

Transseptal Leftventricular Endocardial Pacing is an Alternative Technique in Cardiac Resynchronization Therapy. One Year Experience in a High Volume Center

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Introduction. In patients receiving cardiac resynchronization therapy (CRT), failure rate to implant the left ventricular (LV) lead by the traditional trans-venous approach is 4-8%. Surgical epicardial implantation is considered as an alternative, but this technique is not without morbidity. Evidence from case documentation and from small trial batches demonstrated the viability of endocardial LV lead implantation where surgical epicardial lead placement is not applicable.

Material and Methods. Four patients were implanted with endocardial LV lead using the transeptal atrial approach after unsuccessful transvenous implantation. Implantation of an endocardial active fixation LV leads was successful in all patients with stable electrical parameters immediately after implantation and over the follow-up period. All patients received anticoagulation therapy in order to target the international normalized ratio of 2.5-3.5 and have not experienced any thromboembolic, hemorrhagic events, or infection.

Results. Follow-up echocardiography indicated significant improvement of LV systolic function ($24 + 4.9$ to $32 + 5.1$ %, $P = 0.023$) with a notable improvement of the functional status.

Conclusions. Endocardial left ventricular lead implantation can be a valuable and safe alternative technique to enable LV stimulation in high surgical risk patients where standard coronary sinus implant is unsuccessful.

Key words: biventricular pacing, transeptal lead, transeptal pacing, endocardial stimulation, cardiac resynchronization therapy.

INTRODUCTION

Cardiac resynchronization therapy (CRT), with atrio-biventricular pacing has been a tremendous advance in the treatment of symptomatic congestive heart failure patients presenting with severely impaired left ventricular function associated with ventricular dyssynchrony and intraventricular conduction disturbances [1-3]. The standard approach indicates the necessity for the implantation of an LV pacing lead transvenously into one of the tributary veins of the coronary sinus (CS). However, even with the improvement in dedicated devices and increased operator experience, failure to implant a CS lead has been reported in 4-8% of the cases [4, 5]. Unfavorable CS or vein anatomy, such as CS dissection, occlusion, or abnormal ostium of the CS or focal coronary vein stenosis are the most frequent reasons. Post-implant dislocation of the lead, high pacing threshold or phrenic nerve stimulation also diminishes the effectiveness of LV stimulation [6-8]. In cases of unsuccessful LV lead placement

through the CS, surgical epicardial lead implantation via a lateral thoracotomy or minimal-invasive thoracoscopy is considered the standard alternative method that requires general anesthesia [9-11]. In patients with advanced heart failure, this approach may be linked with a high morbidity and mortality. Endocardial LV lead placement through an atrial transeptal approach has been described previously as an alternative technique to provide CRT in cases where epicardial LV lead implantation is contraindicated or is at increased risk [12-18]. In the following paper we describe the technique that we used and the outcomes of the transeptal endocardial LV implant in patients for whom transvenous CS lead placement had failed and are not eligible for surgical epicardial implantation and have no contraindication for lifelong oral anticoagulation.

Patients

From October 2014 to October 2015, at the Electrophysiology and PM department of Semmelweis University Heart Center, four patients (3 males;

mean age 62.5 years) had undergone endocardial LV lead implantation where LV pacing could not be achieved via the coronary sinus despite the application of interventional techniques including venoplasty. Patients had New York Heart Association III to IV symptoms and had compelling indication for life long systemic anticoagulation. All patients had left bundle branch block (LBBB). Pre-implantation echocardiography revealed severely depressed LV function. Patient's characteristic features are listed in Table 1. Surgical lead implantation was

contraindicated in three patients because of a very high anesthetic and surgical risk. Patient 2 did not sign the consent for epicardial surgical LV lead implantation. In patients 1, 3 and 4, the CRT devices together with the right atrial and ventricular lead were implanted in the first procedure having the port of the LV lead sealed with an IS-1 plug. The transseptal LV lead implantation was performed on a later procedure. In patient 2 the transseptal LV lead implantation was implanted during the first procedure.

