Implantable cardioverter defibrillator treatment : benefits and pitfalls in the currently indicated population

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Chapter 13

Requirement for Coronary Sinus Lead Interventions and Effectiveness of Endovascular Replacement during Long-term Follow-up after Implantation of a Resynchronization Device

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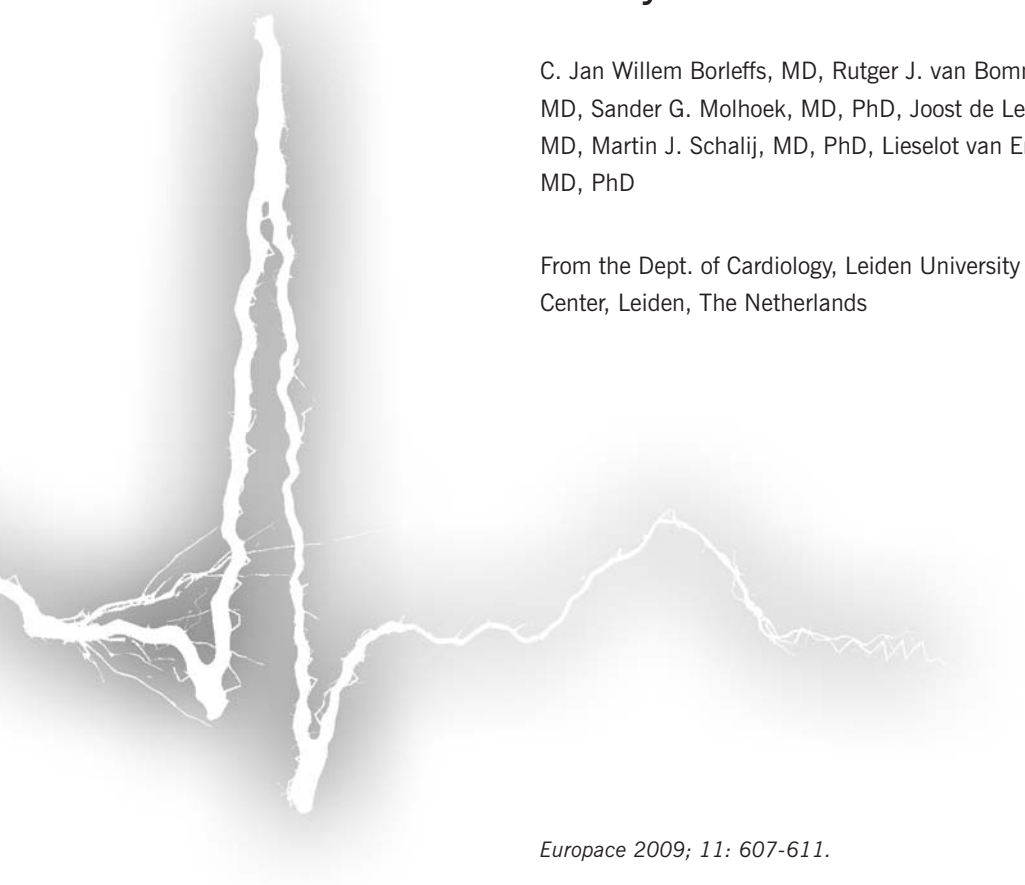

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Abstract

Aims: To assess the requirement for coronary sinus (CS) lead intervention after cardiac resynchronization therapy (CRT) and to evaluate the effectiveness of endovascular replacement.

Methods: All patients receiving a CRT device with CS lead in the Leiden University Medical Center in the period from 1999 to 2007 were prospectively evaluated and followed.

Results: Five-hundred-seventy-seven patients were successfully implanted with a CRT device. Nine (1.6%) patients were lost to follow-up. The remaining 568 patients were included in the analysis. During a median follow-up time of 645 days (interquartile range, 260 to 1148), 7% of patients required a CS lead intervention. Cause of the intervention was an elevated threshold (n=13), loss of capture (n=20), or intractable phrenic nerve stimulation (n=6). Fifteen patients (38%) required a CS lead intervention before first scheduled follow-up (two months after implantation). Thirteen patients (33%) warranted a CS lead intervention more than six months after implantation. The first endovascular replacement was successful in 86% (32 out of 37), while a second endovascular approach failed in 66% (2 out of 3).

Conclusion: The long-term requirement for CS lead interventions is 7%. Endovascular repositioning or replacement is successful in the majority of cases.

