A transcatheter procedure for direct modification of the aneurysmatic left ventricle

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This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-19-00225

Introduction

Left ventricular aneurysms (LVAs) are found in 10 to 30% of patients suffering from anterior myocardial infarction[1]. Traditionally, scar reduction has required the use of invasive surgical techniques[2]. The Surgical Treatment for Ischemic Heart Failure (STICH) trial is a classic trial comparing coronary artery bypass grafting (CABG) alone with a combined procedure of CABG and surgical ventricular reconstruction[3]. Currently, catheter-based procedures for direct modification of the left ventricle are represented by the Parachute device (CardioKinetix Inc., Menlo Park, CA, USA) and the Revivent TC™ device (BioVentrix Inc., San Ramon, CA, USA)[4,5]. We report our single-centre experience and outcomes of 26 patients undergoing the Revivent "Less Invasive Ventricular Enhancement" procedure, which requires no sternotomy, no ventriculotomy, and no extracorporeal or circulatory support.

Methods

THE REVIVENT TC PROCEDURE

The Revivent procedure involves plication and exclusion of the left ventricular (LV) scar using paired micro-anchors. One anchor is implanted surgically into the scarred area of the LV epicardium whilst the other is introduced percutaneously into the right side of the interventricular septum. The most apical aspect of the LV is then excluded. The detailed steps of the procedure are illustrated in **Supplementary Figure 1** and **Supplementary Appendix 1**.

STUDY SUBJECTS, INCLUSION AND EXCLUSION CRITERIA

This is a prospective study of patients who underwent the Revivent TC procedure from January 2017 to January 2019 at a single centre. It has received approval from the Institutional Ethics Committee. All patients provided written informed consent prior to enrolment into this study. The inclusion and exclusion criteria are shown in **Supplementary Appendix 1**.

Results

From January 2017 to January 2019, 26 patients underwent a Revivent TC procedure **(Supplementary Table 1)**. In the follow-up period, two patients suffered from major adverse cardiac events (MACE), which corresponds to a primary event rate of 7.7%. One was re-hospitalised three times for recurrent heart failure; the other patient died on day 56 from multi-organ system failure.

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SUBMITTED ON 01/03/2019 - REVISION RECEIVED ON 1st 23/05/2019 / 2nd 27/09/2019 / 3rd 17/12/2019 - ACCEPTED ON 24/01/2020

LEFT VENTRICLE AND LV ANEURYSM DIMENSIONS

As shown in **Figure 1A**, LV end-diastolic diameters (LVEDD) obtained from the different views were significantly reduced (LVEDD-AP, by echocardiography, 63.6±7.1 to 55.2±7.7 mm, p<0.001), (LVEDD-MA, by cardiac magnetic resonance [CMR], 83.8±10.3 to 73.6±9.9 mm, p<0.001), (LVEDD-LS, by CMR, 61.6±8.7 to 58.4±8.1 mm, p=0.021). LV end-systolic volume (LVESV) (139.5±49.6 to 107.8±43.8 ml), LVSEV index (84.8±25.7 to 65.6±24.4 ml/m²), LV end-diastolic volume (LVEDV) (189.8±57.2 to 158.4±55.0 ml) and LVEDV index (107.8±33.2 to 90.5±31.8 ml/m²) were all significantly reduced (p<0.001). The LV aneurysm end-diastolic diameters measured between the top and bottom of the aneurysm in the two-chamber (LVAEDD2Ch 43.8±12.8 to 32.1±12.4 mm, p<0.001) or four-chamber view (LVAEDD4Ch 40.1±8.8 to 32.2±9.2 mm, p<0.001) and between the neck and the tip of the aneurysm in the four-chamber view (LVAEDD4Ch, neck 41.7±10.6 to 30.1±9.0 mm, p<0.001) by CMR were also significantly reduced.

CARDIAC FUNCTION

A series of echocardiographic and CMR examinations was performed at different time points to determine the progression in cardiac function. Left ventricular ejection fraction (LVEF), determined by echocardiography and CMR imaging **(Figure 1B)**, was significantly improved (echocardiography: 35.6±8.8% vs 45.9±9.8%, p<0.001; CMR: 28.9±8.3% vs 38.6±10.5%, p<0.001).

