Endocardial left ventricular pacing across the interventricular septum for cardiac resynchronization therapy: Clinical results of a pilot study

Q7 James H.P. Gamble, BMBCh, MRCP, Neil Herring, DPhil, FHRS, Matthew R. Ginks, MD, MRCP, Kim Rajappan, MD, MRCP, Yaver Bashir, DM, FRCP, Tim R. Betts, MD, FRCP

From the Oxford Heart Centre, John Radcliffe Hospital, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom.

BACKGROUND Cardiac resynchronization therapy (CRT) is an effective treatment for selected patients with heart failure, but it can be limited by the inability to place the left ventricular (LV) lead via the coronary sinus.

OBJECTIVE The purpose of this study was to develop an alternative approach, placing the LV lead endocardially via an interventricular septal puncture, and to assess the feasibility and safety of this technique.

METHODS All patients were anticoagulated with warfarin (international normalized ratio 2.5–3.5). A superior approach ventricular transseptal puncture using radiofrequency energy was performed. An active fixation pacing lead was delivered to the mapped site of latest electrical activation on the endocardial LV.

RESULTS Twenty patients were recruited, 15 with failed transvenous LV lead placement and 5 nonresponders to CRT. Mean (± SD) age was 67 ± 12, with 80% male, QRS duration 157 ± 14 ms, ischemic etiology 45%, New York Heart Association functional class 2.9 ± 0.4, and LV ejection fraction 28% ± 7%. The procedure was successful in all, with no serious complications. Clinical composite score improved at 6 months in 65% and worsened in 35%. LV ejection fraction improved >5% in 88%, from 28% ± 7% to 41% ± 9%. Six-minute walking distance improved >10% in 64%, from 248 ± 125 m to 316 ± 109 m. One patient suffered a lacunar ischemic stroke after 5 months with partial neurological recovery, associated with labile international normalized ratios. After 2.0 ± 1.0 years of follow-up, 3 patients died (2 pneumonia, 1 heart failure), and 2 patients suffered transient ischemic attacks.

CONCLUSION LV endocardial pacing via interventricular septal puncture in patients for whom standard CRT is not possible is similarly effective and durable, with significant but potentially acceptable risks.

KEYWORDS Cardiac resynchronization therapy; Heart failure; Left ventricular endocardial pacing; Left ventricular pacing site; Pacing lead

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Introduction

Cardiac resynchronization therapy (CRT) has been shown to decrease both hospitalizations and mortality and to improve symptoms and quality of life in patients with impaired systolic function and prolonged QRS duration on the electrocardiogram (ECG).[1] Placement of the left ventricular (LV) lead via the coronary sinus (CS) can be challenging due to adverse CS anatomy or procedural complications.[2] A meta-analysis including 164 studies of LV lead implantation has shown a contemporary rate of failure to place an LV lead of 2.4% (95% confidence interval 1.9–3%).[3] LV lead revision is needed in 5.7 patients per 100 patient-years, although this is more often early postimplant.[3] Replacement of chronic LV leads is not feasible via the CS in at least 20% of cases.[4]

The most established alternative to LV lead placement via the CS is surgical epicardial lead placement, which is limited by an acute and possibly long-term increase in adverse outcomes,[5,6] as well as concern about lead failure rates.[7]

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Furthermore, access to the posterolateral basal LV, where leads are optimal in most patients, is relatively difficult, and leads are often placed anteriorly.[8]

The alternative is endocardial LV pacing. The atrial transseptal approach to LV endocardial pacing was initially described in 1998 and has undergone multiple modifications, but it has remained complex, usually requiring a combined femoral and superior approach to puncture the atrial septum and deliver a lead.[9] Several studies have reported results on small numbers of patients with relatively limited follow-up. The ALSYNC (ALternate Site Cardiac ResYNChronization) study reported results of this route in a larger 138 patient cohort.[10] These techniques are complex, leave lead material in the low-pressure left atrial chamber where lead thrombi are more likely to form,[11] and may expose the mitral valve to damage or insufficiency.[9]

Despite the limitations of current techniques, a developing body of evidence suggests that endocardial LV pacing may have hemodynamic benefits over epicardial pacing via the CS.[9,12,13] Endocardial pacing has also been shown to produce less dispersion of repolarization than epicardial stimulation, which may reduce arrhythmic risk.[14]

Endocardial LV pacing procedures are likely to be associated with higher risk than conventional lead placement via the CS because of the increased complexity and the necessary presence of artificial material in the LV cavity. The latter exposes patients to the potential risk of thrombotic embolization and in particular stroke; therefore, all previous LV endocardial pacing trials have used oral anticoagulation with warfarin, which carries an additional risk associated with bleeding.

