Leadless left ventricular stimulation with WiSE-CRT System – Initial experience and results from phase I of SOLVE-CRT Study (nonrandomized, roll-in phase)

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BACKGROUND Left ventricular (LV) endocardial pacing is a promising method to deliver cardiac resynchronization therapy (CRT). WiSE-CRT is a wireless LV endocardial pacing system, and delivers ultrasonic energy to an LV electrode.

OBJECTIVE The purpose of this study was to present short-term outcomes with the WiSE-CRT system in centers with no prior implanting experience.

METHODS Data were prospectively collected from 19 centers where WiSE-CRT systems were implanted during the roll-in phase of the SOLVE-CRT trial. Patients were followed at 1, 3, and 6 months, including transthoracic echo (TTE) at 6 months.

RESULTS The WiSE-CRT was successfully implanted in all 31 attempted cases, and 30 patients completed the 6-month follow-up. One patient underwent heart transplantation 1 month after implantation, and was excluded. Fourteen (46.7%) patients demonstrated ≥1 NYHA class improvement. TTE data were available in 29 patients. LV ejection fraction, LV end-systolic volume, and LV end-diastolic volume improved from 28.3% ± 6.7% to 33.5% ± 6.9% (P < .001), 134.9 ± 51.3 mL to 111.1 ± 40.3 mL (P = .0004), and 185.4 ± 58.8 mL to 164.9 ± 50.6 mL (P = .0017), respectively. There were 3 (9.7%) device-related type 1 complications: 1 insufficient LV pacing, 1 embolization of an unanchored LV electrode, and 1 skin infection.

CONCLUSIONS We demonstrated a high success rate of LV endocardial electrode placement in centers with no prior implanting experience. Favorable clinical responses in heart failure symptoms and significant LV reverse remodeling were noted.

KEYWORDS Cardiac resynchronization therapy; Heart failure; Leadless pacemaker; Nonresponder; Ultrasound

Introduction

Despite the established role of cardiac resynchronization therapy (CRT) in eligible patients with heart failure (HF) with reduced ejection fraction (EF), major limitations of this device therapy include a high (5%–7%) incidence of unsuccessful coronary sinus (CS) lead position/placement and substantially higher rates (30%–50%) of CRT “nonresponders.” The common causes for unsuccessful CS lead position/placement include anatomical variations (CS valves, tortuosity, small branch caliber), high pacing threshold, and diaphragmatic stimulation.

The Wireless Stimulation Endocardially for Cardiac Resynchronization (WiSE-CRT) system (EBR Systems, Sunnyvale, CA) delivers ultrasonic energy to a left ventricular (LV) endocardial receiver electrode to achieve biventricular pacing and may be a solution to patients who failed conventional CRT. A percutaneously delivered LV endocardial electrode (ultrasound receiver and energy converter) delivers an electrical stimulus that is synchronized to a right ventricular...
The SOLVE-CRT (Stimulation Of the Left Ventricular Endocardium for Cardiac Resynchronization Therapy in Non-Responders and Previously Untreatable Patients) is an international, multicenter prospective randomized trial of the WiSE-CRT system evaluating its efficacy and safety in CRT nonresponders and CRT-eligible patients who were previously untreated.\(^5\) (ClinicalTrials.gov Identifier: NCT02922036). Participating sites without prior WiSE-CRT system implantation experience were allowed to include a minimum of 2 roll-in patients per site. Here we present our collective experience with the WiSE-CRT system in the roll-in phase of the clinical trial.

### Methods

#### Trial design

In SOLVE-CRT, up to 90 roll-in patients were allowed, and the WiSE-CRT system was turned on without randomization (unlike non-roll-in patients that were randomized to WiSE-CRT on vs off). It should be noted that roll-in patient enrollment was terminated in early 2020 owing to the effects of the COVID-19 pandemic.