Introduction

Cardiac resynchronization therapy (CRT) plays an important role in the treatment of advanced heart failure in patients with cardiac dyssynchrony. Biventricular pacing has a positive effect on mortality, exercise tolerance, quality of life and number of heart failure related hospitalizations.[1-5]

Furthermore, a significant clinical improvement, as measured by a change in New York Heart Association (NYHA) functional class occurs in approximately 70-80% of the patients receiving resynchronization therapy.[6-8] The clinical non-response in 20-30% of all CRT recipients is the most important setback in the use of CRT. Further important complicating factors are the success rate of coronary sinus (CS) lead positioning, which is 88-96% in large trials,[3, 8, 9] and the occurrence of CS lead dysfunction in 5-10% of the patients during follow-up.[9, 10] However, currently available follow-up data is often limited to six months following CRT implantation.

Endovascular placement of the CS lead in a branch of the coronary sinus is the approach of first choice. However, this technique has a number of setbacks and is not applicable to all patients because of coronary sinus anatomy, coronary vein anatomy, phrenic nerve stimulation (PNS) and/or dislocation of the CS lead.[11] In all cases of CS lead failure, the clinician has three options of intervening: (1) endovascular replacement; (2) replacement of the endovascular lead by an epicardial lead by means of a (minimally invasive) surgical implant; or (3) transseptal or transapical approach.[12-14] The current study evaluated the incidence and causes of the requirement for CS lead intervention and the effectiveness of endovascular replacement.

Methods

Patients

All 577 patients receiving a CRT device with CS lead in the Leiden University Medical Center in the period from 1999 to 2007 were prospectively evaluated and followed. Patients in whom it was not possible to implant a CS lead during the initial procedure were excluded from the current analysis. Eligibility for CRT was based on the standard guidelines and included advanced heart failure, depressed left ventricular ejection fraction (LVEF <35%) and wide QRS complex (>120 ms).[15]

Device implantation

A coronary sinus venogram was obtained using a balloon catheter, followed by the insertion of the CS lead into one of the posterolateral veins through an 8-F guiding catheter. The following CS lead models were used: Easytrak, Easytrak 2, and Acuity manufactured by

Boston Scientific (Natick, MA [formerly, Guidant, St. Paul, MN]); Attain and Attain-SD, manufactured by Medtronic Inc. (Minneapolis, MN); Aescula, by St. Jude Medical, (St. Paul, MN); and the Enpath, by Enpath Medical Inc. (Minneapolis, MN). The right atrial and right ventricular leads were positioned conventionally. All leads were connected to a dual-chamber CRT or CRT-defibrillator (CRT-D) device of the following models: Contak TR, Contak CD, or Contak Renewal, Guidant Corp.; Insync III, Insync CD, Insync III Marquis, or Insync Sentry, Medtronic Inc; Epic or Atlas, St Jude Medical. Procedural success was accomplished when pulse generator and the 3 leads were positioned without complications.

Before patient discharge, all leads were systematically screened for adequate functioning. This included testing for pacing threshold, sensing, and lead impedance. Additionally, possible presence of PNS was ruled out.

Follow-up

All devices and leads were technically assessed at 3 to 6 months intervals. In case of loss of capture at maximum output, increase of threshold to sub-maximal (>5.5V/1.0ms) values or intolerable PNS a chest roentgenogram was made to evaluate whether gross dislodgement of the CS lead had occurred. In case of PNS, all effort was made to prevent its occurrence, using different technical settings.

In the Dutch health care system, all patients are followed by the implanting center. Since periodical follow-up was performed every three to six months, patients with more than six months of missing data were considered as lost to follow-up.

Left ventricular lead intervention

Before admittance for repositioning of the CS lead, the retrograde venogram of the coronary sinus made at first CS lead implant was reevaluated in order to assess coronary sinus anatomy and to predict the probability of successful endovascular replacement of the CS lead. After repositioning or replacement of the CS lead in an area with a good threshold and sensing, the occurrence of PNS was tested by pacing with high output (10 V). In case of PNS with low output pacing, the CS lead was repositioned to a better location. Furthermore, the CS lead position after replacement was compared with its position after the initial implantation. Endovascular repositioning or replacement of the CS lead was performed by an electrophysiologist at our centre.