Table 1
Characteristic features of patients

Pt no.	Age	Gender	Etiology of cardiomyopathy	NYHA Functional Class	QRS (ms)	LVEF (%)	Follow-up months	MR grade before implantation (I-IV)	ACT before implantation
1	60	M	Ischemic	III	186	28	11	III	Yes (for AF)
2	45	M	non-ischemic	Iva	193	21	10	III	Yes (IVT)
3	70	M	non-ischemic	III-IV	205	27	7	III-IV	Yes (for AF)
4	75	F	Ischemic	III	210	24	6	III	Yes (for AF)

Pt, patient, NYHA, New York Heart Association Functional Class, LV, Left Ventricular, LVEF, Left Ventricular Ejection Fraction, MR, Mitral, regurgitation, ACT, Anticoagulation Therapy, IVT, Interventricular Thrombosis, AF, Atrial fibrillation

MATERIAL AND METHODS

The placement of the LV endocardial lead was done via a combined femoral and subclavian approach. The implantation starts with a standard transseptal puncture from the right femoral vein. The puncture was performed with the guidance of fluoroscopy and with continuous monitoring of the arterial pressure. Following the successful transseptal puncture, confirmed by the left atrial pressure curve, 5000 IU of intravenous heparin was administered. A guide wire (0.035 inch \times 260 cm) was advanced into one of the pulmonary veins and the dilator was removed and the sheath was withdrawn into the right atrium (Figure 1). An angioplasty balloon (8 mm \times 40 mm Fox Plus Abbott Vascular) was positioned across the septal puncture site and was inflated using contrast agent. In a CS guiding sheath a steerable electrophysiological catheter is advanced from the left subclavian area towards the septum of the right atrium. The balloon was deflated then it was withdrawn into the transseptal sheath and the guide wire was maintained in the left atrium (Figure 2). The steerable catheter is pushed on transseptally into the left atrium and then to the left ventricle. Maintaining the electrophysiological catheter in position the guiding sheath is advanced to the left atrium. In cases where the sheath did not advance through the site of the puncture, the angioplasty balloon was again placed at the puncture site and it was inflated and deflated as per the need

(Figure 3). When we identified the optimal pacing site, the electrophysiological catheter was withdrawn into the sheath and the sheath was pushed against the LV wall to ensure stable position. Subsequently, a standard active fixation bipolar lead was screwed into the desired location of the postero-lateral area of the left ventricle (Figure 4). After measuring the pacing and sensing thresholds, the guiding sheath had been removed using a longitudinal slit tool. Maintaining a sufficient slack in the lead, the proximal end was secured in the prepectoral region and connected to the CRT device. In all patients, the atrial lead has been implanted in the right atrial appendage and the right ventricular lead was placed in the right ventricular septum.

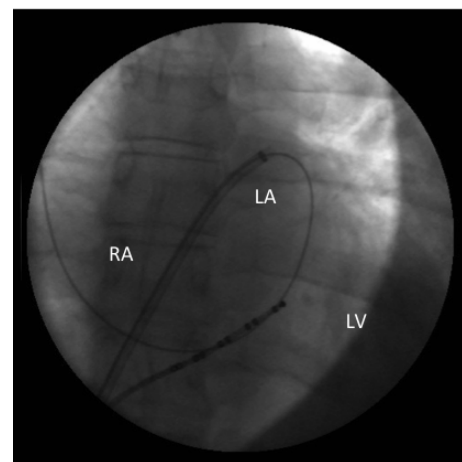


Figure 1. A guide wire in the Left Atrium after successful transseptal puncture.

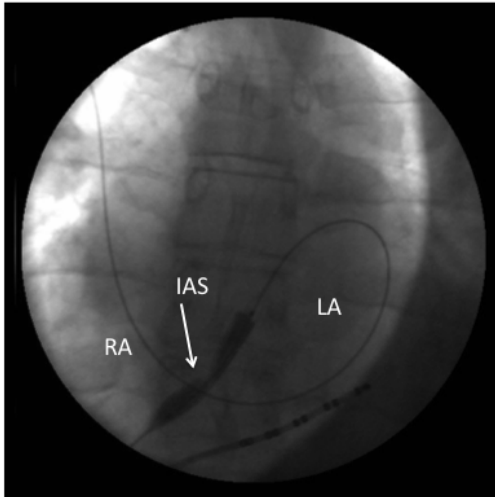


Figure 2 A. Balloon dilatation of the transseptal puncture site.

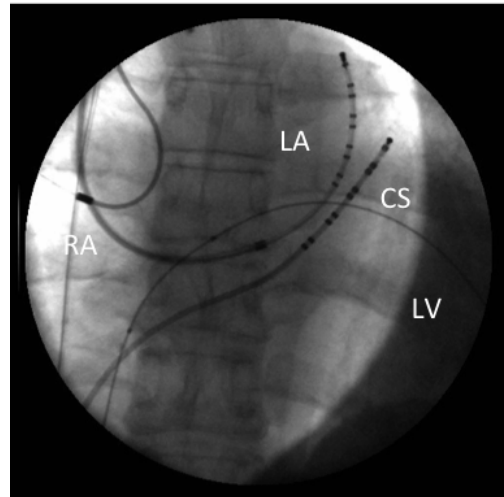


Figure 3A. The EP catheter is advanced transseptally into the left atrium.