#### Study participants

The study population was composed of (1) CRT nonresponders, (2) CRT-eligible patients who were previously untreated with CRT, and (3) CRT-eligible patients deemed too high-risk for conventional transvenous CRT upgrade of implantable cardioverter-defibrillator. The former cohort had previously undergone CRT placement and failed to respond to CRT despite a functional CRT system, guideline-directed medical therapy, and optimal device programming for a minimum of 6 months. CRT nonresponse was defined as EF improvement <5% and worsening or unchanged patient functional status. The second cohort included those with CRT indications but without functioning CS lead, because of either failed lead placement or deactivated CS lead owing to suboptimal lead parameters. Eligible patients were aged 18 years or older and on stable guideline-directed medical therapy.\(^4\)\(^,\)\(^5\)

The major exclusion criteria included right bundle branch block, LV end-diastolic diameter \(\geq 8\) cm, attempted CRT implant within 1 month of enrollment, life expectancy \(<1\) year, chronic hemodialysis, glomerular filtration rate \(<30\) mL/min, mechanical or transcutaneous aortic valves, and recent acute coronary syndrome or stroke. As of August 2019, patients with persistent or permanent atrial arrhythmias with a prior atrioventricular nodal ablation also met inclusion criteria.

All patients had a screening transthoracic echo (TTE) to assess whether an adequate acoustic window was present to ensure optimal delivery of ultrasonic energy from the transmitter to the endocardial electrode. Similarly, LV wall thickness at the target site \(\geq 5\) mm was required for safe anchoring of the LV receiver electrode.

The study was approved by the Institutional Review Board in each participating center, and all participants gave written informed consent.

#### Device implantation

All participating physician investigators underwent implantation training (didactic lecture, animal lab, and battery/transmitter implantation on cadavers). The battery and transmitter need to be implanted first in order to locate the appropriate implanting site for the LV electrode. Staged implantation over 2 days (transmitter/generator implant on day 1 and LV receiver electrode implant on day 2) was mandated.

The location of transmitter implantation was guided by preimplant screening TTE. The transmitter pocket was dissected to the level of the intercostal muscle, then the appropriate acoustic window was reconfirmed with intraoperative TTE before the transmitter was securely sutured to the subcutaneous tissue. A subcutaneous battery pocket in the left lateral thoracic area was created in the same intercostal space at the midaxillary line. A transmitter cable was tunneled from the transmitter pocket to the battery pocket.

Either retrograde transaortic approach via the femoral artery or transseptal approach via the femoral vein was selected based on the physician’s experience and the patient’s clinical characteristics. Transseptal approach was used if patients had peripheral artery disease or a prosthetic aortic valve. Retrograde transaortic approach requires a 12F femoral arterial sheath, whereas atrial transseptal appropriate requires a long steerable sheath (an inner lumen 12F Medtronic FlexCath). A 12F WiSE delivery sheath is then advanced to the LV, and a balloon at the distal end of the delivery sheath is inflated with diluted contrast. The sheath is then advanced to the LV endocardium while contrast is injected to ascertain adequate contact and alignment with the endocardial surface. The use of either transesophageal or intracardiac echo guidance is highly recommended in conjunction with cine imaging and contrast use. An 8F electrode catheter is advanced inside the delivery sheath until approximately 25% of the 9.1 mm electrode body is exposed outside the delivery sheath tip. Generally, the mid to basal lateral LV segments were primarily targeted for electrode placement; however, the other locations were also selected to meet preanchoring requirements, including adequate pacing threshold (<2.5 V at the pulse width of 0.5 ms) and transmitter-electrode relation (distance \(<10\) cm and angulation \(<30^\circ\) ). Site-specific electrical delay measurement (Q-LV) was used as an adjunctive parameter for optimal site selection, and a Q-LV interval \(>90\) ms was considered optimal. Adequate electrode anchoring is confirmed with 2 orthogonal cine views with contrast injection, intracardiac electrogram, and electrical parameters before detachment of the electrode. Activate clotting time was maintained above 200 seconds with intravenous boluses of unfractionated heparin.

