jaa Just accepted article

EuroIntervention

Title: **Early Results of the Revivent TC Procedure for Treatment of Left Ventricular Aneurysm and Heart Failure due to Ischemic Cardiomyopathy.**

Authors: Yan Wang, M.D, PhD; Guosheng Xiao, M.D; Guoming Zhang, M.D; Bin Wang, M.D; Zhi Lin, M.D; Ho David Saiwha, M.D; Hao You, M.D; Keke Lai, M.D; Maolong Su, M.D; Hongmen Wen, MMSc; Jian Wang, MMSc; Lon Annest, M.D, PhD; Gary Tse, M.D, PhD

DOI: 10.4244/EIJ-D-19-00225

Citation: Wang Y, Xiao G, Zhang G, Wang B, Lin Z, Saiwha HD, You H, Lai K, Su M, Wen H, Wang J, Annest L, Tse G. Early Results of the Revivent TC Procedure for Treatment of Left Ventricular Aneurysm and Heart Failure due to Ischemic Cardiomyopathy. *EuroIntervention* 2020; Jaa-720 2020, doi: 10.4244/EIJ-D-19-00225

Manuscript submission date: 01 March 2019

Revisions received: 23 May 2019, 27 September 2019, 17 December 2019

Accepted date: 24 January 2020

Online publication date: 28 January 2020

Title: Early Results of the Revivent TC Procedure for Treatment of Left Ventricular Aneurysm and Heart Failure due to Ischemic Cardiomyopathy

Short title: Results of Revivent TC to Ischemic Cardiomyopathy

Authors : Yan Wang[1], MD, PhD; Guosheng Xiao[1], MD; Guoming Zhang[1], MD; Bin Wang, MD[1]; Zhi Lin, MD[2]; Ho David Saiwha[1], MD; Hao You[2], MD; Keke Lai[3], MD; Maolong Su[4], MD; Hongmen Wen[5], MMSc; Jian Wang[1], MMSc; Lon Annest[6], MD, PhD; Gary Tse[7,8], MD, PhD.

1. Department of Cardiology, Xiamen cardiovascular hospital, Xiamen University, Xiamen, China.
2. Department of Cardiac surgery, Xiamen cardiovascular hospital, Xiamen University, Xiamen, China.
3. Department of anesthesia, Xiamen cardiovascular hospital, Xiamen University, Xiamen , China.
4. Department of Ultrasound, Xiamen cardiovascular hospital, Xiamen University, Xiamen, China.
5. Interventional treatment center, Xiamen cardiovascular hospital, Xiamen University, Xiamen, China
6. Medical Office, BioVentrix, New York, USA
7. Department of Medicine and Therapeutics, Faculty of Medicine, Chinese University of Hong Kong, Hong Kong, China.
8. Li Ka Shing Institute of Health Sciences, Faculty of Medicine, Chinese University of Hong Kong, Hong Kong, China.

Yan Wang and Guosheng Xiao contributed equally to the manuscript.

Corresponding author:

Yan Wang, Department of Cardiology, Xiamen cardiovascular hospital, Xiamen University, Xiamen 361004, China.

E-mail: wy@medmail.com.cn

Classifications

Myocardial infarction, chronic heart failure, left ventricular aneurysm

Abbreviations

LVAs=Left ventricular aneurysms

NYHA=New York Heart Association

ACE=Angiotensin-converting enzyme

ARB=Angiotensin receptor blockers

CMR=Cardiac magnetic resonance

LVESVI=Left ventricular end-systolic volume index

LVEDVI=Left ventricular end-diastolic volume index

LVEF=Left ventricular ejection fraction

RA=Right atrium

PA=Pulmonary artery

RV=Right ventricle

LV=Left ventricle

IMA=Internal mammary arteriography

PEEK=Poly-ether ether-ketone

ACT=Activated coagulation time

TEE=Transesophageal echocardiography

LVEDD=Left ventricular end-diastolic dimension

MACE=Major adverse cardiovascular events

ECMO=Extracorporeal membrane oxygenation

ICD=Implantable cardioverter defibrillator

LVEDV=LV end-diastolic volume

LVESV=LV end-systolic volume

LVAEDD=Left ventricular aneurysm end-diastolic dimension

6MWT=6-minute walk test

STICH=Surgical Treatment for Ischemic Heart Failure

CABG=Coronary artery bypass grafting

Introduction

Left ventricular aneurysms (LVAs) is 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]. Surgical Treatment for Ischemic Heart Failure (STICH) trial is a classic trial comparing coronary artery bypass grafting (CABG) alone with a combined procedure CABG and surgical ventricular reconstruction [3]. Currently, catheter-based procedures for direct modification of the left ventricle are represented by the Parachute device and the Revivent-TC device [4-5]. We report our single-center experience and outcomes of 26 patients undergoing The Revivent "Less Invasive Ventricular Enhancement" procedure, which requires no sternotomy, no ventriculotomy, 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 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 the supplementary data.