The six-minute walk test distance was significantly longer (368.8±40.0 to 461.5±61.2 m, p<0.001). There was no change in NT-proBNP (758.6±1,261.1 to 508.4±399.1 pg/ml, p=0.916) **(Figure 1C)**, but New York Heart Association (NYHA) heart failure class was improved at nine months (2.7±0.6 to 1.7±0.7, p<0.001).

Discussion

This study is the largest prospective study published thus far for patients undergoing left ventricular enhancement using the Revivent TC procedure, which is performed on a beating heart without sternotomy, ventriculotomy, or cardiopulmonary bypass. The main findings are that it effectively reduced LVESV, and improved LVEF, with a good safety profile, as well as acceptable complication rates and mortality endpoints. We demonstrate that this procedure can be performed safely by cardiologists with appropriate training. The novelty is the use of CMR for accurate structural and functional characterisation of cardiac function.

All patients successfully received the implantation of the micro-anchors, with a procedural success rate of 100%, and with no device implantation failure. Only two patients suffered from MACE in the follow-up of nine months. With the accumulation of experience, operative time improved from 360 min for the first case to 240 min for the last case, demonstrating the presence of an acceptable learning curve effect for experienced interventional cardiologists and cardiac surgeons.

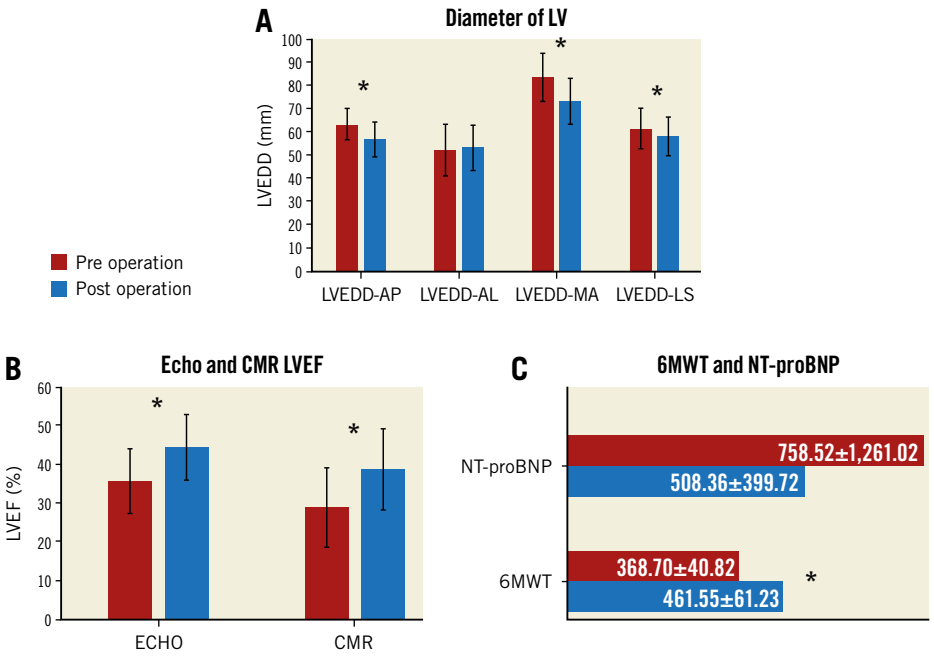

Figure 1. *LV end-diastolic diameter and cardiac function markers pre and post Revivent TC operation. A) LVEDD in different views by echocardiography and CMR. B) LVEF by echocardiography and CMR. C) NT-proBNP and six-minute walking test (6MWT). LVEDD-AL: LV end-diastolic diameter (LVEDD) measured between the anterior and lateral walls in the four-chamber view by CMR. LVEDD-AP: LVEDD measured between the anterior and posterior dimension in the long-axis view on echocardiography; LVEDD-MA: LVEDD measured between the mitral valve and the apex in the four-chamber view by CMR; LVEDD-LS: distance between the lateral wall and the septum on the short-axis view at the papillary muscle level by CMR.*

Limitations

There are several limitations of our study. Firstly, this is an observational study and was not designed to compare outcomes with patients undergoing surgical treatment or receiving only medical therapy. Another limitation is that it is only a single-centre study involving a small number of patients with relatively short follow-up.

Conclusion

The Revivent TC procedure was able to provide significant benefits in terms of left ventricular volume, ejection fraction, six-minute walk test and NYHA heart failure class nine months after the operation. Its long-term efficacy and safety should be confirmed by larger prospective studies with longer follow-up durations.