#### Study follow-up

Patients were followed at 1, 3, and 6 months, then every 6 months up to 2 years and annually for an additional 3 years.
Physical examination, blood work (complete blood count, basic metabolic panel, haptoglobin, liver function test, and IgE), and device interrogation were performed at each follow-up. Clinical assessment with Kansas City Cardiomyopathy Questionnaire (KCCQ) and NYHA class were evaluated at 3 and 6 months, and 12-lead electrocardiogram and TTE were performed at 6 months. An echo core lab independently analyzed the echocardiograms. Echo readers were blinded to the patient treatment assignment or whether implantation was performed in the roll-in phase. The WiSE-CRT was programmed on after the 6 months follow-up for all patients.

Study endpoints
Primary safety endpoint included type I complications through 6 months of follow-up. Type I complications are defined as those caused by a component of the investigational device (WiSE-CRT system transmitter, battery, electrode, catheter, sheath, and/or programming software), or specific procedure-related events including vascular events, stroke, pericardial effusion, and pocket-related events.

The primary efficacy endpoint was mean % change in LV end-systolic volume (LVESV) from baseline through 6 months. Additional efficacy outcomes of interest included the number of subjects with an improvement of LVESV ≥15%, LV end-diastolic volume (LVEDV) ≥10%, and LVEF ≥5%, the number of subjects with improvement of KCCQ Summary Score ≥5 points, and improvement of 1 or more NYHA class. All-cause mortality, cardiac mortality, and HF hospitalizations were also captured.

Statistical analysis
Categorical data were summarized as the proportion of subjects exhibiting the endpoint of interest. Continuous endpoints were summarized as a mean, standard deviation, and sample size. To compare performance values between preimplant (baseline) and follow-up intervals, a paired Student t test was used for normally distributed data and the Wilcoxon signed rank test was used for non-normally distributed data. A χ² test or a Fisher exact test (if the expected cell count was less than 5) were used for among-group comparison of categorical variables. A P value <.05 was considered indicative of statistical significance. Statistical calculations were performed using SAS®9.4 (SAS Institute, Cary, NC).

Results
Patients
Thirty-one patients underwent WiSE-CRT system implantation in the roll-in phase at 19 centers, including 15 in the United States, 1 in the United Kingdom, and 3 in Australia. One patient with NYHA class IV HF underwent heart transplantation after 1 month and was withdrawn from the study. Out of 30 remaining patients, 29 patients completed 6 months follow-up while 1 patient completed only clinical assessment remotely without TTE owing to COVID-19-related restrictions on nonessential testing.
Demographic and clinical characteristics for the 31 enrolled patients are shown in Table 1. Briefly, the mean age was 65.5 ± 10.6 years, and 18 (58.1%) were male. Approximately half of the patients (48.4%) had nonischemic cardiomyopathy. Nine (29%), 21 (67.7%), and 1 (3.2%) patients exhibited NYHA class II, III, and IV symptoms, respectively. The vast majority of patients were on angiotensin-converting enzyme inhibitor / angiotensin-receptor blocker / angiotensin receptor-neprilysin inhibitor (93.5% taking at least 1 of them) and beta blockers (96.8%).

Indications for CRT were (1) NYHA class II–IV, EF ≤35%, left bundle branch block (LBBB) QRS width ≥150 ms (class I) in 16 (51.6%), (2) NYHA class II–IV, EF ≤35%, LBBB QRS width of 130–150 ms (class IIa) in 7 (22.6%), and (3) NYHA class II–IV, EF ≤35%, non-LBBB QRS width ≥150 ms (class IIa) in 8 (25.8%), respectively. Fifteen (48.4%) patients had functional CRT system but the treatment attempt was unsuccessful in 13 (41.9%) and CS lead placement was turned off in 3 (9.7%) patients.

Baseline co-implant devices were dual-chamber pacemaker (n = 2, 6.5%), CRT pacemaker (n = 1, 3.2%), CRT defibrillator (n = 21, 67.7%), and dual-chamber defibrillator (n = 7, 22.5%).

