Journal of Geriatric Cardiology (2017) 14: 261–265

Research Article **· Open Access ·**

Transvenous versus open chest lead placement for resynchronization therapy in patients with heart failure: comparison of ventricular electromechanical synchronicity

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Abstract

Background Transvenous lead placement is the standard approach for left ventricular (LV) pacing in cardiac resynchronization therapy (CRT), while the open chest access epicardial lead placement is currently the most frequently used second choice. Our study aimed to compare the ventricular electromechanical synchronicity in patients with heart failure after CRT with these two different LV pacing techniques. **Methods** We enrolled 33 consecutive patients with refractory heart failure secondly to dilated cardiomyopathy who were eligible for CRT in this study. Nineteen patients received transvenous (TV group) while 14 received open chest (OP group) LV lead pacing. Intra- and inter-ventricular electromechanical synchronicity was assessed by tissue Doppler imaging (TDI) before and one year after CRT procedure. **Results** Before CRT procedure, the mean QRS-duration, maximum time difference to systolic peak velocity among 12 left ventricle segments (LV Ts-12), standard deviation of time difference to systolic peak velocity of 12 left ventricle segments (LV Ts-SD), and inter-ventricular mechanical delay (IVMD) in OP and TV group were 166 ± 17 ms and 170 ± 21 ms, 391 ± 42 ms and 397 ± 36 ms, 144 ± 30 ms and 148 ± 22 ms, 58 ± 25 ms and 60 ± 36 ms, respectively (all $P > 0.05$). At one year after the CRT, the mean QRS-duration, LV Ts-12, LV Ts-SD, and IVMD in TV and OP group were 128 ± 14 ms and 141 ± 22 ms ($P = 0.031$), 136 ± 37 ms and 294 ± 119 ms ($P = 0.023$), 50 ± 22 ms and 96 ± 34 ms ($P = 0.015$), 27 ± 11 ms and 27 ± 26 ms ($P = 0.86$), respectively. The LV lead implantation procedure time was 53.4 ± 16.3 min for OP group and 136 ± 35.1 min for TV group ($P = 0.016$). The mean LV pacing threshold increased significantly from 1.7 ± 0.6 V/0.5 ms to 2.3 ± 1.6 V/0.5 ms ($P < 0.05$) in TV group while it remained stable in the OP group. **Conclusions** Compared to conventional endovascular approach, open chest access of LV pacing for CRT leads to better improvement of the intraventricular synchronization.

J Geriatr Cardiol 2017; 14: 261–265. doi:10.11909/j.issn.1671-5411.2017.04.001

Keywords: Heart failure; Resynchronization; Tissue Doppler imaging

1 Introduction

Cardiac resynchronization therapy (CRT) has been proved to be an effective treatment for patients with heart failure (HF) and a wide QRS complex.[1,2] In 2014, the number of CRT implantations in the mainland of China was 2379. With economic development and increased acceptance both by patients and physicians, this number is expected to be increasing rapidly during the coming years.[3] Restoring the synchronicity of the atrioventricular, interventricular, and intraventricular contractions by permanent pacing of the left ventricle (LV) wall is the primary underlying mechanism of the beneficial effects of CRT.[4] Currently, transvenous insertion of the lead through a side branch of the coronary sinus (CS) is the standard approach of LV pacing. Unfortunately, due to reasons such as venous anatomy, phrenic nerve stimulation, high stimulation thresholds and instability of the lead, transvenous implantation of LV lead has been reported unsuccessful in up to 10% of patients.[5,6] In this case, the open chest access epicardial lead placement by either thoracotomy or video-assisted thoracoscopy (VAT) is often used as a second choice. In the present study, we compared the effects of conventional in-

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Received: February 16, 2016 **Revised:** January 24, 2017
Accepted: January 28, 2017 **Published online:** April 28, 2017

travenous lead placement with open chest access epicardial lead placement of LV pacing on ventricular electromechanical synchronicity for CRT

