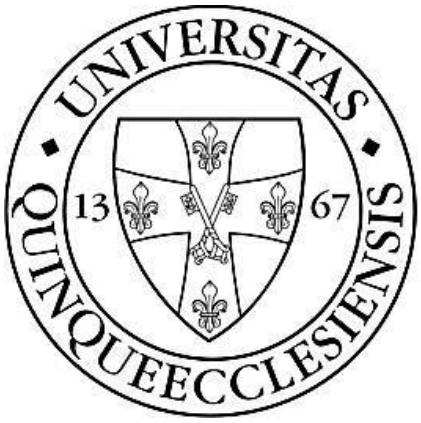
New methods: Pacing therapy to improve patients with advanced heart failure



Ph.D. Thesis

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Acronym list

AV: atrioventricular

CHF: Chronic Heart Failure

CRT: Cardiac Resynchronization Therapy

CS: Coronary Sinus

CT: Computer Tomography

+dP/dTmax: Maximal Rates of Left Ventricular Pressure Change

ECG: Electrocardiogram

EHRA: European Heart Rhythm Association

ESP: End-Systolic Pressure

HF: Heart Failure

IAS: Interatrial Septum

ICD: Implantable Cardioverter Defibrillator

INR: International Normalised Ratio

LA: Left Atrium

LAV: Left Axilar Vein

LBBB: Left Bundle Branch Block

LV: Left Ventricle

LVAD: Left Ventricular Assist Device

LVEF: Left Ventricular Ejection Fraction

LVEDD: Left Ventricular End Diastolic Diameter

LVESD: Left Ventricular End Systolic Diameter

MRI: Magnetic Resonance Imaging

MSP: Multi Site Pacing

NYHA: New York Heart Association

OAC: Oral Anticoagulation

PM: Pacemaker

PP: Arterial Pulse Pressure

QoI: Quality of Life

RA: Right Atrium

RAO: Right Anterior Oblique

RFV: Right Femoral Vein

RIJV: Right Internal Jugular Vein

RV: Right Ventricle

TE: Thromboembolic Event

TEE: Transoesophageal Echocardiography

TIA: Transient Ischemic Attack

TVI: Tissue Velocity Imaging

VAT: Video Assisted Thoracoscopy

SVC: Superior Vena Cava

VKA: Vitamin K Antagonist

VT: Ventricular tachycardia

VTS: Ventricular tachycardia storms

VV: Interventricular

Introduction

Cardiac resynchronization therapy (CRT) has evolved as an effective non pharmacological method of treating patients with heart failure (HF) and left ventricular (LV) dyssynchrony for those who have not responded adequately to medical therapy. CRT requires permanent pacing of the LV wall and restores the synchronicity of the atrio-ventricular, interventricular and intraventricular contractions, resulting in improved clinical outcomes and cardiac performance of advanced HF patients with wide QRS complex. However, a significant percentage of patients treated with CRT do not show an improvement in clinical symptoms or cardiac function. The suboptimal position of the LV pacing lead, an absence of LV dyssynchrony, myocardial scar abundance or suboptimal device programming have been related to a nonresponse to CRT. Furthermore, unsuccessful primary implantation of the LV lead into the coronary venous system has been reported in up to 10 % of patients.

In the last decade the indication for CRT expanded and the improvements in lead and delivery tool technologies made CRT more accessible to patients with HF. The number of CRT recipients in the last years increased enormously. Given the fact that 95% of new CRT patients received coronary sinus (CS) leads and assuming 75% patients survival and 10% CS lead failure over 5 years, a high number of CRT recipients will require CS lead revisions or alternative LV pacing methods. Furthermore, 40% of CS lead revision cases will have no usable side branches for LV lead replacement and will need alternative approaches to LV pacing.

<u>Problems with the current LV lead implantation methods</u>

Currently, in clinical practice the standard first line approach is the transvenous epicardial LV lead placement through a side branch of the CS. The final position of the LV pacing lead depends on the anatomy of the CS, on the performance and stability of the pacing lead and on the absence of phrenic nerve stimulation. Despite all of the available technologies and the placement techniques, in the high volume centers the rate of failed LV lead implantation into the CS side branch or the risk of late lead dislodgement, phrenic nerve stimulation or increasing threshold remains a substantial complication (5-10%) of transvenous CRT.

Alternative CRT methods

The alternative approaches can be classified on the basis of the LV pacing site (*epicardial* or *endocardial)*, and on the basis of access (*closed-chest/percutanous* or *open-chest)*. In the case of the closed chest/percutaneous approach, the lead insertion can be differentiated as transvenous, transapical or transarterial. For example the standard CS side branch lead placement is a transvenous approach and produces epicardial pacing.