Procedural details
General anesthesia was employed for 30 out of 31 transmitter/generator implantations and for 14 out of 31 LV electrode placements on the following day. Intravenous sedation and local anesthetics were used for the remaining procedure. Mean procedure times were 1.5 ± 0.5 hours for transmitter/battery implantation and 1.9 ± 0.7 hours for LV electrode placement, respectively. The LV electrode was successfully placed in all patients either via atrial transseptal approach (n = 5, 16.1%) or retrograde transaortic approach (n = 26, 83.9%). Preanchoring electrical testing was performed in 3.3 ± 2.9 sites per procedure. The final electrode location was recorded for 30 of 31 (96.8%) patients, including 6 (20%) basal lateral LV, 21 (70%) mid-lateral LV, and 3 (10%) apical inferior-lateral LV segment. The Q-LV was measured in 28 of 31 (90.3%) and the mean Q-LV interval was 131 ± 35 ms at the final electrode implant location. For achieving femoral arterial site hemostasis in 26 patients undergoing retrograde transaortic LV implantation, Perclose ProGlide (Abbott Laboratories, Chicago, IL) only, both Perclose ProGlide and Angio-Seal VIP (Terumo, Somerset, NJ), and manual compression were employed in 22 (84.6%), 1 (3.8%), and 3 (11.5%) patients, respectively.

Efficacy results
Fourteen (46.7%) patients demonstrated ≥1 NYHA class improvement, and the reminder of the patients had no changes in the NYHA class (Table 2). None reported worse symptoms. Significant improvements were observed in nearly all domains of KCCQ score (Table 3, Figure 2).
NYHA class at baseline and at 6 months (N = 30)

<table>
<thead>
<tr>
<th>NYHA class</th>
<th>Baseline</th>
<th>6 Months</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>0 (0.0%)</td>
<td>5 (16.7%)</td>
<td>.002</td>
</tr>
<tr>
<td>II</td>
<td>9 (30.0%)</td>
<td>16 (53.3%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>21 (70.0%)</td>
<td>9 (30.0%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
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</table>

111.1 ± 40.3 mL (P = .0004), and 185.4 ± 58.8 mL to 164.9 ± 50.6 mL (P = .0017), respectively (Figure 3). LVEF improved ≥5% in 12 (41.4%) patients while LVESV decreased ≥15% in 10 (34.5%) and LVEDV decreased ≥10% in 10 (34.5%) patients, respectively. There were no significant differences between patients with nonischemic cardiomyopathy (n = 15) and ischemic cardiomyopathy (n = 14) with regard to changes in LVEF, LVESV, and LVEDV. Data on LV pacing pulse delivery for every RV pacing pulse was available in 28 of 31 (90.3%) patients at 6 months, and the successful LV pacing delivery was 93.5% ± 10%.

Safety results
There were 3 (9.7%) type I complications adjudicated by the Clinical Events Committee, including intermittent loss of capture, embolization of inadequately anchored LV electrode, and wound infection. The first patient demonstrated LV capture in approximately 50%–60% of pacing despite multiple attempts to increase pacing capture. In the second patient, the electrode embolized to the right femoral artery and was successfully retrieved before a new electrode was successfully implanted. It was later determined that the electrode was incompletely anchored to the LV endocardium. The wound infection occurred 6 weeks postimplantation in the third patient, and was successfully treated with a course of oral clindamycin.

Additionally, there were 1 patient with iliac artery aneurysm and 5 patients with periprocedural cardiopulmonary events. These events are detailed in Table 4. There was no death or cardiac perforation.

Discussion
In this study, we analyzed efficacy and safety outcomes of 31 patients treated with the WiSE-CRT system during the roll-in phase of the SOLVE-CRT trial. We demonstrated a high success rate of LV endocardial electrode placement, improvement in NYHA class at 6 months for a majority of patients, and modest improvements in echocardiographic parameters of LV remodeling. There were no deaths or LV perforations associated with the procedure.

