0.042), and
documented symptomatic NSVT (HR, 9.1; 95% CI, 2.8–
29.2; P<0.001) were independently associated with appro-
priate shocks. An impaired systemic ventricular function was
not significantly associated with the risk of appropriate
shocks. Twenty-three patients had a systemic right ventricle,
of whom the function was impaired in 17. Excluding these
patients from the analysis did not change the absence of a
significant relation. Seventeen patients (13%) had symptom-
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P=0.001), and had a moderately to severely impaired sys-
temic ventricle (63% versus 28%; P=0.001).

**Risk Score for Appropriate ICD Shocks**

Clinical parameters associated with appropriate shocks after
multivariable Cox analysis were secondary prevention indi-
cation, CAD, and symptomatic NSVT. Table 3 shows the HR
and points attributed to each variable. Three risk categories
were derived from a possible maximum of 4 points: low risk,
0 points; intermediate risk, 1 point; and high risk, 2 to 4
points. Figure 5A shows that the 8-year survival curve to first
appropriate shock was 94%, 57%, and 26% for the low-, inter-
mEDIATE-, and high-risk patients, respectively. Only 1
appropriate shock occurred in the low-risk group. Figure 5B
shows the survival in relation to the previously mentioned
risk factors in 12 743 patients in the Concor database without
an ICD. Survival in the Concor database shows a similar
trend as freedom from appropriate ICD shocks in the study
population: 94%, 82%, and 71% for patients with a low, inter-
mEDIATE, or high risk after 8 years of follow-up.

**Complications and Inappropriate ICD Therapy**

Table 4 summarizes 45 implant-related complications in 40
patients (29%). Lead failure caused multiple inappropriate
shocks in 5 patients. Overall, 41 patients (30%) experienced
86 episodes of inappropriate shocks (221 shocks; range, 1–27
shocks per patient; mean, 5.4 shocks). Inappropriate ATP
preceded inappropriate shocks in 18 of 41 patients. Shocks were delivered on atrial tachyarrhythmias in 69%, sinus tachycardia in 23%, lead fracture in 5%, and T-wave oversensing in 3%. Seventeen patients (41%) also experienced appropriate shocks. Forty-four patients with atrial tachycardias or sinus tachycardias used antiarrhythmic drugs. This percentage did not differ from antiarrhythmic drug use in patients without supraventricular tachycardia (SVT; 49%).

Figure 4B shows the Kaplan-Meier estimate of time to first inappropriate ICD shock in patients with a primary (n = 18) versus a secondary (n = 23) prevention indication. No difference was observed between the groups.

Clinical Parameters Associated With Inappropriate ICD Therapy
In univariate analysis, inducible SVT (HR, 2.6; 95% CI, 0.9–7.2; P = 0.050) and SVT ablation before or after ICD implantation (HR, 2.1; 95% CI, 1.1–4.3; P = 0.026) were associated with inappropriate ICD shocks. In multivariable analysis, only SVT ablation was associated with inappropriate shocks (HR, 2.2; 95% CI, 1.0–4.6; P = 0.040). Interestingly, the presence of SVT before ICD implantation was not associated with a higher risk of inappropriate shock as the result of any cause (HR, 1.0; 95% CI, 0.5–1.8; P = 0.982). In patients without SVT, inappropriate shocks were mainly the result of sinus tachycardia and lead failure (58%). Use of antiarrhythmic drugs (used by <50% of patients) did not alter the risk of inappropriate shocks (HR, 0.9; 95% CI, 0.5–1.8; P = 0.982) nor did implantation of a dual-chamber ICD (HR, 0.8; 95% CI, 0.4–1.5; P = 0.50). Inappropriate shocks occurred more frequently in primary prevention in TOF compared with other cardiac defect (HR, 3.6; 95% CI, 1.0–12.4; P = 0.048).

EPSs and Ablation
EPS was performed in 85 patients (63%). Sixty-three patients (73%) had inducible sustained ventricular arrhythmias, of which 45 (71%) were monomorphic VT, 8 (13%) were polymorphic VT, 7 (11%) were VF, 2 (3%) were both VF and monomorphic VT, and 1 (2%) were both VF and polymorphic VT. Twenty-one patients (33%, 5 primary prevention) with inducible monomorphic VT received appropriate ICD shocks for monomorphic VT, whereas 7 patients (32%, 2 primary prevention) without inducible ventricular arrhythmias had at least 1 appropriate ICD shock. There was no relation between the inducibility of ventricular arrhythmias and the occurrence of appropriate shocks, nor was the incidence of appropriate shocks different between patients who did (34%) and did not (20%) undergo EPS (P = 0.07).