Epicardial pacing techniques

Currently, the open-chest access epicardial lead placement is the most frequently used as a second choice by either thoracotomy or video-assisted thoracoscopy (VAT). Nevertheless, at planned coronary artery bypass graft surgery, valve repair or replacement, the epicardial surgical approach might still remain the first choice. The advantage of this approach is the direct visual control with the possibility of choosing the lead tip position. The risks of lead dislodgement and phrenic nerve stimulation are low and there is no limitation of the CS anatomy. Surgical epicardial LV lead placement has several disadvantages such as the need for general anaesthesia, the presence of epicardial fat, adhesions and it is more invasive than the transvenous approaches. There are several surgical approaches to implant the LV pacing lead.

Median sternotomy is used at planned coronary artery bypass graft surgery and at valve repair or replacement. The **full left thoracotomy** offers the widest accessibility of the lateral LV wall however at present is less applied. The **minimal thoracotomy (minithoracotomy)** offers better survival and a lower incidence of mediastinitis or osteomyelitis. Nowadays, the epicardial LV lead is implanted surgically often through a small left thoracotomy. The LV lead implantation is performed under general anesthesia and on the beating heart. The **Video assisted thoracoscopy (VAT)** offers less postoperative pain and requires smaller incisions. It does not compromise in visualization. The VAT technique should be performed under general anesthesia, single-lung ventilation, standard monitoring and on the beating heart. The VAT approach is a feasible and safe alternative, is well tolerated and it has minimal postoperative recovery. **Robotically assisted surgery:** This technique results in more precise LV lead placement on the ventricular wall and significantly reduces postoperative morbidity and the length of hospitalization. This approach also needs general anesthesia, single-lung ventilation,

standard monitoring and TEE control. However, while robotic surgery was shown to be feasible and safe, its use is restricted largely by cost implications related to purchase and maintenance of technology and its longer operating room time.

Endocardial pacing techniques

In case of endocardial pacing the LV lead has a direct contact with the endocardial tissue. Usually is implanted as closed chest/percutaneous approach, only the lead insertion can be differentiated as transvenous or transapical. The transvenous technique is performed using different veins and the LV lead is introduced into LV via interatrial septum.

Transseptal endocardial LV lead implantation: Transseptal access endocardial LV lead placement was investigated as a means of delivering LV pacing when CRT first emerged as a therapeutic paradigm and currently is used also as third line approach. This approach does offer some major advantages: transvenous access, more lead placement sites, endocardial pacing and there is no need to compromise in LV pacing threshold for positional stability or phrenic nerve stimulation. The procedure does not require general anaesthesia and minimal postoperative recovery is required. However, the major concern is about the long term risk of thromboembolic complication and mitral valve endocarditis related to permanent presence of the transmitral LV lead from the RA.

Transapical endocardial LV lead implantation: For endocardial LV pacing the feasibility of a fundamentally new surgical method was reported in 2008. This method developed in our center (Gottsegen György National Heart Center, Budapest) is based on transapical lead implantation. This new technique combines the minimal invasive surgical approach and the advantage of endocardial pacing. The transapical approach was invented for patients who failed the first attempt through the CS approach and/or with extensive epicardial adhesions. The advantage of this minimally invasive technique is the best accessibility of the all LV endocardial segments without the limitations of the anatomy to reach the most delayed segment of the lateral wall.

The aim of our study

The aim of our study was to compare the outcome of patients undergoing either transapical endocardial or surgical epicardial LV pacing.

A second aim was to determine the long-term outcome, including the cerebral thromboembolic complications of pts who underwent transapical LV lead placement.

Material and methods

The comparison study was a single center prospective randomized study which was approved by Regional Medical Ethical Committee conform the Medical Research Council-Scientific and Ethical Committee guidelines of the 1975 Declaration of Helsinki.

Patient population in the comparison study

23 consecutive patients were identified in whom previous CRT implantation failed. The patients were involved and randomized in the comparison study between 2008 and 2010. All patients were eligible for CRT implantation based on current ACC/AHA and ESC guidelines: all had severe congestive heart failure, NYHA functional class III or IV despite optimized medical treatment; LVEF ≤ 35% and left ventricular end-diastolic diameter ≥ 60 mm. QRS duration was more than 130 ms in all patients. Demographic data are summarized in Table 1.