When conventional transvenous CS lead placement fails, alternative CRT delivery methods include surgical placement of an epicardial lead, and other novel endocardial pacing techniques. Surgical LV lead placement has an inherently higher morbidity and may be technically difficult in patients with prior sternotomy owing to pericardial adhesions. Once placed, however, surgical epicardial LV leads seem to have reasonable long-term performance. Endocardial LV pacing has several potential advantages over epicardial CS lead. First, LV endocardial pacing affords greater freedom of pacing site selection not constrained by the coronary venous anatomy or phrenic capture. Second, LV endocardial stimulation provides a more physiologic pattern of myocardial depolarization, similar to intrinsic endo-to-epicardial depolarization, and is thought to be less arrhythmogenic compared to LV epicardial stimulation.

Prior to the WiSE-CRT system, endocardial LV pacing techniques using a conventional transvenous lead via atrial transseptal, ventricular transseptal, and transapical approach were explored. The transvenous lead approach necessitates lifelong oral anticoagulation with warfarin. Most studies demonstrated significant improvements in LV remodeling and favorable clinical response to CRT; however, its procedural complexity and substantial long-term thromboembolic risk limit wider adoption. The ALSYNC (Alternate Site Cardiac Resynchronization) was the first multicenter trial of LV endocardial transvenous lead pacing (superior transvenous atrial transseptal approach), which enrolled 138 patients who either had a failed transvenous CS lead or had nonresponse to CRT. The procedure was successful in 118 of the 132 attempted cases (89%). The target prothrombin time–international normalized ratio was 2–4. At 6 months, LVESV reduction of ≥15% was observed in 55% while 35% of the patients demonstrated clinical improvement of NYHA class ≥1. During a mean 17-month follow-up, 5 strokes, 14 transient ischemic attack episodes, and 23 deaths were reported, highlighting the alarmingly high thromboembolic risk of traditional endocardial LV leads despite chronic warfarin use.

The WiSE-CRT system provides LV endocardial pacing therapy without the need for permanent oral anticoagulation. Prior nonrandomized studies from selective centers have shown high implant success and improvements in LV remodeling and HF symptoms. Auricchio et al reported 3 first-in-man implantation cases in 2013. The WiSE-CRT received European CE mark approval in 2015. The SELECT-LV (Safety and Performance of Electrodes Implanted in the Left Ventricle) trial prospectively enrolled 35 patients to receive the WiSE-CRT system. The procedure was successful in 34 patients (97.1%). At 6 months, 28 patients (84.8%) reported improved HF symptoms. Mean EF improved from 25.9% ± 6.4% to 33% ± 10.3% (P < .0001) and 21 (66%) demonstrated an increase in EF ≥5%. Acute (<24 hours) procedural complications were observed in 3 patients (VF, electrode embolization, femoral artery fistula). The patient who experienced inprocedural VF died 4 days later. One patient with chronic atrial fibrillation and subtherapeutic international normalized ratio on warfarin had a stroke.

Recently, Sieniewicz et al reported on a multicenter experience of the WiSE-CRT system implantation in the
Post Market Registry. Out of 90 enrolled patients, 85 patients (94.4%) achieved successful LV endocardial pacing. Of these, the LV electrode was placed via the retrograde aortic approach in 82 patients (91%). Acute (<24 hours) procedural complications were observed in 4 patients (4.4%), including 2 patients with cardiac tamponade, 1 with pneumothorax, and 1 with pleural effusion. The patient who developed LV perforation and cardiac tamponade intraoperatively died 4 days after. The most common complication was related to the femoral arterial access (n = 4). During the 6-month follow-up, 4 deaths, 1 stroke, and 1 episode of transient ventricular arrhythmia when a TTE probe was placed in an LV apical position were noted. In the last patient, it was later found that an LV electrode had been placed in the LV apex. Nonsustained ventricular arrhythmia stopped immediately after the probe was withdrawn, and the patient remained asymptomatic. Echocardiographic assessment was available in 43 patients at 6 months. Mean LVEF increased from 30.6% ± 8.9% at baseline to 37.0% ± 11.5% at 6 months (P < .0001) and LVESV reduction of ≥15% was observed in 58.1%.