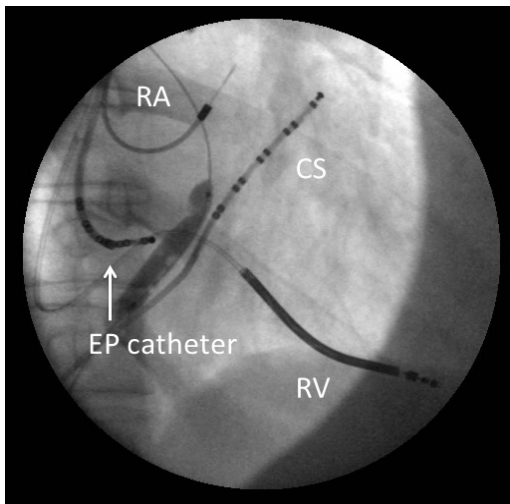


Figure 2B. Advancement of the EP catheter to the right atrium.

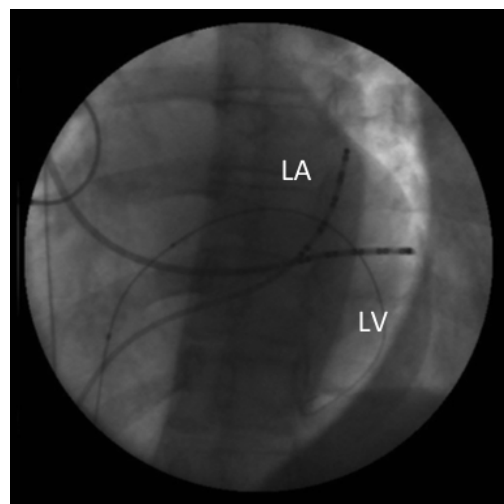


Figure 3B. The EP catheter and the sheath are advanced into the left ventricle.

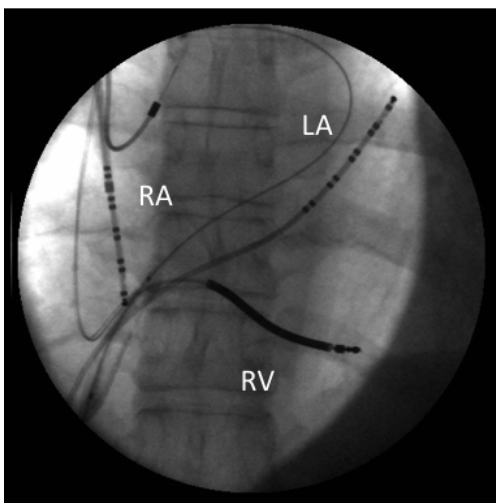


Figure 2C. The balloon is deflated and withdrawn into the right atrium.

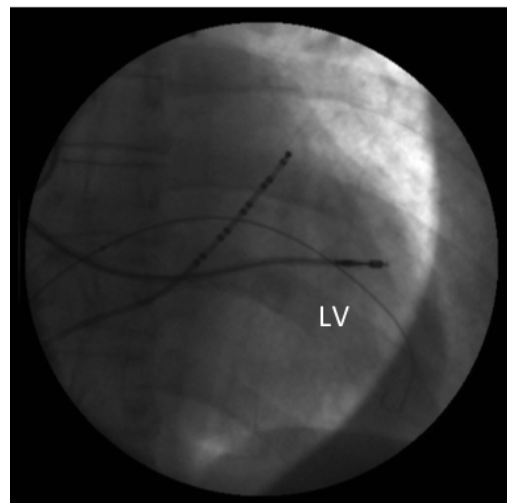


Figure 4A. The active fixation lead is screwed in the left ventricle.

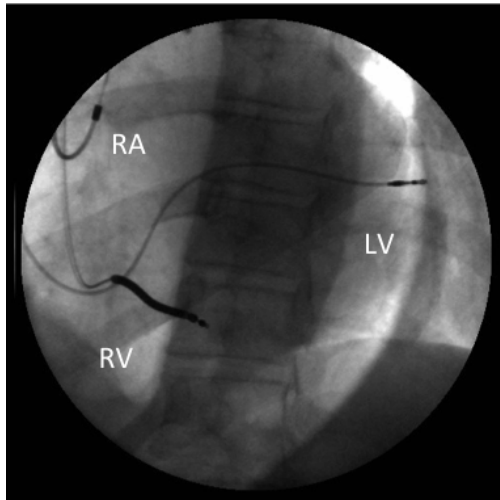


Figure 4B. Final lead position.