2 Methods

2.1 Study patients

Between April 2007 and June 2009, we enrolled 33 consecutive patients who underwent CRT at the Beijing Anzhen Hospital in China into this prospective, non-randomized clinical study. The including criteria were the following: (1) the primary cause of heart failure is dilated cardiomyopathy; (2) patient with New York Heart Association (NYHA) Class Ⅲ/Ⅳ despite optimal pharmacologic treatment; (3) with left bundle branch block and/or QRS complex > 130 ms; (4) with sinus rhythm; and (5) with LV ejection fraction (LVEF) < 35%. Patients with ischemic cardiomyopathy were excluded. The choice of intravenous or open chest access epicardial lead placement of LV pacing was made by patient preference after detailed explanation of both procedures by treating physicians. Twenty one patients preferred intravenous access but two failed and finally received open chest LV lead placement. Informed consent was obtained from all participated patients. The study was approved by the local ethic committee.

2.2 Transvenous lead placement

Transvenous LV lead implantation was performed in the electrophysiology laboratory. The CS lead (Model 4193, Medtronic Inc., Minneapolis, USA) was introduced under fluoroscopic guidance using the standard technique through the left subclavian vein. If lateral epicardial veins were not accessible, or if pacing thresholds were unacceptably high (> 3.5 V/0.5 ms), another branch was chosen. The right ventricular pacing lead was placed into the apex or septum. The LV lead placement was guided by an intra-operative CS occlusive venogram. The left anterior oblique projection was used to assess whether the lead was positioned in a septal, anterior, anterolateral, lateral, posterolateral, or posterior location; the right anterior oblique projection was used to assess whether the lead was positioned at the base, mid, or apical portion of the LV.

2.3 Open chest lead placement

Open chest surgical lead placement was performed in a specially designed hybrid operation room. LV epicardial lead was implanted with minimally invasive surgery. The procedure was done under general anesthetic and with standard monitoring of EKG and pulse oximetry. After the patient was placed in the right decubitus lateral position at 60°, the surgical fields were sterilized. One 1–1.5 cm long incisions was made at the seventh left intercostal space at the posterior axillary line to introduce the thoracoscopy (standard 30°) video camera. A 3 cm incision was made at the fifth intercostal space after collapsing the left lung. Pericardium was then opened and suspended after the identification of the phrenic nerve. Once the lateral wall of the LV was exposed and the marginal arteries identified, a unipolar epicardial lead (Capsure-Epi Models 4965, Medtronic Inc., Minneapolis, USA) was fixed by 4–0 prolene sutures with thoracoscopy assistance. After taking threshold measurements, the proximal tip of the lead was directed into the exterior of the thorax through the anterior thoracoscopy opening living a 20 cm segment into the thoracic cavity to avoid traction from lung expansion. Then it was advanced through the subcutaneous tissue up to the left subclavicular region with the assistance of a rigid guide (Medtronic Inc., Minneapolis, USA). Next, the incision was closed with sutures and another thoracoscopy hole was used to introduce a pleural drain. Then, the patient was placed in the supine position and the subclavian area was sterilized. The intravenous bipolar lead (Model 4074/4574, Medtronic Inc., Minneapolis, USA) was introduced into the right ventricle and right atrium under fluoroscopic guidance using the standard technique. The pocket of the pacemaker was made and the three chamber permanent pacemaker (Model InSync-8042, Medtronic Inc., Minneapolis, USA) was connected with the three leads individually. After the threshold and sensitivity were tested the pocket was closed with sutures.

2.4 Assessment of ventricular electromechanical synchronicity by tissue Doppler imaging (TDI)

Ventricular electromechanical synchronicity was assessed by standard echocardiography (System Vivid 5, Vingmed-General Electric), including Doppler studies as previously described by Yu, *et al*.[7] Briefly, at least three consecutive beats were stored, and the images were analyzed offline with the aid of a customized software package (EchoPac 6.3.6, Vingmed-General Electric). The peak myocardial velocity during the ejection phase (Sm) and the time to peak Sm (Ts) were measured with reference to QRS complex. Standard deviation of time difference to systolic peak velocity of 12 left ventricle segments (LV Ts-SD), and maximum time difference to systolic peak velocity among 12 left ventricle segments (LV Ts-12) were calculated from 12 segments measurements. Inter-ventricular mechanical delay (IVMD) was calculated using aorta and pulmonary artery pre-ejection time (time from the QRS start to the aorta and pulmonary artery flow spectrum start, respectively).