Impact on daily practice

The Revivent TC procedure is a minimally invasive hybrid operation. It is safe, effective, performed on a beating heart without ventriculotomy or cardiopulmonary bypass, and results in a significantly smaller LV, higher EF and improved function with few adverse events.

Funding

The study was funded by research grants from the Xiamen Health Commission (3502Z20179049), Xiamen Science and Technology Bureau (3502Z20151041) and Fujian province (2016-CXB-13).

Conflict of interest statement

L. Annest is an employee of the BioVentrix company. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. Methods.

Supplementary Figure 1. Pictographic representation and angiogram images of the Revivent TC operation.

Supplementary Table 1. Clinical and procedural characteristics of the study population (n=26).

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-19-00225

Supplementary data

Supplementary Appendix 1. Methods

Study subjects, inclusion and exclusion criteria

This is a prospective study of patients who underwent the Revivent TC procedure from January 2017 to January 2019 at a single centre. It has received approval from the Institutional Ethics Committee. All patients provided written informed consent prior to enrolment into this study. The inclusion criteria were: (1) patients aged 18 years or older; (2) with heart failure in New York Heart Association (NYHA) Class II-IV; (3) who have received optimal medical therapy for at least 90 days for heart failure (including statins, any one of angiotensin-converting enzyme [ACE] inhibitor, angiotensin receptor blockers [ARB], β-blocker, aldosterone receptor antagonist or diuretic); (4) significantly enlarged left ventricle with aneurysm formation by both echocardiographic and cardiac magnetic resonance (CMR) imaging criteria; (5) contiguous and transmural antero-septal or apical scar, left ventricular end-systolic volume index (LVESVI) >60 mL/m^2, and left ventricular ejection fraction (LVEF) <40% (6) with a life expectancy of one year or longer. The exclusion criteria were: (1) the presence of viable myocardium in the scar area and future coronary interventions were planned; (2) thrombus in any cardiac chamber; (3) myocardial infarction occurring within 90 days; (4) left ventricular ejection fraction <15%; (5) severely abnormal liver and kidney disease; (6) infectious endocarditis, active sepsis, and patients contraindicated for anticoagulation therapy. Eighty-one patients were screened for the Revivent TC procedure, 35 patients were deemed to be eligible for inclusion and finally 26 patients agreed to receive the Revivent TC.

The Revivent TC procedure

Patients underwent general anaesthesia. Venous access was established through the right internal jugular vein, and an incision was made in the fourth or fifth intercostal

space, depending on the position of the cardiac apex. The procedure was then performed according to the following steps. (1) A proprietary 14 Fr introducer was placed into the right internal jugular, and into the right atrium (RA); a Swan-Ganz catheter was passed into the pulmonary artery (PA) and a 0.025” wire passed into the PA, over which any instrumentation of the right ventricle (RV) could be performed without tricuspid injury. A snare was introduced into the 14 Fr introducer, over the 0.025” wire, and into the RV; the snare was expanded to serve as a fluoroscopic target for needle passage from the left ventricle (LV). (2) The anterolateral LV scar was punctured by the cardiac surgeon, using a pressure-monitored standard 18g, 70 mm needle. Using the pressure monitoring and fluoroscopy for guidance, the needle was passed through the LV, across the interventricular septum, and into the right ventricle, where a guidewire was advanced into the RV chamber. The needle was then removed and replaced with a short 6 Fr catheter sheath over the guidewire, such that its tip was in the RV. An internal mammary arteriography (IMA) catheter was then advanced through the short 6 Fr catheter, such that a 0.018” wire could be advanced to the pulmonary artery or right ventricular apex through the catheter sheath. (3) The 0.018” guidewire was then snared, and the IMA catheter was pulled into the 14 Fr introducer sheath, which was inserted through the internal jugular vein. Using the wire as a “track”, a 6 Fr catheter was advanced from the outside of the lateral LV, through the short 6 Fr and then the 14 Fr introducer and out into the supraclavicular space on the patient’s right side. (4) The initial (snared) wire was replaced with a 0.014” wire, which can be accommodated by the lumen of a poly-ether ether-ketone (PEEK) tether; the tether is passed retrogradely, over the 0.014” and through the 14 Fr introducer, the short 6 Fr, and out of the scar on the lateral LV, through which the initial needle was passed. (5) The hinged (internal) anchor is situated on the right side of the interventricular septum, and a locking (external) anchor is advanced over the tether protruding from the LV. (6) Serial anchors are similarly passed, as dictated by the patient’s anatomy, and external and internal anchors are brought together such that the lateral LV wall is apposed to the septum, excluding the intervening scar; a measured compression of “wall contact plus 1 (one) Newton (N)” is applied to ensure

