Children and young adults treated with transvenous and subcutaneous implantable cardioverter-defibrillators: a 22-year single-center experience and new perspectives

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ABSTRACT
BACKGROUND Over the last several years the evolution of transvenous implantable cardioverter-defibrillator (T-ICD) system and the introduction of subcutaneous ICD (S-ICD) have contributed to the development of the sudden cardiac death (SCD) prevention in clinical practice.
AIMS To report our clinical experience with ICD therapy in children and young adults during the twenty-two years of the follow-up.
METHODS We reviewed the database of ICD recipients choosing 80 consecutive patients (pts) implanted at the age of 6–21 in 1996–2018. We analyzed the rate of appropriate (AT) and inappropriate therapies (IT), mortality, complications and new treatment options.
RESULTS A total of 21/80 patients (26.25%) received ≥1 AT for ventricular tachycardia/ventricular fibrillation (anti-tachycardia pacing or shock) and 25/80 patients (31.25%) had one or multiple IT (P = 0.47). Nine patients (11%) had both AT and IT interventions. During follow-up, 2 (2.5%) cardiac resynchronization therapy (CRT) systems, and 8 (10%) S-ICDs were implanted, 3 heart transplantations were performed, and 1 severe tricuspid valve regurgitation occurred. A total of 6/80 patients (7.5%) died. All deaths occurred in the hypertrophic cardiomyopathy group.
CONCLUSIONS The mortality rate was 6/80 (7.5%) in the twenty-two-year follow-up. The rate of AT vs. IT was almost equal and remained steady in the long observation period. Severe TR might be a serious clinical problem in some patients. Entirely S-ICD for SCD prevention is a feasible and safe therapy in young recipients.

KEY WORDS children, implantable cardioverter-defibrillator (ICD), subcutaneous ICD, sudden cardiac death prevention, transvenous ICD

INTRODUCTION The long term follow-up period of the implantable cardioverter-defibrillator (ICD) in the youngest patients in Poland gave us enough data to share our twenty-two-year experience with cardiologists and pediatricians.

The clinical practice of the last several years has shown that the transvenous ICD system evolution as well as the subcutaneous ICD (S-ICD) (EMBLEM, Boston Scientific) introduction have contributed to the advances in the sudden cardiac death (SCD) prevention. On one hand, there is a continuum between this paper and our previous reports. On the other hand, it also includes very important new information concerning mortality and our own experience with S-ICD in this population. To our knowledge, this study represents the largest group of patients with the T-ICD and S-ICD implanted at a young age in a single center in Poland. The long-term results of SCD prevention are still discussed in a limited number of reports concerning young patients in the perspective of a lifelong therapy.
WHAT’S NEW?
The mortality rate in young implantable cardioverter-defibrillator (ICD) recipients was reported notably higher in a twenty-two-year follow-up than in shorter observation periods.

In the study population, the rate of appropriate and inappropriate therapies turned out almost equal and remained steady during the long observation period. Subcutaneous ICD (S-ICD) appears to be a good therapy option preventing from tricuspid valve regurgitation (TR), which allows to avoid intracardiac and endovascular adhesions.

An entirely subcutaneous system is a feasible therapy in life-threatening arrhythmias preventing some serious transvenous ICD (T-ICD) complications in young patients.

### TABLE 1
Study group characteristics (first implants and upgrades). Etiology, ICD type.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All N = 80</th>
<th>Primary prophylaxis N = 48</th>
<th>Secondary prophylaxis N = 32</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophic Cardiomyopathy (HCM)</td>
<td>43 (53.7%)</td>
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<td></td>
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</tr>
<tr>
<td>Long QT syndrome (LQTS)</td>
<td>8 (10%)</td>
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<td></td>
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<tr>
<td>Primary VF</td>
<td>6 (7.5%)</td>
<td></td>
<td></td>
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<tr>
<td>Right Ventricular Cardiomyopathy</td>
<td>7 (8.75%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dilated Cardiomyopathy (DCM)</td>
<td>5 (6.25%)</td>
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<td></td>
<td></td>
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<tr>
<td>Catecholaminergic polymorphic VT (CPVT)</td>
<td>4 (5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congenital heart disease: Ventricular tachycardia</td>
<td>2 (2.5%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tetralogy of Fallot, Ebstein anomaly</td>
<td>2 (2.5%)</td>
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<tr>
<td>Brugada syndrome</td>
<td>2 (2.5%)</td>
<td></td>
<td></td>
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<tr>
<td>Drug abuse induced cardiac toxicity</td>
<td>3 (3.75%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single chamber</td>
<td>50 (60%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dual chamber</td>
<td>20 (25%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Single chamber epicardial</td>
<td>2 (2.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRT (one de novo, one up-grade)</td>
<td>2 (2.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S-ICD (seven de novo, one as concomitant device)</td>
<td>8 (10%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: VT, ventricular tachycardia; S-ICD, subcutaneous implantable cardioverter-defibrillator; CRT, cardiac resynchronization therapy

