NEW METHODS IN THE NON-PHARMACOLOGICAL TREATMENT OF HEART FAILURE AND VENTRICULAR ARRHYTHMIAS

Doctoral thesis

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INTRODUCTION

Diseases of the heart are among the leading causes of mortality in the world. Heart failure and arrhythmias are common forms of heart diseases, they will become even more important as the ratio of elderly population increases. Because of prolonged treatment they require huge medical expenses. In the last decades non-pharmacological methods play more and more relevant role beside medication.

Resynchronization therapy of heart failure

About 15% of heart failure patient also suffer from intraventricular conduction disturbances, in NYHA stage III and IV this ratio can be higher then 30%. Prolongation of the duration of ventricular depolarization results in dyssynchrony of ventricular conduction, because ventricular segments depolarized in different time will not contract simultaneously. Biventricular stimulation can decrease electrical and mechanical dyssynchrony, duration of left ventricular depolarization and repolarization together with end-systolic volume and mitral regurgitation. Left ventricular contractility and diastolic filling time can be increased. Clinical status and quality of life increase in 70-80% of the patients, and on the whole the number of hospitalisations and mortality will be decreased.

The left ventricular electrode is generally implanted into a side branch of the coronary sinus (CS). The quite high dislocation rate of the CS electrodes is currently an important clinical problem. Instability may complicate the optimal positioning of the lead,

dislocation may cause significant increase of the pacing threshold, loss of capture or phrenic nerve stimulation.

Catheter ablation of ventricular tachycardia

Ventricular tachycardia (VT), which most commonly occurs in patients with structural heart disease, is a life-threatening arrhythmia. Beside medical therapy, patients having high risk for sudden cardiac death are candidates for implantable cardioverter defibrillator (ICD). If VT episodes occur often, catheter ablation is increasingly indicated. Catheter ablation has the potential to control recurrent episodes in nearly all forms of monomorphic VT. Ablation is especially required in the cases of recent episodes, frequent ICD shocks or incessant VT. Although as the result of the technical development a number of new tools (electroanatomical mapping systems, cooled tip catheter, alternative energy sources) help the physician, catheter ablation of ventricular tachycardia (specially in the case of hemodynamic instability) remained one of the biggest challenges of invasive electrophysiology.
Ventricular tachycardia ablation is recommended to perform in special centres with well-trained operators and teams. Respirator, intraaortic balloon-pump, heart surgery and intensive therapy back-up must be available.

AIMS

1. We investigated the effectiveness and safety of coronary sinus stenting to anchor the CS lead position in the cases of postoperative and intraoperative dislocation, microdislocation, instability of the electrode and phrenic nerve stimulation.

2. Effectiveness and safety of a new, minimally invasive method was investigated for the reposition of the distally positioned or dislocated CS lead without opening the pacemaker pocket, if the distal position was resulted in phrenic nerve stimulation.

3. If the transvenous or surgical epicardial implantation of the left ventricular lead is not possible or contraindicated, alternative methods may be effective. We investigated the advantages of electroanatomical mapping during transseptal left ventricular lead implantation.

4. Catheter ablation is indicated, in the cases of frequent ventricular tachycardia episodes causing ICD shocks and/or if antiarrhythmics are not effective. We investigated the effectiveness of VT ablation in our patients late after myocardial infarction.

5. If antiarrythmic medication, device therapy and endocardial catheter ablation are ineffective, epicardial ablation may be performed as last remaining therapy in the case of incessant VT. Our aim was to perform the first epicardial ablation in Hungary for the treatment of incessant VT late after myocardial infarction.

6. Our aim was to treat the frequent VT episodes with catheter ablation in a patient after surgical correction of tetralogy of Fallot.

METHODS

Stabilization of the coronary sinus electrode position with stent implantation

Coronary sinus stent implantation was performed in 248 patients because of postoperative or intraoperative dislocation, intraoperative microdislocation causing significant increase of the pacing threshold, instable lead position and phrenic nerve stimulation near to an acceptable electrode localisation. After positioning of the lead a short (mainly 8-15 mm) bare metal coronary stent was introduced into the target CS side branch via another guide wire through the same CS sheath near to the lead.