RESULTS

All patients had successfully been implanted with LV endocardial leads. Three of our patients

received CRT-D devices, while one patient received a CRT-pacemaker. A sum-up of the device implantation and follow-up parameters is available in Table 2. There was no phrenic nerve stimulation observed at stimulation with 10 V, 0.4 msec. During the follow-up period, no lead dysfunction or dislocation was observed. All patients have been on long-term anticoagulation and the international normalized ratio was maintained between 2.5 and 3.5. There were no hematoma or serious post-procedural bleeding observed due to the use of full anticoagulation during the procedure. None of the patients developed any thromboembolic events on last follow-up. All patients had improvement in the functional status thus symptoms had ameliorated at least one NYHA class. There was a significant improvement in the left ventricular systolic function, from a mean LV ejection fraction of $24 + 4.9$ to $32 + 5.1$ % ($p = 0.023$). We did not observe significant changes in the grade of mitral regurgitation throughout the follow-up period ($p = 0.18$).

Table 2
Implant and Follow-up data of the patients

Pt	1			2			3			4		
Device	Incepta Boston Scientific, CRT-D Miami, USA			Incepta Boston Scientific, CRT-D Miami, USA			Entovis, HF-T, CRT-P, Biotronik GmbH & Co, Berlin, Germany			Protecta XT, CRT-D, Medtronic; Minnesota, USA		
LV lead	Medtronic 5076-65cm			Medtronic 5076-65cm			Medtronic 5076-65cm			Medtronic 5076-65cm		
Success	Yes			Yes			Yes			Yes		
	R wave (mV)	Threshold (Volts/ms)	Impedance (Ohms)	R wave (mV)	Threshold (Volts/ms)	Impedance (Ohms)	R wave (mV)	Threshold (Volts/ms)	Impedance (Ohms)	R wave (mV)	Threshold (Volts/ms)	Impedance (Ohms)
Implant	8.5	0.6/0.4	495	15.5	0.7/0.4	754	20	0.8/0.4	678	7.2	0.75/0.4	754
1 Week postimplant	9.1	0.7/0.4	537	14.7	0.7/0.4	461	21	0.9/0.4	658	7.4	1/0.4	713
3 months postimplant	9	0.7/0.4	430	15	0.7/0.4	490	20	0.8/0.4	589	7.3	0.75/0.4	710
6 months postimplant	9.3	0.7/0.4	483	15.3	0.7/0.4	710	22	0.8/0.4	630	7.2	0.75/0.4	720
Complications	None			none			none			none		
Follow-up NYHA Class	II			II-III			II			II		
LVEF at follow-up	38%			29%			35%			27%		
Grade of MR at follow-up	III			II-III			III			III		
Thromboembolism	None			none			none			none		

Pt, patient, NYHA, New York Heart Association Functional Class, LV, Left Ventricular, LVEF, Left Ventricular Ejection Fraction, MR, Mitral regurgitation

DISCUSSION

For patients in whom transvenous left ventricular lead placement in the tributary veins of the CS is unsuccessful and are ineligible for surgical epicardial implantation, transseptal endocardial LV lead implantation is an alternative method for providing resynchronization therapy. Evidence from case documentation and from small trial batches proved the safety and feasibility of this alternative technique. In 1998 Jaïs *et al.* described the first successful implant of endocardial LV lead using a combined approach with a transseptal puncture from the femoral vein and a snare technique through the right jugular vein [12]. Since then, Leclercq *et al.*

have described several cases of successful LV lead implantation using a direct transseptal approach via the right internal jugular vein [14]. Another group has described a method using direct TS puncture from the left axillary vein [18]. In 2007 Van Gelder *et al.* and Nuta *et al.* described successful endocardial LV lead placement from the subclavian vein into the LV cavity via the interatrial septum, following transseptal puncture through the femoral vein to allow entry of the LV lead from above [15, 16]. In our patients, we used the latter approach.

