# Reverse ventricular remodeling and long-term survival in patients undergoing cardiac resynchronization with surgically versus percutaneously placed left ventricular pacing leads

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**BACKGROUND** A minority of patients undergoing cardiac resynchronization therapy (CRT) use a surgically placed epicardial left ventricular (SPELV) pacing lead. Previous studies of outcomes in patients receiving such leads have been limited to small cohorts with limited follow-up.

**OBJECTIVE** We sought to compare outcomes between patients receiving SPELV pacing leads and patients with traditional percutaneously placed left ventricular (LV) leads.

**METHODS** We extracted clinical data on consecutive patients undergoing the new implantation of a cardiac resynchronization device. Long-term survival and response (defined as an improvement in LV ejection fraction of $\geq$5%) were compared between the 2 groups.

**RESULTS** Between September 3, 2003, and August 6, 2007, 725 patients met inclusion criteria, of whom 96 (13.2%) had an SPELV pacing lead. Over a mean follow-up of 5.1 $\pm$ 2.5 years, there were 310 deaths, 17 heart transplants, and 15 left ventricular assist device placements (342 total end points). In univariate analysis, there was no difference in outcomes between patients with an SPELV pacing lead and patients with a percutaneously placed LV lead both early at 6 months (log rank, $P = .53$) and over a mean follow-up of 5.1 years (log rank, $P = .58$). In multivariate analysis, survival free of left ventricular assist device or heart transplant was similar in patients regardless of lead placement status ($P = .89$). From a subcohort of 455 patients, 297 patients (65.3%) met criteria for response. In multivariate analysis, there was no difference in the rate of response based on lead placement modality.

**CONCLUSION** Patients undergoing epicardial LV lead placement using a surgical approach have outcomes and rates of reverse ventricular remodeling similar to those in patients undergoing LV lead placement using a percutaneous approach.

**KEYWORDS** Surgically placed left ventricular pacing lead; Cardiac resynchronization therapy; Survival; Reverse ventricular remodeling

**ABBREVIATIONS** **CRT** = cardiac resynchronization therapy; **CS** = coronary sinus; **LV** = left ventricular; **LVAD** = left ventricular assist device; **LVEF** = left ventricular ejection fraction; **SPELV** = surgically placed epicardial left ventricular

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## Introduction

Cardiac resynchronization therapy (CRT) is one of the biggest advances in the treatment of advanced heart failure in the past 15 years.[1–4] In the large majority of patients, left ventricular (LV) lead placement is performed using a percutaneous approach. In a minority of patients, however, percutaneous lead placement is not possible because of various factors including challenging coronary sinus (CS) anatomy, unacceptable pacing thresholds, and phrenic nerve stimulation. While percutaneous implantation techniques have improved, in the MADIT-CRT trial: the cardiac-resynchronization therapy for the prevention of heart-failure events trial published in 2009,

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7.5% of patients randomized to the cardiac resynchronization therapy–defibrillator arm received an implantable cardioverter-defibrillator–only device owing to technical problems with CS lead implantation.[3] In patients in whom percutaneous CS lead placement is not possible, a surgically placed epicardial left ventricular (SPELV) pacing lead represents a viable alternative.[5–14] In other patients undergoing a concomitant cardiac surgical procedure, an epicardial LV lead is sometimes placed during the surgery in anticipation of possible future need for CRT. On one hand, surgical placement of an epicardial LV lead offers the advantage of optimal lead positioning typically along the lateral or posterolateral wall. Optimal lead positioning has been shown to improve CRT efficacy.[15] On the other hand, surgical epicardial lead placement involves an invasive surgical procedure, and the long-term durability of epicardially placed leads is uncertain. In terms of outcomes, the current literature[6,12] suggests a trend toward worsened outcomes in patients receiving SPELV pacing leads compared with patients with traditional percutaneously placed leads. These studies, however, have been limited to a small series that have been unable to control for multiple potential confounders and had relatively brief follow-up times. We sought to compare improvements in left ventricular ejection fraction (LVEF) and survival between patients receiving SPELV pacing leads and patients with traditional percutaneously placed CS leads by taking into account multiple possible confounders.

## Methods

This retrospective study involved the analysis of a consecutive cohort of patients who underwent the new implantation of a CRT device at the Cleveland Clinic, Cleveland, OH, between September 3, 2003, and August 6, 2007. The study was approved by the Institutional Review Board of the Cleveland Clinic for retrospective medical record review and performed according to institutional guidelines. Clinical, electrocardiographic, and echocardiographic data were gathered via chart reviews. For inclusion in the final cohort, all patients had an LVEF of $\leq$35% and a QRS duration of $\geq$120 ms. Patients lacking a valid US social security number were excluded. An assessment of mortality was made using the United States Social Security Death Index searched in August 2012. The subsequent left ventricular assist device (LVAD) placement or heart transplant was assessed using the current Cleveland Clinic advanced heart failure therapy registry data. Both short- and long-term survival were compared between patients undergoing surgical epicardial LV lead placement and those undergoing percutaneous lead placement. A multivariate model was constructed to compare outcomes based on lead placement status, accounting for many possible confounders. Patients with available follow-up echocardiograms at least 3 months post-CRT implantation were then analyzed separately and divided into responders and nonresponders. Response was defined as an absolute improvement in LVEF of $\geq$5%. The association between response and surgical LV lead placement was assessed in multivariate analysis.

### CRT device implantation and management

In the cohort as a whole, CRT device implantations were performed transvenously in the vast majority of patients by electrophysiologists targeting a lateral or posterolateral vein for the LV lead position. In instances when a transvenous lead could not be placed owing to technical problems with the procedure, a minimally invasive epicardial lead via a mini-thoracotomy was placed by a staff cardiothoracic surgeon. Alternatively, in the surgical LV lead cohort, LV lead placement was performed at the time of a concomitant cardiac surgical procedure in anticipation of need for CRT in the future. In these patients, the LV lead was hooked up along with the placement of a right ventricular lead and, commonly, an atrial lead either by a cardiothoracic surgeon on the same date or by an electrophysiologist at a later date. CRT devices were commonly programmed with an atrioventricular sensed delay of 100 ms and a paced delay of 130 ms, with optimization performed according to the standard protocols of the Cleveland Clinic. Medications were recorded immediately before the implantation of the CRT device, with subsequent titration of medications made at the discretion of patients' outpatient physicians.

### Statistical analysis

Continuous variables were presented as a mean $\pm$ SD and dichotomous variables as an absolute number and percentage. Comparisons between continuous variables were made using the Student *t* test for parametric variables and a Mann-Whitney test for nonparametric variables. Dichotomous variables were compared using the Fisher exact test. Kaplan-Meier curves were constructed using the log-rank test to assess mortality at 6 months and over the mean follow-up period (5.1 years). A multivariate Cox proportional hazards regression model was constructed to compare survival free of LVAD or heart transplant between patients on the basis of epicardial vs percutaneous LV lead placement status over the follow-up period. Baseline differences between patients based on LV lead placement status with $P < .1$ were entered into the model. In addition, multiple known factors were entered into the model on the basis of a priori knowledge. Missing data, which were uncommon, were handled via "letting the model float." Data with tied failure times were handled via the method proposed by Efron et al.[16] To test the Cox assumption that the hazard ratio between individuals is constant, a time-varying covariate was entered into the model for each variable, with a $P$ value of $>.05$ needed to satisfy this assumption. The cohort with available follow-up echocardiograms was then subdivided on the basis of response. A multivariate logistic regression model was constructed to assess the association between surgical epicardial lead