Table 1. Patient demographics and medical therapy in the comparative study

	Group I.	**Group II.**	**P**
Patient number (n)	11	12	N.S.
Age	59,7±7,9	62,8±7,3	N.S.
Male/female	9/2	8/4	N.S.
NyHA Class	3,5±0,4	3,6±0,4	N.S.
Echocardiografic data			
LVEF (% ± SD)	26,0±7,8	26,4 ± 8,9	N.S.
LA (mm ± SD)	61,0±9,8	60,1±10,7	N.S.
LVESD (mm ± SD)	62,7±10,8	61,1±10,7	N.S.
LVEDD (mm ± SD)	73,7±10,5	68,3 ± 10,8	N.S.
Drug therapy (%)			
ACE inhibitors/ARB-s	100,0	100,0	N.S.
Beta blockers	90,9	100,0	N.S.
Digitalis	54,5	50,0	N.S.
Amiodarone	45,5	50,0	N.S.
Loop diuretics	100,0	100,0	N.S.
Spironolactone	54,5	50,0	N.S.

All patients were on optimal medical therapy (OMT) suggested by HF guidelines. The reason for transvenous failure are summarized in Table 2.

Causes of CS lead placement failure	Group I.	Group II.
Aberrant orifice of CS; no intubation (n)	5	6
Phrenic nerve stimulation ; high threshold (n)	3	2
No suitable CS side branches (n)	1	2
CS lead dislodged more times (n)	2	1
CABG or prostatic valve impl. (n)	-	1

Pts were randomized into either transapical (Group I.) or epicardial surgical LV lead implantation (Group II.). Only patients who were anti-coagulated were eligible to enter the study. None of the pts had evidence of LA or LV thrombi on the preoperative echocardiographic study. Follow up visits were scheduled at 3, 6, 12 and 18 months. Responsiveness to CRT was defined as an improvement >1 NYHA class and/or 10% improvement in LVEF at 6 months. All patients who died before 6 months were considered to be non-responder.

The following baseline and follow up data were compared between groups: LV ejection fraction (LVEF), NYHA class, LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD) and quality of life (QoL).

Lead implantation procedures: The patients were prepared for the operation using general anesthesia. After intra-tracheal intubation the patient was prepared for an infraclavicular incision as well as for a small left thoracotomy.

Transapical approach: Initially transthoracic echocardiography was used to locate the LV apex. Beyond this marked area the procedure commenced with a mini-thoracotomy. Inside the chest a small pericardiotomy was performed above the LV apex. A standard active fixation endocardial pacing lead (Medtronic 4076-85 cm, 5076-52 cm, Vitatron ICQ09B-52 cm, Guidant Flextend 2) was positioned in the LV cavity through the apex. The leads were inserted using Seldinger technique utilizing a peel-way sheath (LI-7 Plus, 7F, Biotronik). After removal of the guide wire, the pacing electrode was inserted into the LV cavity through the sheath and peel-away sheath was removed. Hemorrhaging from the LV was controlled with one or two 5/0 or 4/0 monofilament purse-string sutures around the puncture point (Figure 1). Fluoroscopy was necessary for the intracavital navigation and endocardial fixation of the electrode at the optimal pacing site for CRT (Table 5).