One of the advantages of this interventional alternative technique is that there is no need for general anesthesia and there is minimum post-operative recovery. In comparison to epicardial

pacing, endocardial LV stimulation has some potential advantages. The transseptal access allows a broader choice for the pacing site inside the LV cavity and is not limited by the anatomy of the tributary veins of the CS. In case of a high pacing threshold, the lead can be repositioned to a different site inside the LV cavity, this is often difficult when maneuvering the lead in the cardiac venous system. The risk for phrenic nerve stimulation is low. In our small study population no phrenic nerve stimulation occurred at high energy stimulation and optimal implantation and follow-up electrical parameters were observed (Table 2). Experimental and clinical observations also indicated that LV endocardial stimulation enables a more physiological electrical activation of the left ventricle, with a transmural activation spreading from the endocardium to the epicardium [19, 20]. Better hemodynamic results with higher aortic and mitral time velocity integral, improvement of LV fractional shortening and less ventricular dyssynchrony were reported with endocardial than with epicardial LV stimulation [21, 22]. During follow-up in our patients, we observed that the totally endocardial pacing was correlated with a marked improvement of the LV systolic function and improvement in the functional status of the patients.

The disadvantages of this alternative technique include the risk associated with the transseptal catheterization, the unknown long-term thromboembolic risk, the need for lifetime anticoagulation, risks associated with position of the lead across the mitral valve, and the need of complex procedures to manage device related infections. The transseptal approach via the interatrial septum has been used for various interventional and electrophysiological procedures. Therefore, without any doubt, experienced operators have less risk with this procedure. The use of intraoperative anticoagulation and the need of anticoagulation right after the implantation lead to the increase of the risk of periprocedural bleeding complications. In our small study cohort there has not been any complications related to the procedure nor major hematoma was observed. The main concern is regarding the long-term risks of thromboembolic complications associated with endocardial LV stimulation. It is mandatory to use

anticoagulant therapy in these patients and the recommended target INR is between 2.5 and 3.5 [23, 24]. However, the use of anticoagulation is common in the majority of these patients due to the presence of atrial fibrillation. In all of our patients there was an indication for the use anticoagulant therapy, before the implantation of a transseptal system – three patients for paroxysmal atrial fibrillation and one for intraventricular thrombosis. Long-term follow-up data of the thromboembolic complications in patients who had a transseptal endocardial LV lead implanted are scarce. So far no thromboembolic complications were reported as long as anticoagulant therapy was followed [13, 25-27]. During follow-up no thromboembolic events occurred in our study population. In patients with transseptal CRT with an endocardial LV lead crossing the interatrial septum and the mitral valve, there is a theoretically increased risk of worsening the mitral regurgitation and of mitral valve endocarditis. No significant increase in the grade of mitral regurgitation has been reported with LV endocardial pacing [13-16, 26, 28]. We did not document any significant deterioration of mitral regurgitation in our study patients. To date there is no record of more frequent endocarditis associated with this technique. Throughout the follow-up period we did not have any lead infection.

CONCLUSIONS

Transseptalendocardial left ventricular lead implantation appears to be a valuable and safe second alternative with the benefit of an endocardial pacing site. The disadvantages of this technique are the need for permanent anticoagulation and the lead interaction with the mitral valve, though any significant complications as a result of this phenomena have not been reported until now. Nevertheless, more data is required to evaluate the safety and long-term efficacy of this alternative technique.

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Conflicts of interest: None declared.

Introducere. Implantarea clasică prin abord epicardic transvenos a electrodului de ventricul stâng (VS) pentru a realiza terapia de resincronizare cardiacă (TRC) nu este posibilă în 4-8% din cazuri. La acei pacienți, la care plasarea epicardică chirurgicală a electrodului de stimulare al VS nu este posibilă datorită unui risc

anestezico-chirurgical inacceptabil, implantarea endocardică a electrodului de stimulare al VS poate fi o alternativă viabilă.

Metode. S-a efectuat TRC în cazul a patru pacienți, cu plasarea endocardică prin abord transseptal atrial a sondei de VS, după ce implantarea prin abord epicardic transvenos a fost lipsită de succes. La toți pacienții s-a realizat poziționarea cu succes a unui electrod de stimulare cu fixare activă la nivelul endocardului VS, cu parametrii electrici stabili la momentul implantului și pe perioada de urmărire. Toți pacienții au primit tratament anticoagulant oral cu o țintă a INR de 2,5-3,5. Pe perioada de urmărire nu am observat complicații tromboembolice, hemoragice sau infecțioase.

Rezultate. Toți pacienții au avut un răspuns clinic și structural adecvat cu ameliorarea semnificativă a funcției sistolice a VS ($24 + 4,9$ to $32 + 5,1$ % $P = 0.023$) și a statusului funcțional.

Concluzii. Plasarea endocardică prin abord transseptal atrial a electrodului de stimulare al VS, poate fi o tehnică intervențională alternativă, sigură și valoroasă la acei pacienți la care riscul anestezico-chirurgical este ridicat și poziționarea clasică prin abord transvenos al electrodului de stimulare al VS nu este posibilă.

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