Statistical analysis

Continuous data are expressed as mean and standard deviation or range, median and first and third quartile where appropriate; nominal data are presented as numbers and percentages. Comparison of data was performed with the Student's *t* test for unpaired data and Chi-square tests with Yates correction when appropriate. Non-normally distributed data (NYHA functional class) were compared using the Mann-Whitney U test. Cumulative

incidences were analyzed by method of Kaplan-Meier. Death or heart transplantation were counted as censoring events. For all tests, a p-value <0.05 was considered significant.

Results

Patient characteristics

During the study period, 596 patients were implanted with a CRT device. Five-hundred-seventy-seven patients (97%) successfully received a CS lead. Nine (1.5%) patients were lost to follow-up. The remaining 568 patients were included in the analysis. One-hundred-thirty-four patients died (n=130) or underwent heart transplantation (n=4) with their lead still intact at last follow-up. Median follow-up time was 645 days (interquartile range, 260 to 1148).

Implanted leads consisted mostly of models manufactured by Boston Scientific (n=365) or Medtronic (n=185). The majority of patients (80% men, mean age 66 years, range 36 to 87 years) had ischemic heart disease (60%) and a poor LVEF (25±8%). Leads were connected to a CRT only device in 10% (n=56) or CRT-D device in 90% (n=512). All data are summarized in Table 1.

Requirement for CS lead intervention

During follow-up, 39 (7%) patients required CS lead intervention. Median time to this event was 85 days (interquartile range, 35 to 211 days). Patients with a CS lead, needing

Table 1. Patient characteristics.

	All CS lead	CS lead requiring intervention	p-value
Variable	n=568	n=39	
Age (yrs)	66±10	64±11	0.1
Male gender	452 (80%)	30 (77%)	0.7
Ischemic etiology	343 (60%)	18 (46%)	0.1
LVEF (%)	25±8	24±9	0.4
NYHA functional class			
II / III / IV	105 / 420 / 43	9 / 30 / 0	0.4
QRS (ms)	159±32	164±31	0.3
Medication			
Diuretics	500 (88%)	36 (92%)	0.4
ACE inhibitors	507 (89%)	36 (92%)	0.5
Spironolactone	272 (48%)	19 (49%)	0.9
B-blockers	372 (66%)	27 (69%)	0.6
Amiodarone	141 (25%)	11 (28%)	0.6
CRT-D	512 (90%)	33 (85%)	0.2

CRT-D: cardiac resynchronization therapy-defibrillator; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association

intervention, showed no significant differences in clinical parameters (Table 1: patient characteristics). The incidence of surgical CS lead intervention was found to be 3.3 per 100 patient years (95% CI 2.3-4.5 per 100 patient years). Cumulative event-rate (Figure 1) at one year was 5.8% (95% CI 1.9-9.7%), at two years 6.6% (95% CI 2.3-10.9%), and at five years 8.6% (95% CI 2.2-14.9%). Additionally, no technical failure of the CS lead was observed. In case of reintervention, no difficulties were encountered during removal of CS leads, that was performed by traction.

In 6 (15%) cases, requirement of CS lead intervention was based on the occurrence of intractable PNS. The remaining cases of CS lead intervention were diagnosed by findings during periodical examination. In 20 (51%) patients a complete loss of capture was found and in 13 (33%) cases the intervention was warranted due to an elevated threshold more than 5.5V/0.5ms. In the 20 cases of complete loss of capture and consequently loss of biventricular pacing, 13 patients (65%) had experienced an increase in heart failure symptoms. In addition, dislocation could be verified on roentgenogram in 14 out of 20 (70%) cases of complete loss of capture. In the remaining 25 cases, no sign of dislodgement was visible on roentgenogram. Elevated thresholds, causing the need for lead intervention occurred longest after implantation with a median duration of 180 days (interquartile range, 4 to 376 days), whereas complete loss of capture occurred after the shortest period of time (median 83 days, interquartile range 55 to 174) (Table 2: reasons for the requirement and type of CS lead intervention). The shorter time to diagnosis and the fact that 14 out of 20 (70%) cases of lead dysfunction could be verified on roentgenogram, implies a more severe dislodgement in the patients with a complete loss of capture. Fifteen patients (38%) required a CS lead intervention before first scheduled follow-up two months after implantation. Thirteen patients (33%) were indicated for CS lead intervention more than six months after implantation. It is of note that one patient required a CS lead intervention because of a severely elevated threshold 1415 days after implantation.