### TABLE 2
Comparison of rates of appropriate and inappropriate therapies in primary and secondary prophylaxis

<table>
<thead>
<tr>
<th></th>
<th>All N = 80</th>
<th>Primary prophylaxis N = 48</th>
<th>Secondary prophylaxis N = 32</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate therapies</td>
<td>21 (26.25%)</td>
<td>10 (12.5%)</td>
<td>11 (13.75)</td>
<td>0.17</td>
</tr>
<tr>
<td>Inappropriate therapies</td>
<td>25 (31.25%)</td>
<td>13 (16.25)</td>
<td>12 (15%)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

P value

### RESULTS
The summary of the appropriate and inappropriate therapies is presented in TABLE 2.

In a group of 8 S-ICD patients there was one shock for catecholaminergic polymorphic ventricular tachycardia during exercising with aborted SCD. No inappropriate intervention was observed during 2-year period in this subgroup. IT causes are described in our previous report in detail.¹

### Mortality analysis
The mortality rate was 6/80 (7.5%) including 2 deaths caused by ventricular lead dysfunction, described in the previous report in detail.⁷ Two patients developed end stage heart failure. The first one with the fatal outcome of heart transplantation (HTX) 20 years after ICD implantation occurred in a 37-year-old female patient with hypertrophic cardiomyopathy (HCM). The other woman had a mechanical circulatory support as a bridge to transplant with a complication in the form of a massive lethal intracranial bleeding. Echocardiographic examination of this fatal case is presented in FIGURE 1. In 2 patients, death cause is unknown. All deaths described above occurred in the HCM group.

### METHODS
We reviewed database of T-ICD/S-ICD recipients in our institution consecutively implanted at the age of 6–21 (BMI: 15.6–21.3 kg/m²) in 1996–2018. In the presented study we analyzed the clinical outcome, complications, the mortality rate, the incidence of appropriate (AT) and inappropriate therapies (IT) and new treatment options in the group of 80 pts. The study group characteristics were: mean age at implantation 13.5 years (range: 6–21); weight range: 22–78 kg. The mean follow-up was 135 ± 45 months (range: 1–22 years). The study group was divided into 3 age categories: youngest children: 6–12 years (n = 30), teenagers: 13–17 years (n = 24) and young adults: 18–21 years (n = 26). Mean age of S-ICD recipients was 18 years (range: 15–21). 32 pts (40%) were the survivors of SCD and received ICD as secondary prophylaxis (SP), whereas in 48 patients (60%) implantation was performed on primary prophylaxis (PP) indications. Data were collected during the follow-up visits based on the six-month visit schedule or clinical events, whatever came first.

The relevant authorities of the scientific institution were familiar with the contents of this work and agreed to its publication. The study protocol was approved by local ethics committee. All patients or their legal representatives provided written informed consent to participate in the study and have given written informed consent for image publication. The study group characteristics are presented in Table 1 in detail.

### Statistics
Statistical analysis was performed using the SAS (version 9e, SAS Institute, Cary NC, USA) statistical package. For descriptive purposes, all data are presented as mean ± SD (continuous variables) or numbers and percentages where indicated (discrete variables). The chi-square test was used for qualitative variables. All test procedures were two-sided with a P value of less than 0.05 indicating statistical significance.
One patient (1.25%) developed severe tricuspid valve regurgitation (TR) 6 years after dual chamber T-ICD implantation with the removal of the previously implanted single chamber ICD 11 years earlier in secondary prophylaxis. The reason for this upgrade procedure was ventricular lead dysfunction. TR was treated with Carpentier Edwards Lifesciences Classic Annuloplasty Ring Tricuspid and epicardial ICD system was implanted (Boston Scientific -Inogen MINI VR) in another cardiology center, FIGURE 2. Before this decision, the patient did not contact our team.

Recently the patient was admitted to our hospital with a typical diagnostic panel (electrocardiography, X-ray, 24 hours Holter monitoring, echocardiography). After the heart team assessment, his single chamber ICD was reprogrammed from 50 bpm to VVI 40, with beta-adrenergic blocker dose reduction, just to avoid RV pacing with QRS narrowing from 160 ms (paced) to 126 ms (intrinsic rhythm) and ventricular pacing (VP) reduction from 65% to < 1%. In dual chamber ICD

**Clinical outcome and complications**  
The infection rate (endocarditis, device pocket infection or skin perforation) was 5/80 (6.25%) in the twenty-two-year follow-up. It is described in our previous report in detail. Since the last report there was only one case of pocket infection of T-ICD implanted in another center; we removed T-ICD and implanted S-ICD.