VT ablation before ICD implantation was performed in 8 patients, in whom 6 procedures were successful. SVT ablation was performed in 11 (14%) of the 79 patients with documented SVT before ICD implantation. Remarkably, inappropriate shocks occurred in 24 patients (30%) with documented SVT (9% versus 34% in patients with versus without SVT ablation).

Mortality
There were 20 deaths (15%) during follow-up. The cause of death was known in 15 patients and included congestive heart failure in 9, SCD in 1, ventricular tachyarrhythmia storm in 1, and sepsis after cardiac surgery in 1. Three patients died from a noncardiac cause. No ICD electrograms were available in the patient with SCD. Three patients (2%) underwent heart transplantation for heart failure: 0.2, 5, and 7 years after their ICD implantation.

Discussion
To our knowledge, this is the largest multicenter study on ICD therapy in adults with CHD. Moreover, this study defines clinical parameters associated with appropriate ICD therapy within this population. Both patients with a primary and a secondary prevention indication received many appropriate ICD shocks. Interestingly, most first appropriate ICD shocks occurred within the first 2 years of follow-up. Clinical parameters associated with appropriate ICD shocks included secondary prevention indication, CAD, and symptomatic NSVT. Based on these 3 clinical variables, a risk score to predict the occurrence of appropriate shocks was developed. In patients with a primary prevention indication, symptomatic NSVTs and subpulmonary ventricular dysfunction were associated with appropriate shocks in univariable analysis. These risk factors have not been previously reported. High rates of inappropriate ICD shocks, predominantly due to atrial tachyarrhythmias, were noted in 30% of patients; almost half of these patients also experienced appropriate shocks. Implantation-related complications requiring reinterventions were also common.
ICD therapy is highly effective in preventing SCD in patients with ischemic and nonischemic cardiomyopathy.9–11 In adults with CHD, consensus exists on ICD implantation for secondary prevention of SCD. In this cohort, 19% of patients with a primary prevention indication received appropriate shocks, which is ≈5% per year of follow-up. These findings are similar to the results of ICD outcome in patients with hypertrophic cardiomyopathy,14 arrhythmogenic right ventricular cardiomyopathy,15 long-QT syndrome,16 and SCDHeft10 and somewhat lower than reported in MADIT-II [Multicenter Automatic Defibrillator Implantation Trial II] and DEFINITE [Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation].11 The high rates of appropriate ICD shocks in the primary prevention group in the present study suggest that cardiologists have been successful in identifying high-risk patients. Appropriate ICD shocks are a surrogate marker for SCD and may overestimate the

### Table 2. Clinical Parameters Associated with Appropriate ICD Shocks

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable Analysis</th>
<th>Multivariable Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Overall (n=136)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary prevention indication</td>
<td>1.6</td>
<td>0.8–3.1</td>
</tr>
<tr>
<td>Age, &gt;40 y</td>
<td>1.8</td>
<td>0.9–3.5</td>
</tr>
<tr>
<td>Mild CHD</td>
<td>2.3</td>
<td>1.1–4.6</td>
</tr>
<tr>
<td>Documented CAD</td>
<td>1.8</td>
<td>0.7–4.8</td>
</tr>
<tr>
<td>Symptomatic NSVT</td>
<td>3.2</td>
<td>1.4–7.1</td>
</tr>
<tr>
<td>QRS, &gt;180 ms</td>
<td>0.6</td>
<td>0.2–1.4</td>
</tr>
<tr>
<td>Ventricular dysfunction (EF=35%)</td>
<td>1.4</td>
<td>0.7–2.8</td>
</tr>
<tr>
<td>PV</td>
<td>0.8</td>
<td>0.3–1.8</td>
</tr>
<tr>
<td>SV</td>
<td>1.5</td>
<td>0.7–3.0</td>
</tr>
<tr>
<td>Combined PV and SV</td>
<td>1.0</td>
<td>0.3–3.2</td>
</tr>
<tr>
<td>Inducible sustained ventricular arrhythmias</td>
<td>1.1</td>
<td>0.4–2.6</td>
</tr>
<tr>
<td>Primary prevention (n=68)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, &gt;40 y</td>
<td>2.0</td>
<td>0.6–6.3</td>
</tr>
<tr>
<td>Mild CHD</td>
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<tr>
<td>Ventricular dysfunction (EF=35%)</td>
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<td>1.0–14.9</td>
</tr>
<tr>
<td>PV</td>
<td>3.0</td>
<td>1.2–12.6</td>
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<tr>
<td>SV</td>
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<td>0.5–5.3</td>
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<tr>
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<tr>
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<tr>
<td>Secondary prevention (n=68)</td>
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<td>Age, &gt;40 y</td>
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<td>0.7–3.7</td>
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<tr>
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<tr>
<td>SV</td>
<td>1.5</td>
<td>0.6–3.8</td>
</tr>
<tr>
<td>Combined PV and SV</td>
<td>0.1</td>
<td>0.0–21.9</td>
</tr>
<tr>
<td>Inducible sustained ventricular arrhythmias</td>
<td>1.0</td>
<td>0.3–2.8</td>
</tr>
</tbody>
</table>

ICD indicates implantable cardioverter defibrillator; CHD, congenital heart disease; CAD, coronary artery disease; NSVT, nonsustained ventricular tachycardia; EF, ejection fraction; PV, subpulmonary ventricle; SV, systemic ventricle; VT, ventricular tachycardia; TR, tricuspid valve regurgitation.