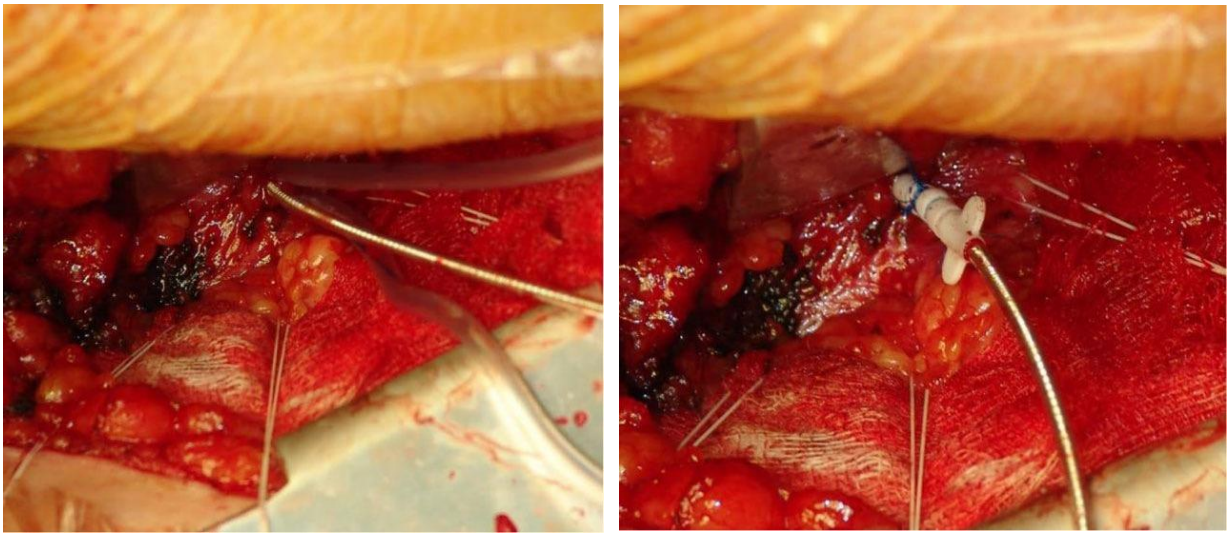
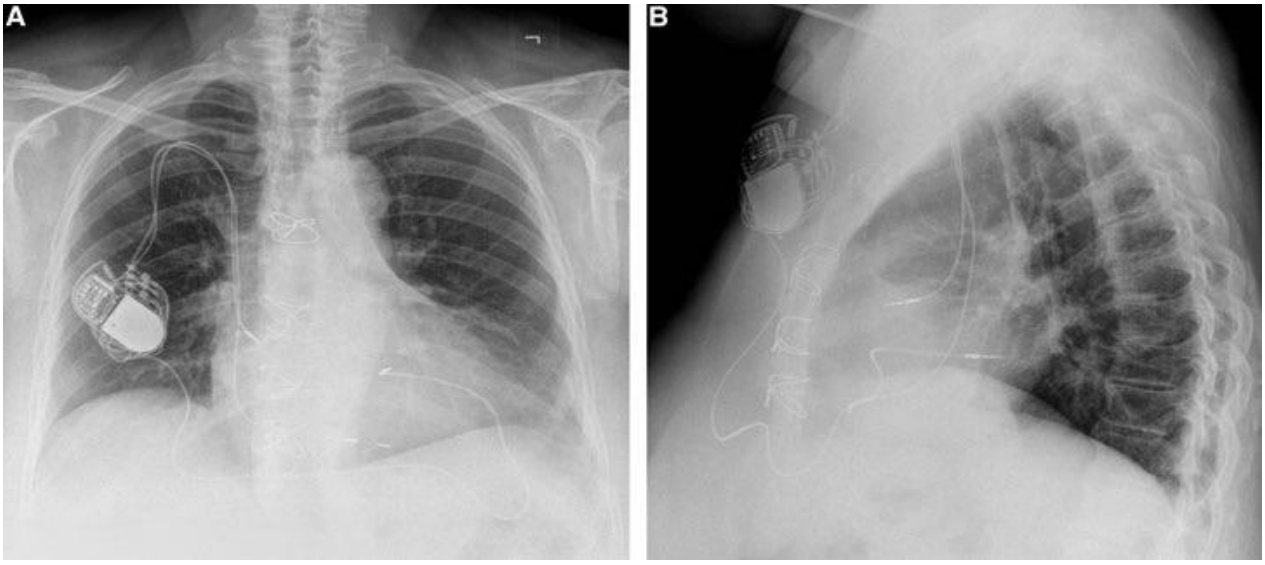


Figure 1. Intraoperative photograph during mini-thoracotomy showing transapical lead insertion and fixation into the LV.

To reach the target area a “J” shaped electrode guide wire was useful. Maneuvering in the LV cavity did not require specific devices and skills. After lead fixation the proximal body of the electrode was tunneled to an infraclavicular pocket using standard technique. Figure 2 A,B.



(A)Postoperative chest x-ray from anteroposterior (AP) projection. (B) Postoperative chest x-ray from lateral (LA) projection.

Perioperative anticoagulation regime was applied as for patients undergoing mitral valve replacement (INR 2,5-3,5). Intravenous heparin was re-started 3 hours after the surgery if bleeding was no longer observed via the pericardial drain.

Epicardial lead implantation: After standard single lumen intubation the patient was placed in supine position with the left chest elevated 30-40°. We performed a large lateral-thoracotomy between intercostal space 4-5. Ensuring sufficient distance the pericardium was opened anterior to the phrenic nerve. The pericardium was fixed with traction-sutures to the skin, rotating the heart to the right and creating optimal exposure of the lateral surface. A unipolar or bipolar epicardial leads (Biotronik, ELC 54-up or 35-up, Medtronic 5071) were attached to the target area and secured with two sutures (Table 5).