durable apposition of the walls without subsequent erosion. (7) In all cases, there was an extension of the LV apex beyond that of the RV; therefore, it was necessary in all cases to place at least one so-called “LV-LV” anchor. To accomplish this, the LV apex was delivered through the incision, and a needle and guidewire passed across, such that the hinged anchor was placed on the epicardium on the right side of the LV apex, with the locking anchor on the left. (8) Careful assessment was made to ascertain that there was no shunt between the left ventricle and the aneurysm, often with repeated LV angiograms. LV and RV angiograms and transoesophageal echocardiography (TEE) were used for guidance throughout all aspects of the procedure.

Perioperative and postoperative management

Patients who underwent the procedure had been on optimised medication for at least three months, including statins, any one of ACEI/ARB, β-blocker, an aldosterone receptor antagonist and a diuretic. Warfarin was initiated postoperatively in all patients undergoing the procedure, with an international normalised ratio (INR) maintained between 2 and 2.5. Daily clopidogrel (75 mg) was added to patients with previous acute coronary syndrome or who had received coronary stents for less than one year. Both medications were discontinued five days before surgery, and patients required bridging therapy with subcutaneous injection of low-molecular weight heparin every 12 hours. Heparin anticoagulation (100 U/kg) was used during the operation, and an activated coagulation time (ACT) was maintained between 300 and 350 s. Warfarin and/or clopidogrel was used postoperatively. All patients received a statin, any one of ACEI, angiotensin receptor blocker or angiotensin receptor–neprilysin inhibitor, a beta-blocker, an aldosterone receptor antagonist, and a diuretic.

Follow-up and outcomes

All subjects received monthly follow-up by a specialist in cardiology (1 month, 3

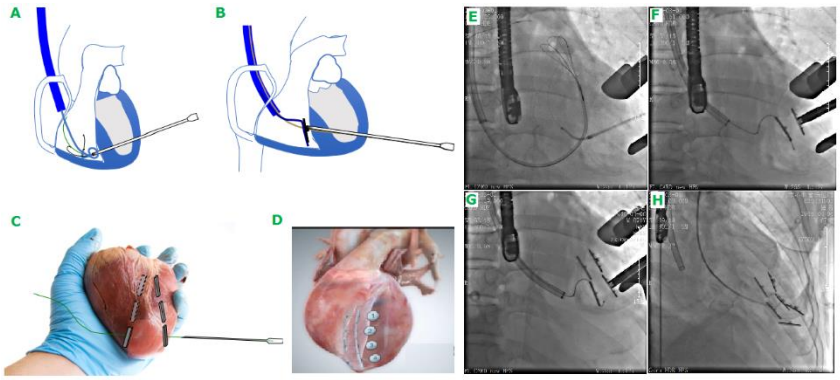
months, 6 months and 9 months after operation). Warfarin and other drug dosages were adjusted as per clinical indications and recorded during each visit. A six-minute walk test was performed and NYHA cardiac function was assessed at each visit. Transthoracic echocardiography (EPIQ 7 Ultrasound system for cardiology; Philips, Amsterdam, the Netherlands) and cardiac magnetic resonance (CMR) (Discovery™ MR750w 3.0T; GE Healthcare, Chicago, IL, USA) were performed nine months after the operation. For CMR, under the control of wireless vector cardiograms, two-dimensional body layers and motion picture images of the long axis and short axis sections of the standard heart were obtained by using one-shot excited semi-Fourier fast spin echo and real steady-state free precession sequence. The left ventricular endocardium and epicardium (papillary muscle and chordae tendineae included in the heart cavity) were delineated layer by layer (from the base of the heart to the apex of the heart). LVEDV, LVESV and LVEF were measured using the software according to Simpson's principle. The difference between the wall thickness at the end of contraction and the wall thickness at the end of diastole was regarded as the change of wall motion. CMR studies were independently analysed by two blinded cardiologists using CAAS MR Solutions 5.0 (Pie Medical Imaging, Maastricht, the Netherlands), and the atrioventricular diameter lines and cardiac function post-processing analysis of the heart were measured.