In the present roll-in phase of the SOLVE-CRT study, despite no prior WiSE-CRT implantation experience in 19 participating sites, the LV endocardial electrode was successfully placed in all patients via either a retrograde transaortic approach or a transseptal approach with minimal risk despite inexperienced operators. Freedom from type I complications was achieved in 28 of 31 patients (90.3%). In this series, the most critical complication was embolization and subsequent retrieval of an unanchored electrode in the LV. Upon detailed review of the cine imaging, it was later concluded that the most common complication was related to the femoral arterial access (n = 4). During the 6-month follow-up, 4 deaths, 1 stroke, and 1 episode of transient ventricular arrhythmia when a TTE probe was placed in an LV apical position were noted. In the last patient, it was later found that an LV electrode had been placed in the LV apex. Nonsustained ventricular arrhythmia stopped immediately after the probe was withdrawn, and the patient remained asymptomatic. Echocardiographic assessment was available in 43 patients at 6 months. Mean LVEF increased from 30.6% ± 8.9% at baseline to 37.0% ± 11.5% at 6 months (P < .0001) and LVESV reduction of ≥15% was observed in 58.1%.

In the present roll-in phase of the SOLVE-CRT study, despite no prior WiSE-CRT implantation experience in 19 participating sites, the LV endocardial electrode was successfully placed in all patients via either a retrograde transaortic approach or a transseptal approach with minimal risk despite inexperienced operators. Freedom from type I complications was achieved in 28 of 31 patients (90.3%). In this series, the most critical complication was embolization and subsequent retrieval of an unanchored electrode in the LV. Upon detailed review of the cine imaging, it was later concluded that the

| Table 3 Kansas City Cardiomyopathy Questionnaire score at baseline and at 6 months |
|---------------------------------|------------------|------------------|-------------------|------------------|
| KCCQ category (number of patients) | Baseline, mean ± SD (min, max) | 6-Month FU, mean ± SD (min, max) | [6 month − baseline], mean ± SD (min, max) | Paired t test P value |
| Physical limitation score (n = 26) | 55.3 ± 26.6 [0.0, 100.0] | 69.4 ± 20.8 [29.2, 100.0] | 14.2 ± 26.3 [-29.2, 55.0] | .0111* |
| Symptom stability score (n = 28) | 44.6 ± 17.2 [0.0, 75.0] | 55.4 ± 21.9 [25.0, 100.0] | 10.7 ± 32.9 [-50.0, 75.0] | .0966 |
| Symptom frequency score (n = 28) | 59.6 ± 19.1 [29.2, 100.0] | 76.5 ± 19.7 [29.2, 100.0] | 16.9 ± 18.3 [-18.7, 54.1] | <.0001* |
| Symptom burden score (n = 28) | 61.9 ± 18.8 [25.0, 100.0] | 79.2 ± 18.8 [33.3, 100.0] | 17.3 ± 24.5 [-33.4, 66.7] | .0009* |
| Total symptom score (n = 28) | 60.8 ± 16.9 [28.1, 100.0] | 77.8 ± 18.3 [38.5, 100.0] | 17.1 ± 19.9 [-26.0, 52.1] | .0001* |
| Self-efficacy score (n = 28) | 88.8 ± 13.3 [62.5, 100.0] | 92.0 ± 14.1 [37.5, 100.0] | 3.1 ± 13.9 [-37.5, 25.0] | .2436 |
| Quality-of-life score (n = 28) | 43.7 ± 22.2 [8.3, 100.0] | 70.5 ± 21.1 [16.7, 100.0] | 26.8 ± 26.3 [-41.6, 66.7] | <.0001* |
| Social limitation (n = 27) | 45.3 ± 24.0 [0.0, 91.7] | 70.0 ± 24.2 [25.0, 100.0] | 24.7 ± 34.3 [-62.5, 83.3] | .0009* |
| Clinical summary (n = 28) | 57.8 ± 18.7 [20.3, 100.0] | 73.2 ± 18.9 [38.0, 100.0] | 15.4 ± 21.8 [-27.6, 53.1] | .0009* |
| Overall summary (n = 28) | 51.6 ± 18.9 [20.6, 100.0] | 71.9 ± 18.3 [29.4, 100.0] | 20.4 ± 23.0 [-31.8, 53.9] | <.0001* |

*Statistically significant P value.