Study subjects, inclusion and exclusion criteria

This is a prospective study of patients undergoing the Revivent TC procedure from January 2017 to January 2019 at a single center. 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 illustrated in the Supplementary Data.

Results

From January 2017 to January 2019, 26 patients underwent Revivent TC(Supplementary table 1). In the follow-up period, two patients suffered from MACE, which corresponding to a primary event rate of 7.7%. One was re-hospitalized three times for recurrent heart failure, and the other patient died on day 56 from multi-system organ failure.

Left ventricle and LV aneurysm dimensions

As shown in Figure 1A, LV end-diastolic diameter (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 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 ±43.8ml), 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, LVEF determined by echocardiography and CMR imaging (Figure 1B) were 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 6-minute walk test 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±1261.1 to 508.4 ±399.1 pg/ml, P=0.916; Figure 1C), but NYHA heart failure class was improved at 9 months (2.7±0.6 to 1.7±0.7, P <0.001).

Discussion

This study reports 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, improved LVEF, with a good safety profile, as well as acceptable complication rates and mortality endpoints. We demonstrate that this procedure can be safely performed by cardiologists with appropriate training. The novelty is the use of CMR for accurate structural and functional characterization of cardiac function.

All patients successfully received the implantation of the microanchors, with a procedural success rate of 100%, and with no device implantation failure. Only two patients suffered from MACE in the follow-up of 9 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.

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 low number of patients with relatively short follow-up.

Conclusion

The Revivent TC procedure could provide significant benefits in terms of left ventricular volume, ejection fraction, 6-minute walk test and NYHA heart failure class 9 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 is a minimally invasive hybrid operation. It is safe, effective, performed on a beating heart without ventriculotomy or cardio-pulmonary 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

Lon Annest is one member of BioVentrix company. All authors have no conflicts of interest to declare.

References

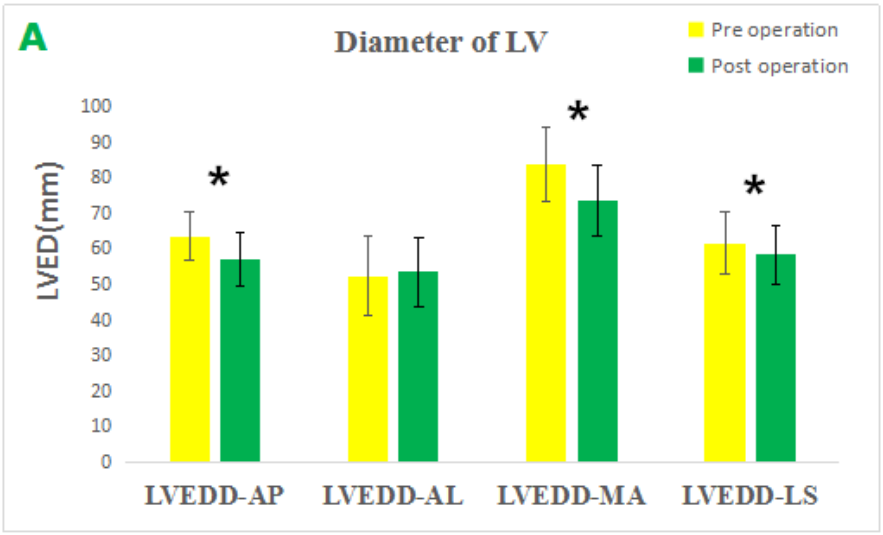
1. Sutton MG, Sharpe N. Left ventricular remodeling after myocardial infarction: pathophysiology and therapy. Circulation Jun 27 2000;101:2981-2988.
2. Jones RH, Velazquez EJ, Michler RE, Sopko G, Oh JK, O'Connor CM, Hill JA, Menicanti L, Sadowski Z, Desvigne-Nickens P, Rouleau J-L, Lee KL. Coronary Bypass Surgery with or without Surgical Ventricular Reconstruction. New England Journal of Medicine 2009;360:1705-1717.