### Primary Prevention Indication

ICD therapy is highly effective in preventing SCD in patients with ischemic and nonischemic cardiomyopathy.9–11 In adults with CHD, consensus exists on ICD implantation for secondary prevention of SCD. In this cohort, 19% of patients with a primary prevention indication received appropriate shocks, which is ≈5% per year of follow-up. These findings are similar to the results of ICD outcome in patients with hypertrophic cardiomyopathy,14 arrhythmogenic right ventricular cardiomyopathy,15 long-QT syndrome,16 and SCDHeft10 and somewhat lower than reported in MADIT-II [Multicenter Automatic Defibrillator Implantation Trial II] and DEFINITE [Defibrillators in Nonischemic Cardiomyopathy Treatment Evaluation].11 The high rates of appropriate ICD shocks in the primary prevention group in the present study suggest that cardiologists have been successful in identifying high-risk patients. Appropriate ICD shocks are a surrogate marker for SCD and may overestimate the

### Table 3. Risk Score for Appropriate ICD Shocks in the Total Cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>Points Attributed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary prevention indication</td>
<td>3.6</td>
<td>1</td>
</tr>
<tr>
<td>Documented CAD</td>
<td>2.7</td>
<td>1</td>
</tr>
<tr>
<td>Symptomatic NSVT</td>
<td>9.1</td>
<td>2</td>
</tr>
</tbody>
</table>

CAD indicates coronary artery disease.
risk for SCD. Some of these shocks, however, were presumably life-saving. This suggests an important role of ICD therapy in preventing SCD in adults with CHD.

Clinical Parameters Associated With Appropriate ICD Therapy

To our knowledge, this is the first study to highlight the importance of symptomatic NSVTs as a significant determinant of appropriate ICD therapy in the general CHD population. Khairy et al reported NSVT as an independent predictor of appropriate ICD therapy in patients with TOF and primary prevention of SCD, but they did not report whether NSVT was symptomatic.7 Despite lack of guidelines on ICD therapy in patients with CHD, there appears to be consensus on ICD implantation for secondary prevention of SCD. In the present study, patients with resuscitated cardiac arrest and sustained VT were best served by ICD therapy. In 37 patients with transposition of the great arteries and intra-atrial baffles, high rates of appropriate shocks were also reported in patients with a secondary (28.6%) but not a primary (4.3%) prevention indication. Herein, the risk factors that were identified in small specific subpopulations prove valid in the entire cohort.

The population of adult patients with CHD is growing and aging, ischemia, infarction, and myocardial fibrosis might form the mechanism of sustained VT and SCD. This is supported by our finding that even patients with mild CHD, who were older and in a worse clinical condition, were at risk of receiving appropriate ICD shocks.

Risk Score

We developed an easily applicable scoring system to predict the probability of appropriate ICD shocks that may be helpful in decision making to implant an ICD. However, the variables used in the scoring system are inherent characteristics of the population to which the model was applied. These clinical variables were associated with survival in the Concor database, which showed a trend similar to the freedom of appropriate shocks in the current study.

Evidently, survival does not equate to appropriate shocks, but this finding supports the clinical relevance of the variables proposed.

Clinical Parameters Not Associated With Appropriate ICD Therapy

QRS prolongation has been associated with SCD and mortality in patients with heart failure and TOF.6,17–19 In the present study, there was no association between ICD therapy and QRS duration. In our high-risk group of patients, the severity of ventricular dysfunction (systemic or subpulmonary ventricle) was not associated with appropriate ICD shocks during follow-up, which is in line with the findings of the MADIT II trial.20 This might be explained by the fact that quantification of ventricular EF was frequently lacking; thus, qualitative data that are less accurate were used. There may be a difference between an impaired systemic right and left ventricle. However, the numbers in this study are too low to demonstrate such an effect. When the systemic right ventricles were excluded from the analysis, the lack of significance remained unaltered. Left ventricular end-diastolic pressure was not routinely measured or reported in the current cohort;
hence, we cannot confirm or negate the finding of Khairy et al that left ventricular end-diastolic pressure >12 mm Hg is associated with appropriate ICD therapy in patients with TOF. Inducible sustained ventricular arrhythmias before ICD implantation did not correlate with appropriate shocks during follow-up. Remarkably, patients with TOF, the largest group of ICD recipients, were not at higher risk of receiving appropriate ICD shocks.