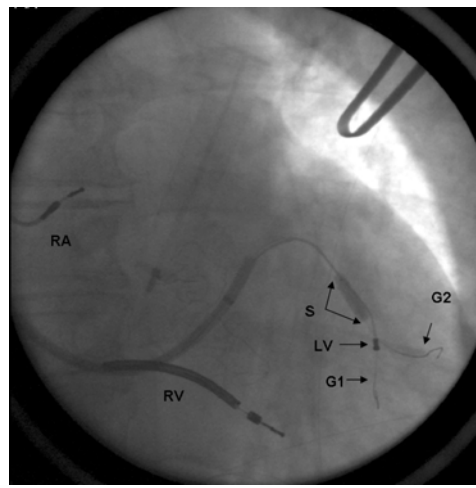

Figure 1. Inflation of the stent to anchor the coronary sinus lead. *S:* stent. *LV:* left ventricular (CS) lead. *G1:* guide wire of the electrode. *G2:* guide wire of the stent.

The stent was deployed 5 to 30 mm proximal to the tip of the electrode with a pressure of 6 to 20 atmospheres *(Figure 1.)*. Left ventricular (LV) pacing threshold and impedance were controlled after the implantation, in every six months and at any patient visit.

Minimal invasive reposition of the coronary sinus electrode

Minimal invasive coronary sinus lead reposition was performed in nine CRT patients with phrenic nerve stimulation and distal CS lead position on a par 6 (max. 17) months after the implantation. CS was cannulated with left Amplatz 2 type guiding catheter after the puncture of the femoral vein, and on a guide wire a stent was positioned beside the electrode into the CS side branch, or if it was not possible, into the CS near to the ostium of the side branch. Ablation catheter („B" curve) was introduced into the right atrium via the femoral vein. The ablation catheter was looped around the atrial part of the CS lead with bended tip, then the catheter and the CS electrode was drawn backward slowly into the direction of the inferior vena cava *(Figure 2.)* If the first position was not acceptable, the lead was pulled back further proximally. After accepting the new position, CS lead was stabilized with inflating the previously positioned stent. Left ventricular pacing threshold and impedance were controlled after the implantation, in every six months and at any patient visit.

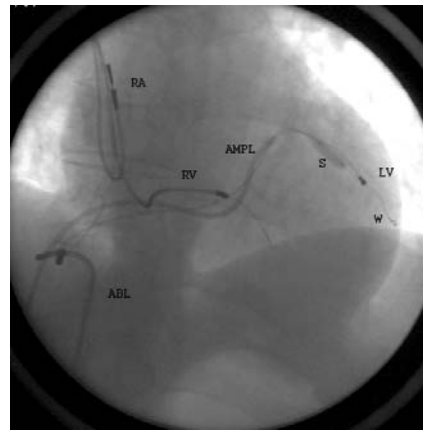

Figure 2. *Abl:* ablation catheter. *Ampl:* Amplatz guide catheter before the ostium of the CS side branch. *LV:* coronary sinus elekctrode after withdrawn, pacing trheshold is acceptable, no phrenic nerve stimulation. *S:* inflation of the stent. *W:*guide wire of the stent. *RV*:right ventricular lead, *RA*:right atrial lead.

Transseptal endocardial left ventricular lead implantation

Transseptal endocardial left ventricular lead implantation was performed in two patients after previous heart surgery and unsuccessful transvenous CS electrode implantation. After transseptal puncture via the femoral vein the location of the puncture was marked using CARTO electroanatomical mapping system. The marked point was identified with the CARTO catheter via the left subclavian vein, and the catheter and a long sheath were introduced into the left ventricle. The region of the latest left ventricular activation was identified with the CARTO system, and an active fixation pacemaker electrode was positioned to there via the sheath. After full dose LMWH treatment oral anticoagulation

therapy was used to prevent thromboembolic complications. INR was considered in the range of 3.5-4.5.