FU = follow-up; KCCQ = Kansas City Cardiomyopathy Questionnaire.
electrode needle was not fully anchored, evidenced by the presence of contrast material between the anchoring needle and the LV myocardium. The second electrode was successfully deployed with satisfactory electrical parameters.6

It should also be noted that there were 5 (16.1%) non–type I cardiopulmonary complications related to the procedure. Two complications were directly related to underlying congestive HF, highlighting the tenuous volume status of this cohort. It is reassuring to note that there was no cardiac tamponade or death related to the procedure in this study. Cardiac perforation is one of the most serious complications associated with WiSE-CRT implantation and has been observed in prior studies.21,23 The improved design of the delivery system (a balloon-tipped catheter) and meticulous operator training emphasizing atraumatic engagement of the catheter tip to the endocardium likely contributed to the absence of cardiac perforation in the present study.

Notably, 47% of patients demonstrated NYHA class improvement, and the observed echocardiographic improvements were comparable to the findings in the prior studies.26 As shown in Table 3, scores improved by 10–25 points in most domains, consistent with clinically significant changes.

Table 4 Device- or procedure-related adverse events

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device-related (type I) acute complications</td>
<td></td>
</tr>
<tr>
<td>Intermittent loss of capture</td>
<td>1</td>
</tr>
<tr>
<td>LV electrode embolization</td>
<td>1</td>
</tr>
<tr>
<td>Device-related (type I) subacute complication</td>
<td>1</td>
</tr>
<tr>
<td>Wound infection (6 weeks postimplant) treated with oral antibiotics</td>
<td></td>
</tr>
<tr>
<td>Procedure-related</td>
<td></td>
</tr>
<tr>
<td>Iliac artery aneurysm</td>
<td>1</td>
</tr>
<tr>
<td>Hypotension treated with IV fluid, subsequently treated with IV diuresis</td>
<td>1</td>
</tr>
<tr>
<td>Acute CHF, treated with IV diuresis</td>
<td>1</td>
</tr>
<tr>
<td>Urosepsis, treated with IV and oral antibiotics</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory suppression related to pain medication, treated with BiPAP</td>
<td>1</td>
</tr>
<tr>
<td>VT triggered by crossing the aortic valve with delivery catheter, treated with cardioversion</td>
<td>1</td>
</tr>
</tbody>
</table>

CHF = congestive heart failure; BiPAP = bilevel positive airway pressure; IV = intravenous; LV = left ventricular; VT = ventricular tachycardia.
symptomatic improvements are not a reliable indicator of treatment efficacy owing to potential placebo effects. A marked placebo effect was consistently observed in the control arm of prior pivotal CRT trials. This is particularly relevant, as all patients in this cohort underwent placement of the “investigational” device and were aware that the device was turned on. Follow-up duration is rather short (6 months), and long-term device performance (effective LV capture, battery longevity) and clinical outcomes were not ascertained in this analysis. The number of patients who were screened out owing to inadequate acoustic window during the roll-in phase is unavailable. In the SELECT-LV study, 7.7% of the enrolled patients did not have adequate acoustic window, and did not undergo implantation attempt. In this study, 48% of the participants received the device on the basis of “CRT nonresponse.” There is no uniform consensus on the definition of the nonresponse status, and this group of patients may be markedly heterogeneous and inherently differ from the patients previously untreated with CS lead.

**Conclusion**

We demonstrated a high success rate of LV endocardial electrode placement in centers with no prior implanting experience. Favorable clinical responses in HF symptoms and significant LV reverse remodeling were noted. No procedure-related death or cardiac tamponade was observed in this analysis.

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