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REVIEW

# Patient selection for LIVE therapy: From clinical indications to multimodality imaging individual case planning

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## Abstract

**Background:** Less Invasive Ventricular Enhancement (LIVE) with Revivent TC is an innovative therapy for symptomatic ischemic heart failure (HF). It is designed to reconstruct a negatively remodeled left ventricle (LV) after an anterior myocardial infarction (MI) by plication of the scar tissue. Its indications are specific, and as with any other structural heart intervention, the success of the procedure starts with appropriate patient selection. We aim to present the indications of the technique, crucial aspects in patient selection, and individual case planning approach.

**Methods and results:** After clinical evaluation, transthoracic echocardiography is the first imaging modality to be performed in a potential candidate for the therapy. However, definitive indication and detailed case planning rely on late gadolinium-enhanced cardiac magnetic resonance imaging or multiphasic contrast-enhanced cardiac computed tomography. These imaging modalities also assist with relative or absolute contra-indications for the procedure. Individual assessment is done to tailor the procedure to the specifics of the LV anatomy and location of the myocardial scar.

**Conclusion:** LIVE procedure is a unique intervention to treat symptomatic HF and ischemic cardiomyopathy after anterior MI. It is a highly customizable intervention that allows a patient-tailored approach, based on multimodality imaging assessment and planification.

KEYWORDS
heart failure, LIVE, Revivent TC, ventricular restoration

## 1 | BACKGROUND

Heart failure (HF) is an increasingly important source of morbidity and mortality in developed nations, and ischemic cardiomyopathy (ICM) is the most common cause.[1] Despite adequate treatment, with prompt percutaneous coronary intervention (PCI), up to 50% of patients lose 18% or more of left ventricular (LV) mass due to an acute myocardial infarction (MI).[2] Following primary PCI, guideline-directed medical therapy (GDMT) decreases the degree of LV remodeling, consequently reducing the development of ICM. Notwithstanding optimal GDMT after early reperfusion therapy, negative LV remodeling (defined as an increase of LV end-diastolic volume > 20% from baseline) has been observed in approximately one third of acute MI patients.[3] This increased LV volume is associated with major cardiac events, such as

  

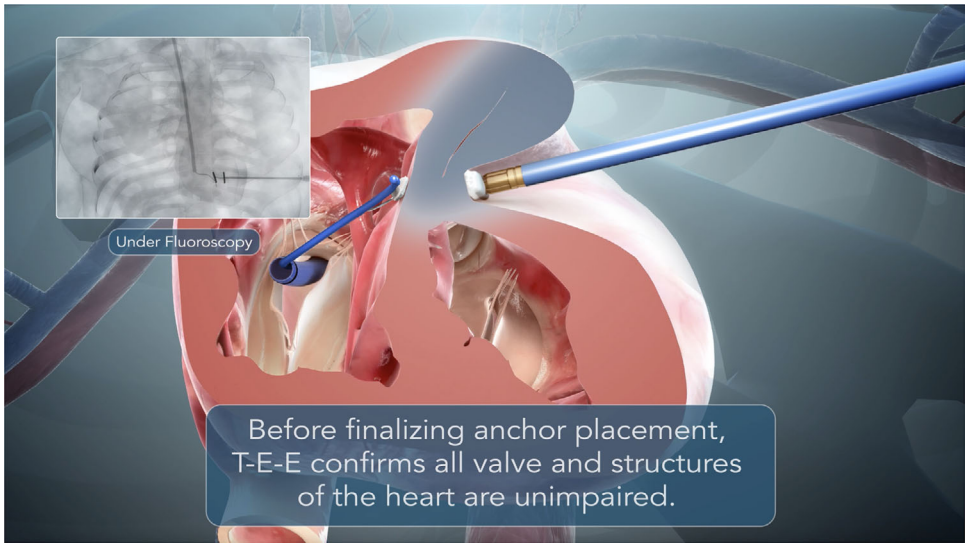


**FIGURE 1** Internal and external anchor deployment

congestive HF, functional mitral regurgitation, apical aneurysm, risk of ventricular arrhythmia and sudden cardiac death. It is also related with decreased survival.[4]