There were 2 cardiac resynchronization therapy (CRT-D) implantations: one upgrade of the existing dual chamber T-ICD and one de novo implantation due to the widely accepted criteria for resynchronization therapy.

HTX was performed in 3 patients (3.75%): 1 fatal described above, and 2 with good clinical outcome. One patient (aged 32) with dilated cardiomyopathy (DCM) had HTX 9 years ago, 8 years after ICD implantation, and is now in good clinical condition. The other patient (aged 40) with a right ventricle cardiomyopathy had HTX 6 months prior to the submission of this article, 21 years after ICD implantation.

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and therefore the indication for EPS can change with time. We repeated EPS in 2 patients several years after the first investigation. Regardless of the previously diagnosed ventricular tachyarrhythmias, one patient had atrioventricular nodal re-entrant tachycardia (AVNRT) and the other atrial tachycardia (AT). The elective radiofrequency (RF) ablation is planned in both cases.

**DISCUSSION** The presented 22-year-long follow-up period from the early childhood, through adolescence till adulthood enables a realistic assessment of ICD therapy results from the perspective of a lifelong therapy.

The rates of AT and IT remain on a constant level comparable to the one from the ten years’ follow-up report. The incidence of AT vs. IT 10 years ago and now, was 22% patients vs. 26.25% patients and 21% patients vs. 31.25% patients, respectively. This difference is not statistically significant. The previous reports concerning AT/IT rate were similar to our results.

In several studies the AT/IT rate was similar to our results. 20.8% patients had appropriate ICD interventions and (27.1%) experienced an adverse ICD-related events including 23 inappropriate ICD interventions occurring in nine patients (9.4%) and 26 device-related complications requiring surgical revision observed in 20 patients (20.8%).

IT and lead malfunction occurred in 41% of patients reported by Maron group. In published data of another Polish registry, the ICD therapy was associated with high complication rates: 57% patients had at least one complication, such as inappropriate ICD intervention, clustered ICD therapy, dislodgement or malfunction of an ICD lead, or an infection-related event.

The mortality rate (7.5%) is notably higher in the twenty-two-year follow-up than reported in shorter observation periods and in another cohort. All deaths occurred in the HCM group in the present study.

The presented HCM population (the majority of the study group) manifested advanced heart failure and severe ICD therapy complications. This explains high mortality rate compared with general good prognosis in this disease.

Our tertiary referral center data represent a high risk cohort.

In the setting of permanent pacemaker or ICD leads, the mechanisms of the tricuspid regurgitation are well recognized recently. Cardiac implantable electronic devices lead implantation results in clots formation on the surface of the tricuspid valve as early as 12 hours after the procedure with the development of the so called neoendocardium. This process leads to valve cusp swelling, fibrosis, adhesions and scar formation. It may result in an acute valve regurgitation as early as 4–5 days after implantation.

Holter memory (Fortify DR) before epicardial VVI system implantation, numerous episodes of atrial tachycardia/atrial fibrillation with rapid ventricular response around 180 bpm were detected and documented. We decided to perform scheduled electrophysiological study (EPS) in our center. In case of a supraventricular arrhythmia confirmation, RF ablation would be beneficial to diminish the risk of inappropriate therapies.

Eight S-ICD systems were implanted (SP: n = 1, PP n = 7), including 7 de novo implantations and one as a co-implant (FIGURE 3). The presented patient with concomitant devices had a conversion of T-ICD due to a ventricular lead fracture twice. The chronological order of events was as follows: single chamber T-ICD implantation in 2003, transvenous lead extraction (TLE) and re-implantation of the new lead in 2010, another ventricular lead damage with a lead alert in 2016 and patient’s refusal to accept TLE. The S-ICD system was finally implanted with lead 3401 to diminish the risk of the lead insulation damage. Good clinical outcome was observed for 3 years.

One HCM patient revealed highly symptomatic II/III atrio-ventricular block 24 years after VVI ICD implantation after aborted SCD. The elective system upgrade is planned with atrial and His bundle pacing leads implantation.

It should be kept in mind that supraventricular and ventricular arrhythmias can coincide, and therefore the indication for EPS can change with time. We repeated EPS in 2 patients several years after the first investigation. Regardless of the previously diagnosed ventricular tachyarrhythmias, one patient had atrioventricular nodal re-entrant tachycardia (AVNRT) and the other atrial tachycardia (AT). The elective radiofrequency (RF) ablation is planned in both cases.

