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Safety of mid-septal electrode placement in implantable cardioverter defibrillator recipients — Results of the SPICE (*S*eptal *P*ositioning of ventricular *ICD E*lectrodes) study

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ABSTRACT

Background: Detrimental effects of right ventricular (RV) apical pacing have directed the interest toward alternative pacing sites such as the RV mid-septum. As safety data are scarce for implantable cardioverter defibrillator (ICD) recipients the study aims to evaluate ICD lead performance in the mid-septal position.
Methods and results: A total of 299 ICD recipients (79% male, aged 65.2 ± 12.1 years, 83% primary prevention of sudden cardiac death) were randomized to receive the RV ICD electrode either in a mid-septal (n = 145) or apical (n = 154) location. Event-free survival was evaluated at 3 (primary endpoint) and 12 months (secondary endpoint). Events included a composite of lead revision, suboptimal right ventricular electrode performance (including defibrillation thresholds (DFT) > 25 J) or lead position not in accordance with randomized location. Event-free survival at 3 (12) months was observed in 80.6% (72.3%) of patients randomized to a mid-septal and in 82.2% (72.1%) of patients randomized to an apical lead position, p = 0.726 (p = 0.969). Pre-defined margins for non-inferiority were not reached at 3 or 12 months. High DFT was found in 7 patients (5.0%) of the mid-septal and in 3 (2.2%) patients of the apical group (p = 0.209).
Conclusion: In ICD recipients electrode positioning to the RV mid-septum or the RV apex results in slightly different rates concerning the survival free of lead revision, suboptimal right ventricular electrode performance or non-randomized lead position. Non-inferiority of the mid-septal lead location cannot be concluded. This should be taken into consideration when a mid-septal lead position is pursued.
Clinical trial registration: ClinicalTrials.gov identifier NCT00745745.

1. Introduction

The placement of an implantable cardioverter defibrillator (ICD) has become standard therapy for primary and secondary prevention of sudden cardiac death [1–3]. Typically, the right ventricular (RV) lead is placed in the apical region because this location is easily accessible, provides for lead stability and usually goes along with adequate values for sensing, pacing and defibrillation thresholds. However, pacing the RV apex is also associated with a non-physiologic ventricular activation pattern [4], functional mitral regurgitation [5], myocardial perfusion abnormalities [6,7], adverse left ventricular remodeling [8], and reduction in ejection fraction [9–11].

As unnecessary RV apical pacing has been proven to increase morbidity and mortality in ICD recipients, programming strategies aim to avoid it [12–14]. However, in a subset of ICD patients (e. g. those with concomitant ventricular antibradycardia pacing indication) right ventricular pacing typically cannot be avoided and therefore may be candidates for alternative pacing sites. Among others [15], a promising alternative pacing site is the RV mid septum, which is associated with preserved left ventricular ejection fraction among pacemaker recipients with frequent ventricular pacing [16–18].

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There are few data on RV mid-septal ICD lead positioning. Therefore, the aim of the SPICE (*S*eptal *P*ositioning of ventricular *I*C*D* *E*lectrodes) trial was to evaluate the safety of this alternative electrode position in comparison to the traditional RV apical site over a follow-up of three months and an additional mid-term follow-up (12 months).

2. Methods

Details of the rationale and design of the prospective, randomized, multi-center, single-blinded SPICE trial (ClinicalTrials.gov identifier NCT00745745) have previously been reported [19].

In brief, patients with an indication for ICD therapy including cardiac resynchronization therapy according to the respective international guidelines [1] were enrolled. Major exclusion criteria were pre-existing right ventricular pacemaker or ICD electrodes, pacemaker dependency and circumstances that dissuade the induction of ventricular fibrillation during the implantation procedure.

Patients were randomized in a 1:1 ratio to receive the RV electrode (Riata™ or Durata™, St. Jude Medical, Sylmar, CA, USA) either in a mid-septal or an apical position. Leads were placed according to fluoroscopic criteria (19, see also Fig. 1). At the end of the implantation procedure ventricular fibrillation was induced. In a first step termination of the induced ventricular fibrillation was attempted with a 20 J shock (thereby providing a 10 J safety margin for standard 30 J energy devices). In case of a failed defibrillation test with 20 J, a second shock was delivered at 25 J (conferring a 10 J safety margin with high energy ≥35 J devices). Defibrillation threshold is defined as lowest successful shock energy that was delivered for VF. In case of an inadequate safety margin for the defibrillation threshold one of the composites of the primary endpoint was reached and the further procedure was left to the physician's discretion (e.g. they were permitted to leave the randomized lead location, alter shock polarities, add or remove a vena cava superior coil, etc.). Study participants were followed for events during three months (primary endpoint) and twelve months (secondary endpoint) on an intention-to-basis. Events included any of the following: (1) final RV lead position differing from randomization group; (2) defibrillation threshold > 25 J at first test sequence during implantation; (3) poor RV lead measurements at implantation or during follow-up (pacing threshold ≥2.0 V at 0.5 ms, sensing threshold < 5.0 mV, abnormal lead impedance ≤ 250 Ω or ≥1500 Ω); (4) need for an additional RV pace/sense electrode during initial implantation or during follow-up; (5) inability to terminate ventricular fibrillation or ventricular tachycardia with maximal shock energy for episodes that occur after implantation; (6) need for RV lead replacement or repositioning during follow-up; (7) death. Therefore, patients were routinely followed at 3, 6 and 12 months post-implantation and at additional follow-ups if clinically indicated. At these follow-ups the patients underwent necessary testing in order to determine the endpoints and the data were monitored (including deaths) over the same time period. Any death was reviewed and classified as cardiac or non-cardiac by the steering committee.