Endovascular replacement

Of the 39 patients warranting CS lead re-intervention, two directly received an epicardial left ventricular (LV) lead because of unfavorable CS anatomy. In 37 patients, endovascular replacement was attempted of which 86% (n=32) was successful during follow-up. In these patients, a median of 867 days (interquartile range, 647 to 1123 days) of stable long-term biventricular pacing was achieved after repositioning. The remaining five patients needed a second intervention during further follow-up. In two of these patients, clinicians chose to implant an epicardial lead because of unfavorable CS anatomy and the experience during the previous attempt. In three patients, a (second) attempt of endovascular replacements was made in which the rate of success was 33% (n=1) (Figure 2). This patient demonstrated adequate biventricular pacing during a follow-up of 1574 days after the sec-

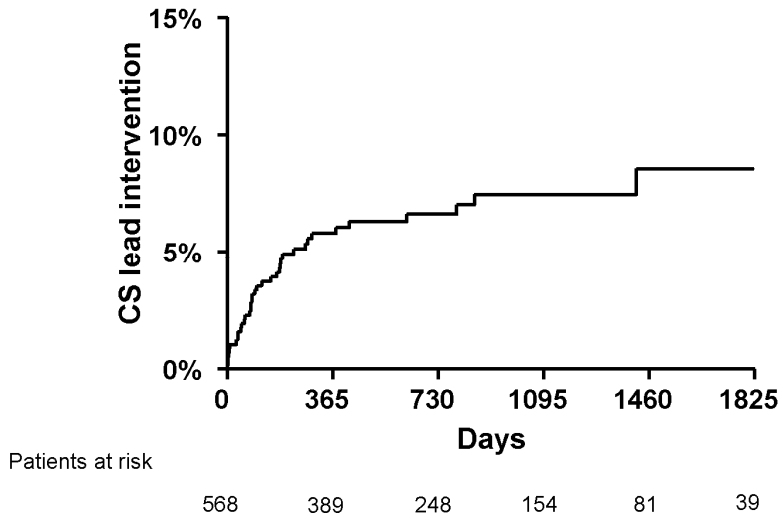

Figure 1. Cumulative requirement for CS lead intervention.

Table 2. Reasons for the requirement of CS lead intervention.

	Reason for intervention	Median time to intervention
	N	Days (1st – 3rd quartile)
Total	39 (100%)	85 (35-211)
Elevated threshold	13 (33%)	180 (4-376)
Loss of capture	20 (51%)	83 (55-174)
Phrenic nerve stimulation	6 (15%)	83 (16-167)

ond replacement. The two patients with an unsuccessful second attempt for endovascular intervention both received an epicardial lead.

It is of note that the same branch of the CS could be used in 21 out of 37 (57%) first attempts at endovascular intervention and most leads were placed at the posterolateral region.

Out of the 37 performed first endovascular CS lead replacements, the old lead was re-used 11 (30%) times. Cases, in which leads could be re-used occurred a shorter period after the initial implantation (re-use of lead: 126±128 days after implantation vs. usage of a new lead: 213±311 days after implantation, p=0.5). The angiographic study, performed at CS lead intervention, demonstrated changes in coronary venous anatomy, such as occlusion or narrowing of the initially used branch, in six cases. In the three cases of second attempts for endovascular replacements, the clinician chose to use a new lead in every case.

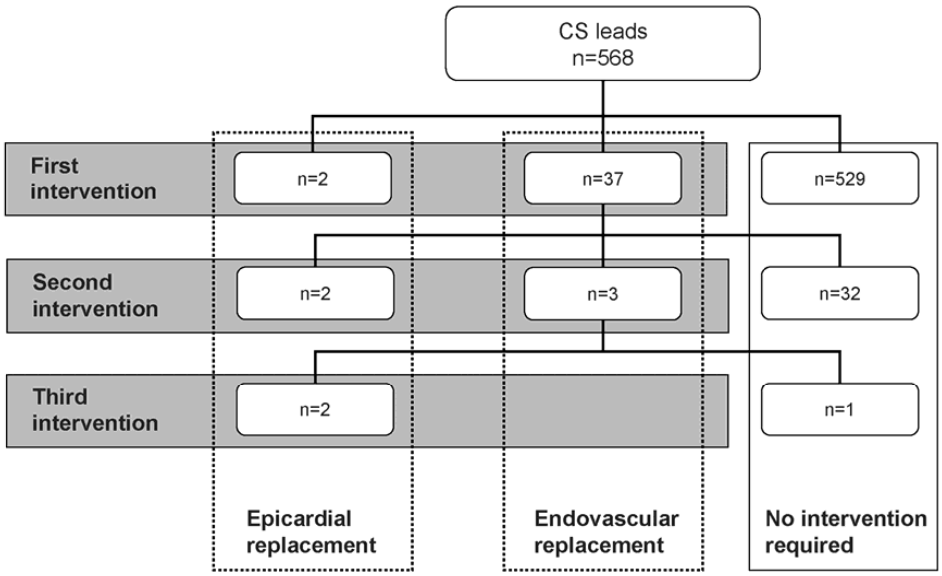

Figure 2. Flow-chart of the requirement and type of CS lead intervention.