2.5 Patient follow-up

After CRT, all patients were treated with diuretics, angiotensin-converting enzyme inhibitor (ACEI) or angiotensin-2 receptor antagonists (ARA II), beta-blockers, and digitalis. Postoperative follow-up was done on an outpatient basis, with TDI, electrocardiography and X-ray every three months.

2.6 Statistics

Categorical variables are presented as frequency and percentage. Continuous variables are presented as mean ± SD. Categorical variables were compared with χ^2 test, and continuous variables were compared with Student t test. All statistical analyses were performed using SPSS version 19.0 (IBM, Chicago, IL).

3 Results

3.1 Clinical characteristics of study patients

The demographics and clinical characteristics of the patients at baseline are listed in Table 1. Patients in the transvenous and open chest LV lead groups were similar with respect to age, gender, LVEF, NYHA class, QRS duration, and use of medications. More than 90% patients of each group were treated with diuretics, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and beta-blocker therapy.

3.2 Baseline and post-CRE ventricular electromechanical synchronicity

As shown in Table 2, there were no significant differences regarding the TDI assessed ventricular a synchronicity indexes between TV and OP group at baseline. In patients of both groups, interventricular and intraventricular synchronicity improved significantly. However, compared with patients of the TV group, LV Ts-12 and LV Ts-SD decreased much more significantly both immediately after CRT (data not shown) and at one-year follow-up. One year after CRT, the mean LV Ts-12, LV Ts-SD in TV and OP group were 136 ± 37 ms and 294 ± 119 ms (P = 0.023) and 50 ± 22 ms and 96 ± 34 ms (P = 0.015), respectively, whereas the decrease of IVMD was similar between TV and OP groups.

3.3 Procedure and follow-up outcomes

The mean procedure duration (skin to skin) of the LV lead implantation was 53.4 ± 16.3 min for OP group and 136 ± 35.1 min for the TV group (P < 0.05). There was no surgical or hospital mortality in the entire series. One patient in the TV group developed pocket infection and one patient in the TV group had pneumonia during hospitalization. The mean postoperative stay was relatively longer for the OP group than the CS-lead group (7.4 ± 3.2 *vs*. 5.2 ± 2.8 days, P < 0.05). QRS-duration decreased from 163 ± 22 to 128 ± 14 ms in the OP group and from 167 ± 19 to 141 ± 22 ms in the TV group. The mean intra-operative pacing threshold of the LV lead was 1.25 ± 0.8 V in the OP group and 1.75 ± 0.6 V in the TV group at 0.5 ms (P < 0.05). During one-year follow up, the mean left ventricle end-diastolic diameter (LVEDD) decreased from baseline of 71.3 ± 9.8 mm to 67.3 ± 9.5 mm, and the mean LVEF increased from 28.1% ± 7.7% to 33.0% ± 7.6% in the TV group, while in the OP

Table 1. Baseline clinical characteristics of study patients.

	TV group (n = 19)	OP group (n = 14)	P value
Age, yrs	62 ± 8	64 ± 10	0.72
Gender (male/female)	11/8	9/5	0.68
LVEF, %	33.0 ± 0.8	32 ± 0.7	0.84
LVEDD, mm	67.3 ± 9.5	70.3 ± 12.8	0.59
NYHA class	3.2 ± 0.2	3.2 ± 0.3	0.86
QRS duration, ms	167 ± 19	163 ± 22	0.78
Use of diuretics, %	95	93	-
Use of ACEI or ARB, %	100	100	-
Use of beta-blocker	100	100	-

Data were presented as meam ± SD or otherwise indicated. ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; LVEDD: left ventricle end-diastolic diameter; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; OP: open chest lead placement of left ventricular pacing; TV: introvenous lead placement of left ventricular pacing.