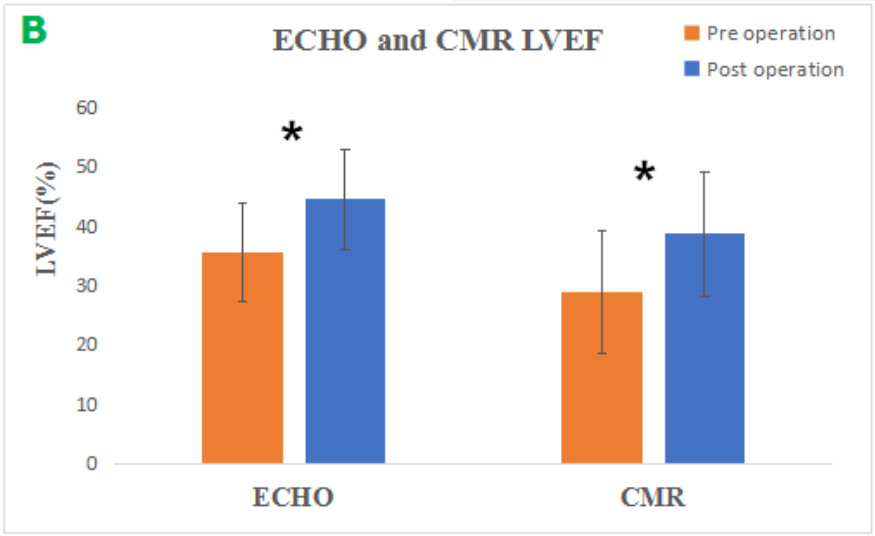
3. Michler RE, Rouleau JL, Al-Khalidi HR, Bonow RO, Pellikka PA, Pohost GM, Holly TA, Oh JK, Dagenais F, Milano C, Wrobel K, Pirk J, Ali IS, Jones RH, Velazquez EJ, Lee KL, Di Donato M, Investigators ST. Insights from the STICH trial: change in left ventricular size after coronary artery bypass grafting with and without surgical ventricular reconstruction. J Thorac Cardiovasc Surg Nov 2013;146:1139-1145 e1136.
4. Kitamura M, Schmidt T, Kuck KH, Frerker C. Heart Failure Interventions Targeting Impaired Left Ventricles in Structural Heart Disease. Curr Cardiol Rep Feb 12 2018;20:8.
5. Yun CH, Sun JY, Templin B, Lin SH, Chen KM, Wu TH, Hung CL, Liu CC, Hsu HH, Alaiti MA, Fares A, DeCicco A, Bezerra HG. Improvements in Left Ventricular Diastolic Mechanics After Parachute Device Implantation in Patients With Ischemia Heart Failure: A Cardiac Computerized Tomographic Study. Journal of cardiac failure 2017;23:455-463.

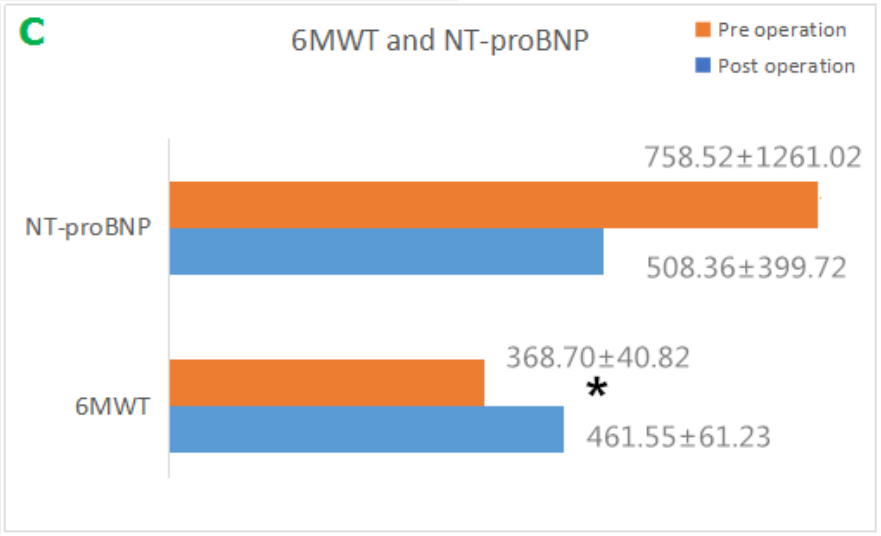
FIGURE LEGEND

Figure 1. LV end-diastolic diameter and cardiac function markers pre- and post-Revivent TC operation.

A: LVEDD in different view by echocardiography and CMR. B: LVEF by echocardiography and CMR. C: NT-proBNP and 6-minute walking test (6MWT).







Supplementary methods

Study subjects, inclusion and exclusion criteria

This is a prospective study of patients undergoing the Revivent TC procedure from January 2017 to January 2019 at a single center. It has received approval from the Institutional Ethics Committee. All patients provided written informed consent prior to enrolment into this study. As shown in Figure 1, 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 1 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. 81 patients were screened for Revivent TC, 35 patients were deemed to be eligible for inclusion and at last 26 patients agreed to receive the Revivent TC.