Device implantation and pacing mode

23 patients received CRT devices for biventricular pacing (Medtronic InSync System model 8040 or 8042, Biotronik Stratos LV, Medtronic InSync Sentry 7298; Biotronik model Lumax 300 HF-T, Kronos LV-T; StJude Atlas). Pacing was delivered in biventricular DDD mode. At implant all patients were in sinus rhythm. Active pacing was selected by programming the atrial-synchronous mode with the atrioventricular (AV) delay determined using hemodynamic evaluation. The AV-delay was optimized based on M mod echocardiography (transmitral TVI). Interventricular (VV) optimization was not performed. The VV time was empirically programmed to – 20 ms (LV first paced).

Substudy with transapical patients: long term follow-up

In our center between October 2007 and September 2013, 26 consecutive patients with ischemic (12 pts) and dilated (14 pts) cardiomyopathy after failed transvenous LV lead implantation underwent transapical LV lead placement as a last resort therapy. All transapical patients from comparison study (11 pts) were included in the long term follow-up substudy. The baseline clinical data and demographic characteristics of all transapical LV lead implanted patients in our center are included in Table 3. The inclusion/exclusion criteria, the surgical procedures, the device implantation and the pacing mode was idem. Twelve patients underwent CRT-PM implantation while in fourteen patients CRT-D device implantation was performed (Table 4). The decision between ICD or pacemaker was not easy because we can't implant in all patients ICD-CRT devices. The reason has many

factors but one of them was commonly financial.

Table 3: Baseline clinical and demographic characteristics in transapical group, 26 pts.

Parameter at enrolment	**Mean ± SD or %**
Age (years)	61± 10
Sex	
Male	19 (73%)
Female	7 (27%)
Cardiomyopathy	
Dilated cardiomyopathy (DCM)	14 (54%)
Ischemic cardiomyopathy (ICM)	12 (46%)
New York Heart Association functional class (NYHA)	
II.	2 (8%)
III.	17 (65%)
IV.	2 (8%)
Left ventricle ejection fraction (LVEF%)	26.7±6.63
Left ventricle end-systolic diameter (LVESD,mm)	75.08±17.15
Left ventricle end-diastolic diameter (LVEDD,mm)	62.56±11.62
Intrinsic QRS duration (ms)	167.85±24.05
Drug therapy	
ACE inhibitors, ARBs	21/26 (80%)
Beta-blockers	21/26 (80%)
Digoxin	6/26 (23%)
Amiodarone	9/26 (34%)
Loop diuretics	20/26 (77%)
Spironolactone	15/26 (57%)

Table 4: Type of CRT devices and transapical LV leads

Type of CRT devices	**Number (n=26)**
Biotronik Lumax	6
Biotronik Stratos	8
Biotronik Entovios	1
Medtronic Syncra	1
Medtronic Insyc/Concerto	7
St. Jude Atlas/Promote	2
Boston Scientific Cognis	1
Type of transapical LV leads	**Number (n=26)**
Vitatron ICQ09B	4
Giant Flextend 2	1
St. Jude 1888T	8
Medtronic 5076	7

Medtronic 6944	1
Medtronic 4076	5

All patients were scheduled for regular visits at 1, 3, 6 months and every 6 months after that. Additional visits or hospitalizations were registered. The INR level was checked and corrected to be in the range between 2.5 and 3.5 generally monthly but if required daily. During the median follow-up period of 40 ± 24.5 months, we collected data on mortality rate, reoperation rate, and cerebrovascular event rate. Emergency CT scan was performed in patients with symptomatic and/or suspected ischemic thromboembolic event. Asymptomatic patients underwent an elective, non- contrast enhanced cerebral CT scan examination at median follow-up of 40 ± 24.5 months in order to determine any silent TE event possibly related to the presence of the LV endocardial lead.

Statistical analysis

Continuous variables were shown as mean ± SD, if normally distributed, and compared with the Student's t test. In case of non-normal distribution of data, median with corresponding interquartile ranges were reported, and the Mann-Whitney U test was used for comparison. Categorical data was expressed in percentages and compared with Fisher's exact test. Simultaneous comparison of > 2 mean values were performed by one-way analysis of variance. A two-tailed p value < 0.05 was considered as significant. All statistics were performed using SPSS (version 16.0) for Windows (SPSS Inc, Chicago, Il, USA).