Table 2. Baseline and post-CRT ventricular electromechanical synchronicity of the 2 + 8 study groups.

	TV group (n = 19)			OP group (n = 14)		
	Baseline	Post-CRT	P value	Baseline	Post-CRT	P value
LV Ts-12, ms	397 ± 36	294 ± 119	< 0.05	391 ± 42	136 ± 37	< 0.05
LV Ts-SD, ms	148 ± 22	96 ± 34	< 0.05	144 ± 30	50 ± 22	< 0.05
IVMD, ms	60 ± 36	27 ± 26	< 0.05	58 ± 25	27 ± 11	< 0.05

CRT: cardiac resynchronization therapy; IVMD: Inter-ventricular mechanical delay; LV: left ventricular; LV Ts-SD: standard deviation of time difference to systolic peak velocity of 12 left ventricle segments; LV Ts-12: maximum time difference to systolic peak velocity among 12 left ventricle segments; OP: open chest lead placement of LV pacing; TV: introvenous lead placement of LV pacing.

group, the respective changes were 70.3 ± 12.8 mm to 62.3 ± 6.5 mm and 28.1% ± 7.7% to 33.0% ± 7.6%. Comparisons of either LVEDD or LVEF changes between TV and OP group showed no statically significant differences.

One patient in the TV but none in the OP group died. One patient in OP group and two patients in TV group were re-admitted because of worsening heart failure. The mean LV pacing threshold increased significantly from 1.7 ± 0.6 V/0.5 ms to 2.3 ± 1.6 V/0.5 ms ($P < 0.05$) in TV group while it remained stable in the OP group.

4 Discussion

The major finding of our present study is that, compared with conventional endovascular approach through a side branch of the CS, open chest access with mini-thoracotomy LV lead implantation for CRT may leads to better improvement of the ventricular electrical synchronicity, as indicated by the greater decrease of QRS-duration, and better improvement of intraventricular synchronization, as indicated by the greater decrease of tissue Doppler indices for intraventricular synchronicity, including LV Ts-12 and LV Ts-SD. Our study also suggests that surgical epicardial lead implantation might have a more stable pacing threshold thanscoronary sinus lead implantation.

In clinical practice, the transvenous epicardial LV lead placement is currently recommended by almost all related guidelines as the standard first-line approach. However, with this technique, the final position of the LV pacing lead depends on the anatomy of the CS, therefore, the implantation at desired sites is not always possible. Furthermore, the transvenous LV lead placement has been reported to be unsuccessful in 5% to 10% of patients even in high volume centers,[5,6] due to reasons such as CS anatomy, the risk of late lead dislodgement, phrenic nerve stimulation, and the increasing threshold. In recent years, numerous techniques and technologies have been specifically developed to provide alternatives for the CS LV pacing,[8] but the open chest access epicardial lead placement by either thoracotomy (which actually is the first used approach for LV lead pacing) or VAT, remains the most frequently used second choice.

However, the clinical relevance of our findings should be interpreted with cautions. First, Several studies suggests a trend toward worsened outcomes in patients receiving open chest epicardial pacing compared with patients with traditional transvenous LV pacing placed leads;[9,10] Second, both Predictors of Response to CRT (PROSPECT) trial[11] and EchoCRT[12] study showed that even after validation by blinded core laboratories, no echocardiographic measure of dyssynchrony could reliably predict the response to CRT, and no current clinical guidelines recommends echocardiographic measures of dyssynchrony for selection of patient receiving CRT.[13,14] Actually, in our present study, despite the significantly better improved of ventricular synchronicity achieved by open access LV lead pacing as compared to transvenous LV pacing, we found similar clinical and echocardiographically assessed outcomes between the two groups.

In conclusion, our study showed that implantation of epicardial leads via minimally invasive video-assisted thoracoscopy is a safe and reliable procedure for CRT, and might lead to better improvement of the intraventricular synchronization as compared with conventional endovascular approach.

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