We have developed an alternative route, placing the LV lead endocardially through an interventricular septal puncture.[15,16] We now report the results of a formal pilot study assessing this technique.

Methods

The study was approved by the local Research Ethics Committee and is registered at ClinicalTrials.gov (Identifier: NCT01818765). The study included adults who satisfied the European Society of Cardiology criteria for CRT[17] who had a failed attempt(s) at placing an LV epicardial lead via the conventional CS route and in whom the treating clinicians had assessed that a viable lead could not be placed via this route using available technology. The risks and benefits of surgical epicardial vs transvenous endocardial lead placement, including the use of lifelong oral anticoagulation, was discussed with all potential patients.

In addition, we recruited nonresponders to conventional CRT (nonresponse defined as no improvement in New York Heart Association (NYHA) functional class and a <15% reduction in end-systolic or end-diastolic volume on echocardiography at 6 months), with nonoptimal LV lead position (defined as an LV lead position outside the anterolateral, lateral, or posterolateral basal and midventricular segments), and without other evident reasons for nonresponse. All patients were carefully assessed for their suitability for long-term warfarin therapy and were commenced on warfarin if they were not already receiving anticoagulation therapy, at least 1 month before the procedure to allow stability.

Clinical follow-up

Our primary objective was to investigate whether LV endocardial pacing via the transventricular septal route is safe and feasible. Accordingly, our primary endpoint was freedom from adverse effects at 6 months postprocedure. As a secondary endpoint, we assessed response to CRT using the Packer clinical composite score (CCS), which categorizes heart failure patients as improved, unchanged, or worsened, categorizing all patients who die or are hospitalized as worsened.[18] In addition, we used the NYHA functional class, the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L) quality-of-life score, and the 6-minute walk test to assess clinical response. Echocardiographic response was assessed with 2-dimensional echocardiography at baseline and 6 months by an accredited echocardiographer and defined as a >5% absolute increase in LV ejection fraction (EF) and >15% relative decrease in LV end-systolic volume.

Patients were followed-up in person at 3 months and 6 months and then up to 2 years telephonically. All comparisons were made between the baseline and 6-month assessments, using the Wilcoxon signed-rank test for nonparametric variables such as NYHA functional class and EQ-5D-5L scores, and paired *t* tests for the other normally distributed continuous variables.

Procedural methods

We have previously described our implant technique.[15] All procedures were performed with the patient under general anesthesia with continuation of warfarin (international normalized ratio [INR] 2–3). We gained access via the subclavian/axillary vein, and a steerable sheath (Agilis, St. Jude Medical, MN) was guided by left ventriculography Q1 to position the straight end of a standard 0.035-inch guidewire against the interventricular septum. Radiofrequency energy was applied using a surgical diathermy pen to the wire, and the septum was punctured. The dilator and sheath were then passed into the LV, and intravenous heparin was given.

A decapolar catheter (Enquiry, St. Jude Medical) and the NavX electroanatomic mapping system (St. Jude Medical) were used to produce an endocardial LV geometry and activation map during right ventricular (RV) pacing to locate the site of latest electrical activation, which was the latest activated area without low activation amplitudes suggesting scar.

The sheath was exchanged for a splitable, steerable sheath (SelectSecure, Medtronic, Minneapolis, MN) and used to deliver a pacing lead to the site of late electrical activation. Standard active fixation 6Fr pacing leads (Medtronic 5076) and the lumenless 4.1Fr lead (SelectSecure, Medtronic) were used. All patients were anticoagulated (INR 2.5–3.5) after the procedure.