**FIGURE 3** Chest X-ray: S-ICD as a co-implant i.e. conversion of T-ICD to S-ICD due to ventricular lead dysfunction. Concomitant devices: T-ICD with lead dysfunction.
As of 2016 we have been using entirely subcutaneous system for SCD prevention in Poland. Since then, we have implanted 55 S-ICDs in our center in total (Figure S1). If there are no indications for permanent pacing or CRT therapy, we choose this solution in young patients.9,10 In adolescents with body weight of more than 30 kg, the S-ICD procedure is a feasible technique in a typical chest generator position (Figure S2). However, there are some reports in younger children, e.g. aged 3 years and body weight of 13.5 kg, with the generator in the abdominal pocket.26 There is also a report on a hybrid approach of a subcutaneous ICD coil and the second coil placed posteriorly, sensing via epicardial pacing leads in a patient weighed 7.3 kg.27 The clinical practice shows that in the youngest children, the intrathoracic defibrillator system is generally used, instead of transvenous one.

Perspectives

On the basis of our experience, S-ICD opens a new treatment perspective for primary electrical or structural heart disease, preventing from SCD with the heart and vessels unaffected. It offers young patients good visual and aesthetically pleasing results (FIGURE 6). S-ICD system diminishes the risk of the lead insulation damage due to its lead multistrand cable-core design, no lumen and no systolic and diastolic cyclic friction within the heart. The S-ICD may be implanted using anatomical landmarks, which reduces X-ray dose significantly. The subcutaneous system eliminates the risk of lead-related infective endocarditis, cardiac perforation.

Furthermore, cusp stiffness, lead adherence to the valve and its immobilization may cause incomplete closure. Cusp perforation or valve laceration are possible as well.20 Valve obstruction can be caused by lead placed between leaflets or its entrapment in the tricuspid valve apparatus. This phenomenon is presented in FIGURE 4. Concomitant RV apex pacing may deteriorate RV function with atrioventricular and interventricular dysynchrony and further annular dilatation and vicious circle initiation.

The incidence of TR varies in the literature ranging between 1.2% and 15%.17‑18 In the presented study the percentage is remarkably low (1.25%).

In our S-ICD group we did not observe any surgical complications during the whole period of follow-up, and it is concordant with another Polish report.21 S-ICD is still underused in Poland in comparison to other European patients.22 Approximately 7% S-ICD inappropriate shock rate is reported in the literature. Twenty five percent of patients (n = 4/15) had device-related complications requiring surgical intervention: three skin erosions at the superior parasternal incision and one pocket infection reported by Silvetti et al.23 All things considered, we regard S-ICD implantation superior to T-ICD in eligible patients. Compared to T-ICD, S-ICD implantation appears to be a simpler option which allows to avoid TLE complications in terms of TR prevention.24‑25 As presented in the results section, in patients with severe TR we would choose S-ICD as a preferable option as opposed to the epicardial system.

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and pneumothorax. Actual maximal device energy output is 80 J, which is higher than necessary for defibrillation in low-weight children. Therefore, advanced experimental trials are conducted in order to develop a smaller and lower energy pulse generator system, with a miniaturized lead. It is estimated that 35 J energy should be sufficient for this purpose in small children of mere weight of 5–10 kgs.  

**Study limitations** This is prospective, observational and non-randomized study, but in this kind of population there is no randomized large scale data published. Some aspects of patients’ profiles were considered the data of minor importance, therefore patients’ medications, baseline electrocardiographic and echocardiographic parameters were not taken into account. We did not continue psychological problems analysis, but since 2010 our patients were followed in local centers. Despite the lack of these data, psychological problems are a well-recognized complication described in numerous publications.

**Conclusions** The mortality rate was 6/80 (7.5%) in the 22-year-long follow-up. All deaths occurred in the hypertrophic cardiomyopathy group. The appropriate and inappropriate therapies rate measured, turned out almost equal in the study population and remained on a constant level in the long observation period. Severe tricuspid valve regurgitation might be a serious clinical problem in some patients, therefore echocardiography screening for this complication should be recommended in the perspective of a lifelong therapy. Entirely subcutaneous system (S-ICD) for SCD prevention appears to be a feasible and safe therapy option in young patients.

**SUPPLEMENTARY MATERIAL**

Supplementary material is available at www.m.p.pl/kardiologiapolska.

**ARTICLE INFORMATION**

**CONFLICT OF INTEREST** Michał Lewandowski, Paweł Syska: lecture honoraria, travel expenses coverage by Boston Scientific and Biotronik, Paweł Syska: lecture honoraria, travel expenses coverage by Medtronic, Ilona Kowalka declares no conflict of interest.

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**REFERENCES**