Radiofrequency catheter ablation of ventricular tachycardia after myocardial infarction

Radiofrequency catheter ablation was performed with electroanatomical mapping in 52 postinfarction patients, in altogether 59 cases because of frequent or incessant VT. Left ventricular ejection fraction (LVEF) was 34% (interquartile range, IQR: 28,5%-38%). Before the ablation, majority of the patients received beta-blocker and amidarone therapy. Repeated ablation was performed in six cases, three ablations in one patient. Incessant VT was the cause of the ablation in twenty cases.
Isthmus region(s) and exit point(s) were the primary targets of ablation, but in most of the cases further substrate modification was also done. After the ablation VT induction was performed. If the „clinical VT" remained inducible, the procedure was continued. Ejection fraction (LVEF) measured before the ablation was compared in patients with and without recurrence of VT. Ratio of VT recurrence was also collated between LVEF $< 35\%$ and LVEF $\geq 35\%$ groups.

Epicardial catheter ablation of incessant ventricular tachycardia after myocardial infarction

Endocardial catheter ablation was performed in a patient because of frequent VT episodes requiring ICD shocks late after myocardial infarction. The patient had not any VT for two months. After that slow (120 bpm) incessant VT was detected, repeated

endocardial ablation was unsuccessful. Because we were not able to terminate the incessant VT during the third endocardial attempt, epicardial ablation was decided as the last treatment option. After a successful puncture with a Touhy 17-Gr needle and using a long sheath, cooled tip ablation catheter was introduced into the pericardial space. The exit point of the VT was identified on the grounds of early activation, identical pace-map and entrainment mapping.

Radiofrequency catheter ablation of ventricular tachycardia after surgical repair of tetralogy of Fallot

The 39-year-old patient underwent surgical repair of tetralogy of Fallot in childhood. Because of frequent VT episodes ICD implantation and several times catheter ablation was performed in other institutes. VT often recurred causing ICD shocks against high dose of antiarrhythmic medication. Catheter ablation was decided using electroanatomical mapping. Ablation lines were created from the surgical scar to the pulmonary valve and to the tricuspid valve.

RESULTS

Stabilization of the coronary sinus electrode position with stent implantation

Coronary sinus side branch stenting was performed in 248 cases to anchor the lead. Pericardial effusion, CS or side branch perforation, dissection was not detected due to stenting. Follow-up period was 15±9 (max. 52) months. Follow-up is longer than 6 months in 188 cases, longer than two years in 59 patients. During follow-up 29 patients died. Electrophysiological measurements demonstrated stable pacing threshold and impedance values after stenting. After six months statistically significant but clinically not important changes of the pacing threshold and impedance were measured. Pacing threshold decreased from 1.0 V (IQR: 0.6-1.7 V) to 0.8 V (IQR: 0.6-1.3V), (p=0.003) *(Figure 3)*, impedance changed from 607 Ohm (IQR: 527-650 Ohm) to 575 Ohm (IQR: 491-659 Ohm) (p=0.017) (*Figure 4*). After two years statistically significant changes were not found. Pacing threshold changed from 0.9 V (IQR: 0.6-1.5 V) to 1.0 V (IQR: 0.5-1.5 V) (p=0.968) *(Figure 3)*, impedance decreased from 611 Ohm (IQR: 520-710 Ohm) to 565 (IQR: 500-661 Ohm) (p=0.128) *(Figure 4)*. Impedance measurements did not suggest fracture of the lead or insulation failure.

In one case left ventricular capture was not possible with maximal pacing energy in the early postoperative period. X-ray control showed proximal dislocation of the CS electrode. In this case the only suitable position was very proximally in the lateral CS side branch, because distally phrenic nerve stimulation was detected. The undersized stent was implanted into the ostium of the side

branch and it was not able to prevent the dislocation. The electrode was re-implanted into an anterolateral side branch.

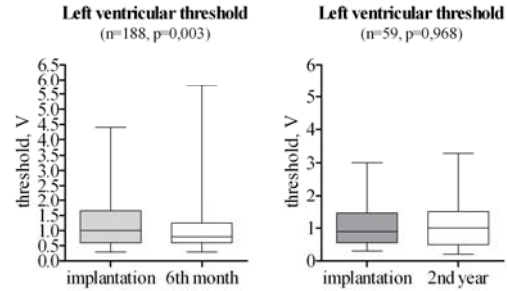

Figure 3. Changes of the left ventricular threshold after six months (n=188) and two years (n=59). Although the decrease of the threshold after six months is statistically significant, it has no clinical importance.