Discussion

The current study aimed to specifically describe the need for CS lead intervention during long-term follow-up and to assess the successfulness of endovascular repositioning. The main findings of the current study can be summarized as follows: 1) Endocardial CS lead performance during long-term follow-up is excellent; 2) Replacement or repositioning was necessary in 7% of patients; 3) Cases in which evaluation of the coronary sinus venogram favored an attempt of endovascular replacement of the CS lead had a success rate of 86% (32 out of 37) at first attempt and 33% (1 out of 3) in second attempt; 4) Thirty-three percent (n=13) of CS lead interventions were made more than six months after implantation; 5) In case of clinical or technical evidence for CS lead malfunction, only 36% (n=14) could be verified on roentgenogram.

Although CRT has become an established treatment in patients with advanced heart failure, clinical use of biventricular pacing still has to cope with some serious setbacks. Firstly, 20-30% of implanted patients does not show clinical improvement.[6-8] Secondly, implantation of a biventricular system succeeds only in 88-96% of patients,[3, 8, 9] and finally, during follow-up the need for CS lead intervention is warranted in 5-10% of implanted patients.[9, 10] Since endovascular replacement of the CS lead is the least invasive (in contrast to epicardial placement), the current study sought to evaluate the incidence and causes of the requirement of CS lead intervention and the effectiveness of endovascular replacement.

During follow-up, high thresholds, complete loss of capture, or intractable PNS prevented adequate left ventricular pacing in 7% of our population. Compared with other device-related complications, this is a substantial number of cases requiring an invasive procedure to resolve. To replace a CS lead, the clinician has to find the best side branch of the coronary sinus, which can be assessed by reevaluation of the retrograde venogram of the coronary sinus, made at the initial implantation. Due to more experience and improved technical possibilities there is a high success rate in the initial endovascular implantation of CS lead into one of the branches of the coronary sinus.[1, 8] Our data show that in case of a subsequent CS lead intervention, the endovascular approach is successful in 86% of cases, making it a very reasonable therapeutic option to restore biventricular pacing and its accompanying beneficial effects.

CS lead dislodgement can occur shortly after implantation but was seen as late as 4 year after implantation. Although the median follow up in our population was 645 days (interquartile range, 260 to 1148), there might well be an underestimation of the percentage CS lead dislodgements. This is also shown in our analysis of the cumulative incidence, which can reach up to 8.6% five years after implantation. The same underestimation is likely to have occurred in some large studies with relatively short follow of less than one year.[3, 8] Only the CARE-HF study has a comparable long mean follow of 29.4 months and also showed a 6% CS lead dislodgement, results comparable to our CRT population.[16]

Phrenic nerve stimulation is tested during implantation by high-voltage pacing (up to 10 V). Nevertheless, chronic PNS is reported in up to 12% of CRT recipients.[8] During follow-up PNS can also arise de novo because of changes in body position or (micro) dislodgement of the CS lead. Changing the pacing output and/or pacing configuration can resolve the problem most of the time but repositioning of the CS lead is necessary in some cases. In our population only 6 patients (1.3%) needed a CS lead replacement due to intolerable PNS, which is 15% (6/39) of all patients with CS lead failure.

Three patients underwent a successful second endovascular replacement but during further follow-up, two of them needed an epicardial lead placement after renewed CS lead malfunction. A second replacement procedure should therefore be carefully evaluated. However, the number of patients receiving a secondary replacement in this study is limited.

In total, six patients received an epicardial LV lead without complications periprocedural or during follow-up. Nevertheless, taking in account the invasiveness and time consumption of an epicardial approach and the 86% effectiveness of the endovascular approach, clinicians should favor the endovascular. It is of note that before intervening, all cases in the current study were reevaluated by venogram of the coronary sinus to determine the possibility of endovascular replacement.

Conclusion

The long-term requirement for CS lead interventions is 7%. Endovascular repositioning or replacement is successful in the majority of cases.

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