Inappropriate ICD Therapy and Complications

In line with previous studies, inappropriate shocks were observed in 30% of patients, predominantly because of atrial tachyarrhythmias (69%). Antiarrhythmic drug therapy did not reduce inappropriate ICD shocks for SVT, albeit <50% of patients with SVT were using antiarrhythmic drugs. Therefore, in this population, ICD implantation should be combined with therapy for atrial tachyarrhythmias. In particular, device programming, prolongation of detection time, and increasing the tachyarrhythmia detection rate may further reduce inappropriate ICD shocks caused by SVT, especially in younger patients. SVT ablation before ICD implantation reduced the risk of inappropriate shocks with 25% and should be considered in patients with documented SVT. The most prevalent implantation-related complication was lead failure, causing inappropriate shocks in 5 patients. In patients with CHD, high rates of lead-related complications have been previously reported. Implantation of an entirely subcutaneous ICD may be considered in patients who do not require cardiac pacing. However, experience in CHD is limited.

Study Limitation

The limitations of the present multicenter study include its small sample size, purely retrospective nature, practice variation between centers, differences in indication for ICD therapy, variation between operators in implantation techniques and programming, and variances in the complexity of CHD. Moreover, a high-risk control group without ICD implantation is obviously lacking, which precludes the quantification of survival benefits. This is illustrated by the fact that ~1% of the patients in the databases received an ICD. This percentage differed among the various defects, between 0.2% and 7.4%. However, application of the risk factors to survival in the Concor database showed a qualitatively similar pattern. A prospective analysis of the risk factors reported herein would, of course, be preferable, but is not available. This would further strengthen the association of the clinical parameters we identified herein with the risk of appropriate shocks.

Conclusion and Clinical Implications

ICD therapy is effective in primary and secondary prevention of SCD in adults with CHD during long-term follow-up. Although the indications for ICD implantation are not uniform, the identification of high-risk patients by a cardiologist seems accurate, as reflected by the high rates of appropriate shocks. Patients with a secondary prevention indication, CAD, and symptomatic NSVT are at highest risk of receiving appropriate shocks. Because the population of adults with CHD is growing and aging, assessment of CAD might be warranted in older patients. Also, quantification of the systemic and subpulmonary ventricle and documentation of NSVTs might add to the patient care in this population. Morbidity is, however, considerable because of the relatively high rate of inappropriate shocks and implantation-related complications. Therefore, the risk/benefit ratio of ICD therapy should be carefully assessed in individual patients. In patients with SVT, ablation before ICD implantation should be considered because this reduces the risk of inappropriate shock by 25%.

Disclosures

J.R.d.G. is supported by grant 2009T021 from The Netherlands Heart Foundation.

References


**CLINICAL PERSPECTIVE**

Sudden cardiac death is a major cause of mortality in adults with congenital heart disease (CHD) and might be prevented by implantable cardioverter defibrillator (ICD) therapy. The number of patients with CHD who receive an ICD is steadily increasing. However, in this population, contrary to the patients with ischemic or nonischemic cardiomyopathy, the indication for ICD implantation is poorly defined and little is known about the efficacy of ICD therapy. Therefore, we conducted a multicenter study to determine the long-term outcome of ICD therapy in adults with CHD and developed a simple risk score model for appropriate ICD discharges. Overall, 136 adults with CHD and ICD (mean age ± SD, 41 ± 13 years; 67% male) were identified. The indication for ICD implantation was primary prevention in 50% of patients. Thirty-nine patients (29%) received effective appropriate ICD shocks during a median follow-up of 4.6 years. Patients with a secondary prevention indication, coronary artery disease (CAD), and symptomatic nonsustained ventricular tachycardias were at highest risk of receiving appropriate shocks. Based on these clinical features, a risk score was developed to evaluate the likelihood of appropriate ICD shocks. The 8-year Kaplan-Meier curve to first appropriate shock was 94%, 57%, and 26% for low-, intermediate-, and high-risk patients, respectively. More important, morbidity was considerable because of the relatively high rate of inappropriate shocks (30%) and implantation-related complications (29%). Therefore, the risk/benefit ratio of ICD therapy should be carefully assessed in individual patients. In patients with supraventricular tachycardias, ablation before ICD implantation should be considered because this reduced the risk of inappropriate shock by 25%. In addition, because the population of adults with CHD is growing and aging, assessment of CAD might be warranted.
Implantable Cardioverter Defibrillator Therapy in Adults With Congenital Heart Disease: Who Is at Risk of Shocks?


Circ Arrhythm Electrophysiol. 2012;5:101-110; originally published online November 17, 2011;
doi: 10.1161/CIRCEP.111.966754

Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3149. Online ISSN: 1941-3084

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