Left ventricular end-diastolic dimension (LVEDD) was measured in the long-axis view by echocardiography, and in both the four-chamber and short-axis views by CMR. LVEDD-AP refers to the LV end-diastolic diameter (LVEDD) measured between the anterior and posterior dimension in the long-axis view on echocardiography. LVEDD-AL refers to the LVEDD measured between the anterior and lateral walls in the four-chamber view by CMR. LVEDD-MA refers to the LVEDD measured between the mitral valve and the apex in the four-chamber view by CMR. LVEDD-LS refers to the distance between the lateral wall and the septum on the short-axis view at the papillary muscle level by CMR.

Procedural success was defined as completion of anchoring, and subsequent volume reduction/exclusion of scar without the need for conversion to open surgery. The safety endpoint was defined as major adverse cardiovascular events (MACE), which includes death, recurrent acute myocardial infarction, stroke, emergency surgery, and/or hospitalisation due to cardiac events. Efficacy outcomes were left ventricular end-systolic volume and left ventricular ejection fraction measured by echocardiography and CMR. The efficacy endpoint was LV and LVA volume, left ventricular ejection fraction, cardiac function, NT-proBNP and six-minute walk test (6MWT). Of these, NT-proBNP was determined at nine months only, but the 6MWT and NYHA functional class were assessed at each visit. Secondary endpoints included the severity of tricuspid and mitral regurgitation.

Statistical analysis

The characteristics of the included patient cohort were compared between before and nine months after the procedure. All measurement values are reported as means±SD. If the data were normally distributed, a paired t-test was used; otherwise, the signed-rank Wilcoxon test was used. All statistical analyses were conducted using Statistical Package for Social Sciences (SPSS), Version 25.0 (IBM Corp., Armonk, NY, USA). Two-sided p-values of <0.05 were considered statistically significant.



Supplementary Figure 1. Pictographic representation and angiogram images of the Revivent TC operation.

A) Guidewire from the LV anterolateral can be snared in the RV by a snare sent through the internal jugular vein - right atrium - right ventricle.

B) Internal anchor (LV-RV) was sent through the guidewire from the jugular vein to the LV anterolateral wall.

C) External anchors (LV-LV) were advanced through a left-sided minithoracotomy and deployed on the LV epicardium.

D) Three or four pairs of anchors were implanted.

E) Guidewire from the LV anterolateral was snared in the pulmonary artery by a snare sent through the internal jugular vein.

F), G) & H) Three pairs of anchors in one patient. The first and second anchors were internal anchors, the third one was an external anchor.

Supplementary Table 1. Clinical and procedural characteristics of the study population (n=26).

Characteristics	Outcome
Age, years	57.8±12.5
BMI	21.2±10.0
Smoker	20 (76.9%)
EuroSCORE II	
<3%	18 (69.2%)
3%~6%	4 (15.4%)
≥6%	4 (15.4%)
Comorbidities	
Diabetes	10 (38.5%)
Hypertension	9 (34.6%)
Atrial fibrillation	2 (7.7%)
Right bundle branch block	3 (11.5%)
Time between AMI and operation, months (mean±SD)	32.4±39.3
The nearest time after AMI, months	5
The longest time after AMI, months	168
Time from last LAD PCI to operation, months (mean±SD)	23.7±21.2
The nearest time after PCI to LAD, months	5
The longest time after PCI to LAD, months	67
Number of LAD stenoses ≥70 (%)	3 (11.5%)
Stenosis of LCX stenoses ≥70 (%)	0 (0%)
Stenosis of RCA stenoses ≥70 (%)	1 (3.8%)
Total anchors, n (mean±SD)	2.7±0.7
Procedural success (%)	26 (100%)
Operation time, min (mean±SD)	304.3±69.3
Longest operation time (3 anchors)	499 min
Shortest operation time (3 anchors)	240 min
Operation to general ward, days (mean±SD)	6.9±2.8

AMI: acute myocardial infarction; BMI: body mass index; LAD: left anterior descending; LCX: left circumflex artery; LVA: left ventricular aneurysm; PCI: percutaneous coronary intervention; RCA: right coronary artery; SD: standard deviation