In patients with a negatively remodeled LV, in whom the LV volume is increased, LV ejection fraction (EF) is depressed because of increased wall tension and less efficient myocardial fiber orientation and anterior myocardial scar tissue of at least 50% transmurality, surgical ventricular reconstruction is an established therapy that can be considered. Its drawbacks are that this is a highly invasive open-heart surgical procedure performed with the use of extracorporeal circulation (ECC) and cardioplegic myocardial arrest.[5] Less Invasive Ventricular Enhancement (LIVE) technique with Revivent TC system (BioVentrix Inc., San Ramon, CA, USA) has been developed as an equally effective therapy to reconstruct the LV to decrease LV volume, reconstruct its physiologic shape and reduce LV wall tension. All this is aimed to improve LV performance leading to reduction of HF symptoms, increase quality of life, and improve survival.[6]

## 2 | LIVE THERAPY OVERVIEW

LIVE therapy is a hybrid procedure, based on teamwork between a cardiac surgeon, an interventional cardiologist and an imaging cardiologist/radiologist. It is performed in a hybrid operative room under general anesthesia. It requires a small left thoracotomy, and depending on the strategy, a right internal jugular vein access (RIJV).

LV shape and size are restored on a beating heart, without ECC by plication and exclusion of the scarred myocardium. This is achieved by implantation of a series of titanium microanchors (5 mm × 25 mm) brought together over a poly-ether-ether-ketone tether (1.7 mm × 1.0 mm) to exclude the scarred myocardium. This is either achieved as an LV-LV approximation, or as a right ventricular (RV)-LV approximation, depending on the scar distribution. In the RV-LV approach, internal anchors are deployed over-the-wire, through the RIJV, on the right side of the ventricular septum (Figure 1).

The procedure is guided by multimodality imaging, with constant fluoroscopic and transesophageal echocardiography (TEE) monitoring. A baseline LV angiogram is executed, and every catheter exchange and anchor deployment is done with fluoroscopic monitoring. A final LV angiogram is performed to confirm that all akinetic and/or dyskinetic segments were excluded. TEE is used to assess baseline LV volumes and compare them with the final result. Continuous valvular assessment is also important, mainly of the tricuspid valve, due to snaring maneuvers and catheter exchange below this structure.

The LIVE procedure most recent results were presented at the European Society of Cardiology 2020 Congress.[7] No early or intra-hospital mortality was reported. A mean of 2.3 anchor pairs (median 2) were used to reshape the LV. Echocardiographic data showed an increase in LV EF from 31.4 ± 9.2% to 40.0 ± 12.4% (change +29.8%, $P < 0.001$) and LV end-systolic volume index (LVESVI) reduction from 66.6 ± 29.3 ml/m$^2$ to 40.7 ± 21.5 ml/m$^2$ (change −38%, $P < 0.001$) and LV end-diastolic volume index reduction from 92.8 ± 39.2 ml/m$^2$ to 60.6 ± 25.9 ml/m$^2$ (change −33.2%, $P = 0.001$) after the procedure. In the mean follow-up period of 9.8 months, NYHA class improved a median of 1 grade and there was no late mortality. The biggest single center experience on the therapy was recently presented at EuroPCR 2021[8] reporting no short-term mortality and 84% survival at 45 months on a 27 consecutive patient cohort, treated between October 2016 and January 2021. At latest follow-up, 96% of surviving patients were in NYHA-class I–II, compared to 19% preoperatively.

Recently, to robustly demonstrate that the LIVE procedure with the Revivent TC system is more effective than GDMT alone for the treatment of ischemic HF, a randomized controlled trial—Revivent TC versus Guideline Determined Medical Therapy (REVIVE-HF, NCT03845127)—has been developed and started patient enrolment in 2019. Results are expected in 2022.