Results

Outcome data from the comparison study

19 patients completed the 18 months follow up (the follow up time was ranging from 18 months to 34 months). In the transapical group one patient died suddenly 10 months after implantation. Pathology showed no device or lead related complications and device interrogation showed no arrhythmias. In the epicardial group three patients died in the follow up period. One patient died within the first 30 postoperative days, however, death was not related to the procedure. This patient had significant mitral valve regurgitation (II-III), coronary disease, paroxysmal atrial fibrillation, severe diabetes and was in NYHA IV. The other two patients died from cardiac related problems: one of sudden cardiac death and the other of progressive heart failure. In both groups significant QRS duration

reduction was observed, however, there were no statistically significant difference between group I and II (Table 5).

Table 5: LV Lead positions and QRS duration after trans-apical or epicardial CRT

		Group I.	Group II.
QRS (ms)	before	138,9 ±24,9	137,8±25,2
QRS (ms)	after	117±17.2	126±24.7
	anterior (n)	-	1
basal	lateral (n)	4	4
	posterior (n)	6	-
	inferior (n)	-	-
	anterior (n)	-	1
mid	lateral (n)	1	4
	posterior (n)	-	1
	inferior (n)	-	-
	anterior (n)	-	-
apical	lateral (n)	-	1
	inferior (n)	-	-

A transapical approach was used in 11 patients (Group I.) and a successful implant of an LV endocardial lead was obtained in all. Lead dislocation was detected in two patients. In one patient it occurred during closure of the pericardium. In another patient dislocation was observed on the second postoperative day. Lead repositioning could be performed without re-opening of the pleural cavity. During the study period 12 patients (Group II.) were randomized to surgical epicardial LV-lead placement. After surgical placement of a LV-lead one patient presented with a high pacing threshold requiring refixation of the displaced epicardial lead. Mean procedure duration was shorter in the transapical group than in the epicardial. The postoperative hospital stay was longer for patients receiving epicardial leads compared to transapically placed LV-endocardial leads due to minor postoperative issues such as postoperative pain (Table 6).

Table 6: Comparison of intraprocedural and postprocedual data

	Group I.	Group II.	P
Operation time (min)	106±23,3	130,1±32,3	<0,05
Fluoroscopy time (min)	7,5±4,8	-	N.A.
Postoperative days (in hospital)	6,4±4,2	11,3±6,8	<0,001
Reoperations needed (n)	2	1	N.S.

During follow up LVEF has improved from 26,0±7,8 % to 39,7±12,5 % in the trans-apical group, and from 26,4±8,9 % to 31,5±11,5 % in the epicardial group. There was a substantial decrease in LV diameters in both groups (Table 7).

Table 7: Comparison of the outcome of the patients

	Group I.			Group II.			
	before CRT	after CRT	p*̊	before CRT	after CRT	p*	p**
LVEF (%±SD)	26,0±7,8	39,7±12,5	<0,001	26,4±8,9	31,5±11,5	<0,05	
LVEDD (mm±SD)	73,7±10,5	70,4±13,6	<0,001	68,3±10,8	68,4±7,2	N.S.	
LVESD (mm±SD)	62,7±10,8	55,8±15,5	<0,001	61,1±10,7	57,5±8,7	<0,05	
NYHA class (±SD)	3,5±0,4	2,2±0,4	<0,001	3,6±0,4	2,7±0,4	<0,001	
∆ LVEF (%±SD)		13,7±10,6			5,1±6,8		N.S.
∆ LVEDD(mm±SD)		3,3±2,8			0,1±3,2		<0,01
∆ LVESD (mm±SD)		6,9±5,4			3,6±3,2		<0,05
∆ NYHAclass(±SD)		1,3±0,4			0,9±0,4		N.S.

Improvement of the NYHA class was observed in both groups. Acute LV-lead sensing did not significantly differ between the groups (11,0±5,6 mV vs. 11,2±6,0 mV; p=NS). Acute and chronic - capture thresholds of the LV-leads were significantly lower in the trans-apical group (0,5±0,2 V/0,4 ms vs. 1,8±1,5 V/0,4 ms; p<0,01 and 0,7±0,2 V/0,4 ms vs. 3,5±1,2 V/0,4 ms; p<0,001). Pacing at 10.0 V/0,4 ms did not result in phrenic nerve stimulation in any patients. There were no clinical signs of thromboembolic events during the mid-term follow up (completed 18 months).