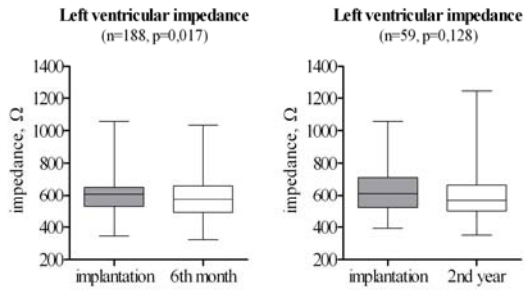

Figure 4. Changes of the left ventricular impedance after 6 months (n=188) and two years (n=59) Although the decrease of the impedance after six months is statistically significant, it has no clinical importance. Injury of the CS insulation insulation was not detected with impedance measurements.

LV pacing threshold increased from 2.2 to 5.6 V in one patient, dislocation was not founded. Scar formation in the myocardium beside the lead may explain the phenomenon. Pacing energy was increased, and further increase of the pacing threshold was not measured. Clinically important pacing threshold increase was not detected in the other 246 cases. Phrenic nerve stimulation affected

by patient position was found in five cases without macroscopic dislocation. Reprogramming of the device (decreasing the pacing voltage, increasing impulse duration) was effective in four patients, while the lead was repositioned in one case.
In three patients we had to explant the biventricular system. The cause was pocket infection in two cases, while endocarditis with vegetation formation on the electrode due to sepsis in one patient (3, 5 and 18 months after the implantation, respectively). The stented CS lead was extracted transvenously without any complications in all of the three patients. Macroscopic injuries of the insulation were not seen. One patient was sent to heart transplantation because of progressive heart failure after 27 months. Heart surgeon was able to pull out the stented lead easily. The stent was covered with a visible sheath even on the part touching with the lead. Macroscopic damages were not found, examinations with special microscops did not show significant injuries.

Minimal invasive reposition of the coronary sinus electrode

Coronary sinus was cannulated successfully via the right femoral vein in all of the nine patients. Guide wire and coronary stent was introduced into the target side branch in seven cases. In the other two patients we were not able to introduce the guide wire into the side branch because of occlusion or tortuosity of the side branch ostium. In these two cases bigger stents (Express Vascular 6.0*14 or 18 mm, Boston Scientific) were positioned into the CS proximally from the ostium of the lateral, but distally from the ostium of the posterolateral or lateral CS side branch.
Withdrawal of the CS lead with the ablation catheter was successful and acceptable new lead position was achieved in all

cases. Phrenic nerve stimulation was not detected using the maximal voltage and different pulse durations. The mean LV pacing threshold was 1.6 ± 1.1 V and the mean pacing impedance was 565 ± 62 Ohm at the implantation. The final lead position was stabilized with stenting, the stent was inflated in the side branch in seven patients, and in the main stem of the CS in two cases. Duration of the whole procedure was 28 ± 9.5 (18-42) minutes, fluoroscopy time was 11.5 ± 7.4 (4-22) minutes. Postoperative echocardiography did not reveal pericardial effusion in any case.
The mean follow-up period was 7.7 ± 4.6 (0.5-14) months. During this time phrenic nerve stimulation was not detected in 8 of the 9 patients. In one case phrenic nerve stimulation was apparent at double pacing threshold voltage when the patient lied on the left side at one month after the procedure. X-ray showed stable lead position and decreasing of the pacing voltage successfully solved the problem.
Electrophysiological measurements demonstrated stable pacing threshold and pacing impedance values, there were no statistically significant changes in these parameters compared to the implantation measurements. On the last patient visit the mean LV pacing threshold was 1.6 ± 1.4 V (p=ns). Impedance measurements (588 ± 54 Ohm; p=ns) did not suggest any signs of insulation failure or damage of the CS lead.