The Revivent TC procedure

As described by Klein (11), patients underwent general anesthesia, 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 the steps as described in the Supplementary data. (1)A proprietary 14Fr 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 an 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 14Fr 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, 70mm needle. Using the pressure monitoring and fluoroscopy for guidance, the needle was passed through the left ventricle, 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 6Fr catheter, such that an 0.018" wire could be advanced pulmonary artery or right ventricular apex through the catheter sheath. (3)The 0.018" guidewire was then snared, and IMA was pulled into the 14 Fr introducer sheath, which is inserted through the internal jugular vein. Using the wire as a "track", a 6Fr catheter was advanced from the outside of the lateral LV, through the short 6F and then the 14Fr introducer and out into the supraclavicular space on the patient's right side. (4)The initial (snared) wire was replaced with an 0.014" wire, which can be accommodated by the lumen of a poly-ether ether-ketone (PEEK) tether; the tether is passed retrograde, over the 0.014" and through the 14Fr Introducer, the short 6Fr, and out 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 on so-called "LV-LV" anchor. To accomplish this, the LV apex was delivered through the incision, and a needle and guide wire 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 is made to ascertain that there is no shunt between the left ventricle and the aneurysm, often with repeated LV angiograms. LV and RV angiograms and transesophageal echocardiography (TEE) were used for guidance throughout all aspects of the procedure.

Perioperative and postoperative management

Patients who underwent the procedure had been on optimized medication for at least 3 months, including statin, any one of ACEI/ARB, β-blocker,an aldosterone receptor antagonist and a diuretic. Warfarin was initiated post operatively on all patients undergoing the procedure, with an 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 (100u/Kg) was used during the operation, and activated coagulation time(ACT) was maintained between 300-350s. Warfarin and/or clopidogrel was used postoperatively. All patients received a statin, any one of angiotensin-converting enzyme inhibitors, 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. 6-minute walk test and NYHA cardiac function was performed at each visit. Transthoracic echocardiography (Philips EPIQ 7 Ultrasound system for cardiology) and cardiac magnetic resonance (CMR) (GE 750w 3.0T) were performed 9 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 tendinalis 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 analyzed by two blinded cardiologists using CAAS MR solutions 5.0, and the atrioventricular diameter lines and cardiac function post-processing analysis of the heart were measured respectively.

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. As in Figure 2, 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 the anchor, and subsequent volume reduction/exclusion of scar without the need for conversion to open surgery. Safety endpoint was defined as major adverse cardiovascular events, (MACE), which includes death, recurrent acute myocardial infarction, stroke, emergency surgery, and/or hospitalization due to cardiac events. Efficacy outcomes were left ventricular end-systolic volume and left ventricular ejection fraction were measured by echocardiography and CMR. The efficacy endpoint is LV and LVA volume, left ventricular ejection fraction, cardiac function, NT-ProBNP and 6-minute walk test (6MWT). Of these, NT-ProBNP was determined at 9 months only, but 6-minute walk test and NYHA functional class were assessed at each visit. Secondary endpoints include the severity of tricuspid and mitral regurgitation.

Statistical analysis

The characteristics of the included patient cohort were compared between before and 9 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. (IBM SPSS version 25.0, Armonk, NY). Two-sided P-values of <0.05 will be considered statically significant.

Supplementary table 1

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

Characteristics	Outcome
Age	57.8±12.5
BMI	21.2±10.0
Smoke	20 (76.9%)
Euro SCORE 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 stenosis ≥70 (%)	3 (11.5%)
Stenosis of LCX stenosis ≥70(%)	0 (0%)
Stenosis of RCA stenosis ≥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

BMI:Body Mass Index, AMI:acute myocardial infarction, LAD:left anterior descending, PCI: percutaneous coronary intervention, LCX:left circumflex artery, RCA: right coronary artery, SD:Standard deviation, LVA: left ventricular aneurysm.

Supplementary Figure 1

Pictographic representation and angiogram images of the Revivent TC operation.

A: Guidewire from LV anterolateral can be snared in RV by a snare sent through internal jugular vein - right atrium - right ventricle. B: Internal anchor (LV-RV) was sent through guidewire from jugular vein to LV anterolateral wall. C: External anchors (LV-LV) were advanced through a left-sided minithoracotomy and deployed on the LV epicardium. D: 3 or 4 pairs of anchors were implanted. **E**: Guidewire from LV anterolateral was snared in pulmonary artery by a snare sent through internal jugular vein. F, G, H: 3 pairs of anchors in one patient, the first and second anchor were internal anchors, the third one was an external anchor.