<u>Long term follow-up results of 26 transapical LV lead patients</u>

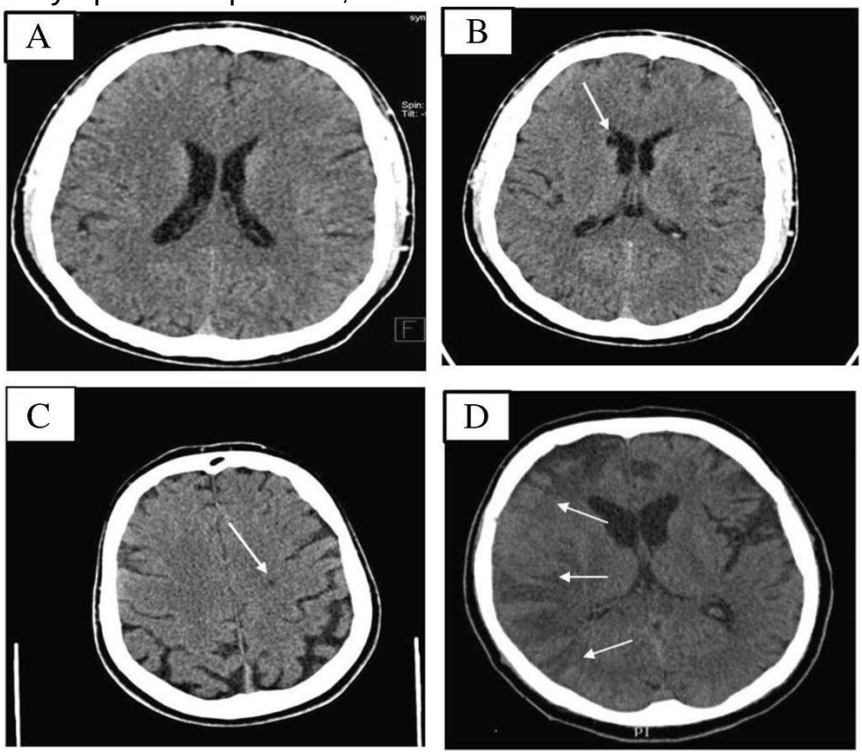
During the median follow-up period of 40 ± 24.5 months, 3 out of 26 patients with transapical CRT were crossed over to epicardial LV lead implantation; consequently, 23 patients could be followed-up as pts with transapical LV lead implantation. The mortality rate was determined utilizing the National Registry Office database. Eleven out of 23 (47 %) patients with transapical CRT survived after a median follow-up of 40 ± 24.5 months. One patient was lost to follow-up. Ten patients died due to exacerbated heart failure while one patient suffered sudden cardiac death. Two out of the three patients crossed over to an epicardial CRT system underwent right-sided infective endocarditis (3 months and 3 years after initial transapical approach) and one patient because pericardial tamponade. Furthermore, two cases of CRT-pocket infection were observed and two cases CRT-

pocket hematoma. Reimplantation was necessary in one patient, after interruption of anticoagulation therapy, due to transapical LV lead fracture causing the deterioration of heart failure, 5 years after the primary procedure. Repositioning of the transapical LV lead was necessary in three cases: two early dislocations and one late lead dysfunction.

Table 8: Complications in the transapical group during long term follow-up (26 pts.)

Complication type	Nr	Characteristic
Endocarditis right sided	2	3 months after implantation 3 years after implantation
Pericardial tamponade	1	1 month after implantation
Pocket infection	2	
Pocket haematoma	2	
LV Lead fracture	1	5 years after implantation
LV Lead dislocations	3	2 early dislocations 1 late dislocation
TE with symptoms	3	2 days, 2 and 4 months after implantation
TE without symptoms	2	detected by cerebral CT

During the long term follow-up period, atrial fibrillation was detected in ten out of 26 patients. In 3 patients were documented symptoms of thromboembolic complications. In asymptomatic patients, the CT scan examination revealed minimal extension chronic ischemic lesions in two cases (Fig. 3).



Non-contrast enhanced cerebral CT scan of patients after TALV lead implantation:

a., no abnormality
b., 6 mm lacuna in the right-sided nucleus caudatus
c., 4 mm hypodensity in left-sided centrum semiovale
d., middle cerebral artery occlusion with right-sided fronto-temporo- parietale extension

Discussion

The major finding from the comparison study is, that the alternative method developed at our center for endocardial CRT is a feasible approach. Our data suggest that transapical endocardial CRT with 18-months follow-up period presented promising outcomes with potential advantages such as shorter procedure time, decreased postoperative burden and the best accessibility of the all LV endocardial segments without the limitations of the anatomy to reach the most delayed segment of the lateral wall compared to epicardial LV lead implantation techniques. The major finding of the long term follow-up of the transapical approach is that, although transapical CRT can be used as an alternative method for CRT in selected heart failure patients, it represents a worrisome thromboembolic complication rate compared to traditional transvenous CRT.