Transseptal endocardial left ventricular lead implantation

Transseptal puncture via the femoral vein, cannulation of the puncture site with the CARTO catheter via the subclavian vein using the elctroanatomical map and implantation of the active fixation pacemaker lead into the region of the latest left ventricular

activation was successful in both patients. Left ventricular pacing threshold was suitable (0.6 V; 0.5 ms and 0.8 V; 0.5 ms). Perioperative complication (haematoma, pericardial effusion, thromboembolic event) was not detected. During follow-up (15 and 10 months) general condition of both patients got better, they needed less amount of diuretics. Hospitalisation was not required because of worsening of heart failure. Left ventricular pacing threshold remained stable, pacing impedance measurements did not show any sign of lead injury. Thromboembolic event did not occur.

Radiofrequency catheter ablation of ventricular tachycardia after myocardial infarction

In our patient group "mors in tabula" did not occur. Primary success was achieved in 97% of the ablations, namely clinical VT was not inducible after 57 ablations using programmed ventricular extrastimulation. During follow-up (median: 10 months, IQR: 3,5-31 months) 17 patients died. Fourteen of them had VT recurrence, in ten cases the ablation was performed because of incessant VT. Four patients died during the first month, only one of them because of untreatable ventricular tachyarrhythmias. The ICD did not detected any VT in 52% of the patients, in further 35% significant decrease of the number of VT episodes requiring ICD shocks was found. Ejection fraction of patients without VT recurrence (38 %, IQR: 30-40%) was significantly higher compared with the VT recurrence group (30% (IQR: 25-30%) (p=0,0032). Ratio of VT recurrence was significantly higher in patients with LVEF < 35% collated with the LVEF ≥ 35% group (p=0,0252, odds ratio: 4,24, 95 % confidence interval :1,33 and 13,57) *(Figure 5)*.

	LVEF<35%	LVEF≥35%	altogether
VT recurrence	17	8	25
no VT recurrence	9	18	27
altogether	26	26	52

Figure 5. Recurrence of VT episodes was significantly higher in patients with seriously depressed left ventricular function.

Epicardial catheter ablation of incessant ventricular tachycardia after myocardial infarction

The incessant VT (which was permanent for one and a half months) stopped in the fifth second during the first epicardial application of radiofrequency energy in the region of the earliest left ventricular activation. After three more applications ventricular tachyarrhythmia was not inducible with programmed ventricular extrastimulation using neither right nor left ventricular pacing (550, 400 and 330 ms basic cycle length with single and double extrastimuli).

Ablation was performed without any complications. During three-year follow-up only two VT episodes were observed. They were terminated successfully by the ICD after the first attempt of antitachycardia pacing. ICD shock was not necessary. The patient is now in NYHA I-II functional stage.

Radiofrequency catheter ablation of ventricular tachycardia after surgical repair of tetralogy of Fallot

Following the ablation, VT was induced neither with programmed extrastimuli nor with isoproterenol infusion. During follow-up of twenty months, a single occurrence of monomorphic VT was

observed, which was successfully terminated by the ICD using antitachycardia pacing. At that time the patient was receiving 50 mg of metoprolol daily. Having 200 mg amiodarone and 75 mg metoprolol daily, he is currently free from arrhythmias.

CONCLUSION

1. Coronary sinus side branch stenting is an effective and safe method to anchor the position of the CS lead. The implanted stent did not hamper the extraction of the lead in our practice, if it was necessary later.

2. Withdrawn of the coronary sinus lead with ablation catheter is an effective and safe treatment of phrenic nerve stimulation caused by distal CS lead position.

3. In special cases transseptal endocardial left ventricular lead implantation guided by electroanatomical mapping may be a real treatment option.

4. In the cases of frequent ventricular tachycardia episodes causing ICD shocks and/or if antiarrhythmic drugs are not effective, radiofrequency catheter ablation may be an efficient and successful therapy for patients late after myocardial infarction. Recurrence of VT episodes was significantly higher in patients with seriously depressed left ventricular function.

5. If antiarrhythmic medication, device therapy and endocardial catheter ablation are ineffective, epicardial ablation may be attempted as last remaining therapy in the case of postinfarction incessant VT.

6. Catheter ablation may be an effective treatment of frequent VT episodes in patients after surgical correction of tetralogy of Fallot.

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