In addition to the fluoroscopy-guided validation of RV lead positioning during implantation by the operating physician, the final lead position was evaluated by an independent adjudication committee member blinded to the patient's randomization arm. In case of disagreements a second adjudication committee member reviewed the lead position for a final decision. The classification of the actual lead position allowed the determination of feasibility of electrode placement in the randomized position and gave basis for as treated analysis (secondary endpoints). Another secondary endpoint was the impact of cardiac resynchronization therapy (CRT) on the primary endpoint.

3. Statistics

The sample size calculation was based on a non-inferiority hypothesis and assumed a 10% occurrence of RV lead-related events and a 16% drop-out rate during follow-up. Pre-set values were 5% for the significance level and 80% for the power. To test for non-inferiority of the RV mid-septal versus the RV apical group, the 95% confidence intervals for the differences in event-free survival were calculated and non-inferiority was assumed if the lower limit of the 95% confidence interval did not exceed −0,10 (−10%). Based on these assumptions, a total of 286 patients (143 patients per group) were calculated to be required to determine non-inferiority [19].

Statistical analyses were performed using the software SAS 9.2 for windows (SAS Institute Inc., Cary, NC, USA) and PASW 17.0 for windows (SPSS Inc./IBM, Armonk, N.Y., USA). Continuous data are presented as mean ± standard deviation unless otherwise stated, and comparisons between the groups were carried out using the Student's t-test or the Wilcoxon test, where appropriate. Categorical variables are presented as frequencies and percentages, and comparisons between the groups were performed using the Chi-square test or Fisher's exact test, where appropriate. p-Values <0.05 were considered statistically significant.

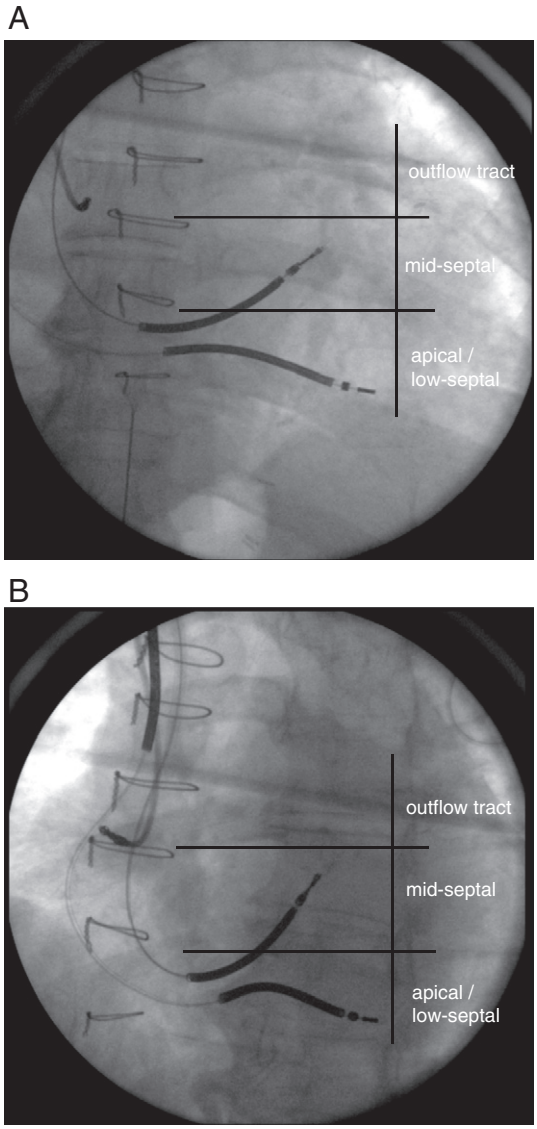

Fig. 1. 1A–1B: Fluoroscopic criteria for lead placement: Right ventricular mid-septal versus apical lead positions in AP-projection (1A) and left anterior oblique 30° (1B) in a patient not participating in the trial (figures taken from [18]). In order to distinguish between outflow tract, mid-septal or apical region the RV septum is divided into three thirds using the AP view, mid-septal lead position is then verified in the LAO projection by the lead tip pointing toward the spine.