Rational for alternative approaches

Despite the technological progress aimed at improving success and reducing complication rates during CRT device implantation, in some cases the delivery of a LV pacing lead through the CS still fails. The reasons for the failed procedures are related to difficulty obtaining CS access, navigating the venous tributaries and obtaining a stable and functional location from which to pace the lateral wall of the LV. In the last years the reported rate of failure to place an LV lead via the CS has decreased steadily over time but remains an existing problem.

Endocardial vs. epicardial pacing

A lot of studies have demonstrated that LV pacing site is a critical parameter in optimizing CRT. LV lead placement in the CS side branch results in epicardial pacing, which is less physiological, reversing the pattern the normal LV wall activation. In the HF patients with CRT, endocardial biventricular pacing provides more homogenous intraventricular resynchronization than epicardial biventricular pacing and is associated with better LV filling and systolic performance. CRT delivered at best LV endocardial sites is more effective than via pre-implanted coronary sinus lead pacing. Epicardial pacing may be more pro-arrhythmic than endocardial LV pacing, since reversal of the direction of activation of the LV wall, as occurs during biventricular pacing, leads to a prominent increase in QT and transmural dispersion of repolarization. Ventricular tachycardia storms

(VTS) and recurrent monomorphic ventricular tachycardias have been clinically observed after the initiation of CRT with epicardial LV pacing.

Nowadays when CS lead placement for transvenous LV pacing has failed the most frequently used surgical alternative is the epicardial pacing lead implantation via limited thoracotomy. As alternative to surgical epicardial LV lead implantation techniques was developed first the percutaneous LV lead implantation via atrial septum. As alternative to transseptal endocardial CRT we developed a fundamentally new method, the transapical LV lead implantation, which provides access for pacing any segment of the LV. Life-long anticoagulation is mandatory for these patients (similarly to transseptal CRT). For safety reasons we aimed a target INR level equivalent with mitral prosthetic valves. During mid-term follow-up we did not observe any TE events in this group of patients treated with the transapical technique, but this finding has changed during long-term follow-up. The transseptal and the transapical CRT are endocardial approaches and becomes increasingly utilized for pacing of the free-wall of the LV in patients when an epicardial approach failed. Therefore, it is important to recognize that for patients with contraindication to anticoagulation, epicardial LV lead implantation is the only remaining therapeutic option if the standard percutaneous implantation fails.

Thromboembolic (TE) risk in the transapical patients

In our long term follow-up study, two major stroke and one transient ischemic attack occurred during median follow-up of 40 ± 24.5 months. One out of two TE events happened early after the interruption of anticoagulation therapy due to the necessity of transapical LV lead reoperation. The stroke or transient ischemic attack occurs usually in patients whom anticoagulation was temporarily interrupted or switched to heparin. It was the time when the physicians responded to concerns about perioperative TE by treating moderate- to high-risk device surgery patients with heparin bridging and the papers before 2010 recommended this as standard of care. Subtherapeutic INR levels frequently appear in everyday practice. According to previous studies, only two thirds of patients are within the target INR level. The duration of decreased anticoagulation control is associated with increased risk of stroke. Current international thrombosis guidelines suggest continuation of vitamin K antagonists (VKA) in high risk patients. Lead components may also influence the risk of stroke. The thrombogenicity of polyurethane

leads may be lower than those of silicone. The presence of an intraventricular anodal electrode may represent an unknown factor as the source of intracavital thrombus formation. The movement of the transapical LV electrode may generate increased turbulent blood flow in the LV generating thrombus formation.

Conclusions

1.,Our data demonstrated the feasibility of the transapical endocardial CRT as a second alternative for patients with advanced HF who failed the first attempt through the CS implantation and/or with extensive epicardial adhesions.

2.,The transapical CRT approach presented promising outcomes with potential advantages such as shorter procedure time, decreased postoperative burden and the best accessibility of the all LV endocardial segments without the limitations of the anatomy to reach the most delayed segment of the lateral wall compared to epicardial LV lead implantation techniques.

3.,Although transapical CRT can be used as a second alternative method for CRT in selected HF patients, it represents a worrisome thromboembolic complication rate compared to traditional transvenous or surgical epicardial LV lead implantation. At the same time is very important to emphasize the fact, that our long term follow-up data were collected in the period of heparin bridging which affected significantly the higher rate of thromboembolic events.

4.,Our data suggest that during application of the new developed wireless systems or other devices, leads etc. used as destination therapy in end-stage HF patients, one of their major complications is the occurrence of TE events. To decrease the risk of thromboembolism, regarding the surface of the currently used devices/leads in the LV, further technological developments are required.

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