**TABLE 1** Overview of imaging modalities

| Modality | What to look for |
|---|---|
| Screening | |
| TTE | Akinesia and dyskinesia of apex, apical septum, and anterior wall |
| | Residual function of other segments |
| | Biplane (Simpson) or 3D volumetry and LVEF (avoid foreshortening) |
| | Apical thrombus (consider contrast imaging) |
| | Increased pulmonary pressure and low RV-function |
| Planning | |
| MRI and CT | Location and distribution of the scar |
| | Transmurality of the scar (MRI only) |
| | Wall motion abnormalities |
| | Ventricular wall diameters (esp. CT) |
| | Accurate volumetry |
| | Additional structures and/or devices, for example, location of RV device leads, CABG (4D) (CT) |

Abbreviations: 3D/4D, three/four dimensional; CABG, coronary artery bypass graft; CT, computed tomography; LVEF, left ventricular ejection fraction; MRI, magnetic resonance imaging; TTE, transthoracic echocardiography.

## 3 | PATIENT SCREENING

Potential candidates for LIVE therapy present with symptomatic HF (NYHA class ≥ II) due to cardiac dysfunction caused by a previous anterior MI, despite maximal GDMT. They typically have increased LV systolic volume (LVESVI > 50 ml/m$^2$) and an EF below 45%, both due to a discrete, contiguous, acontractile (akinetic and/or dyskinetic) scar located in the antero-septal, apical region of the LV. The myocardial scar needs to be at least 50% transmural to provide sufficient support and resistance to the plicating anchors. Alternative myocardial scar locations can also be considered for treatment, as lateral wall scar. Furthermore, patients with purely dyskinetic LV anterior or antero-apical walls that could be described as classic or "true" LV aneurysms are good candidates for LIVE therapy. There should be sufficient scar maturation or fibrotic tensile strength developed to provide adequate support (and prevent "pull through" and wall lesion) for the anchors. As such, the initial ischemic myocardial event should have taken place at least 90 days before the intervention. After appropriate clinical assessment, imaging is essential to assess indication, eligibility, and potential contra-indications for the therapy (Table 1—multimodality imaging overview; Table 2—exclusion criteria). This stepwise approach is described below.

### 3.1 | Transthoracic echocardiography

Initial assessment includes transthoracic echocardiography (TTE), where the focus is to look for akinetic and/or dyskinetic areas within the left anterior descending (LAD) artery myocardial territory—LV anterior wall, anterior septum, and apex. For that purpose, the apical 2-, 3- and 4-chamber views, respectively, are most commonly used. Standard echocardiographic equipment is used, including harmonic imaging with a 3.5 MHz broadband transducer, with capture of at least 3 beats per view (5 beats/view in atrial fibrillation at a normal heart rate). Additionally, contractility of the basal segments is assessed, in order to estimate both the baseline residual function after the reconstruction and—more importantly—the potential for improved myocardial performance. Valvular heart disease and RV size and function are also evaluated. A contrast-enhanced examination is not mandatory, although it further increases diagnostic accuracy of intracardiac thrombus, which is a relative contra-indication for the procedure. 3D echocardiography may optimize the quality of TTE screening, by providing more accurate volume and EF assessment, identification and quantification of akinetic and/or dyskinetic areas and by creating a 3D LV model. Figure 2 summarizes key aspects in TTE screening for the LIVE procedure.

**TABLE 2** Exclusion criteria and appropriateness of imaging modality

| | Echo | MRI | CT |
|---|---|---|---|
| Inadequate myocardial viability | ++ | +++ | +++ |
| Intraventricular thrombus | ++ | +++ | +++ |
| Pulmonary arterial pressure > 60 mm Hg | +++ | + | + |
| Calcified ventricular wall in the area of intended scar | – | + | +++ |

Appropriateness strength of each imaging modality for different exclusion criteria: (–): method not suited for assessment, (+): poor, (++): good, and (+++): excellent appropriateness, respectively.

### 3.2 | Cardiac magnetic resonance imaging

If the patient is considered suitable for the technique by clinical and initial TTE evaluation, a late gadolinium contrast enhanced (LGE) cardiac magnetic resonance (CMR) is requested in order to precisely define the location and transmurality of the myocardium scar. Furthermore, LGE CMR gives important information about LV geometry, volume, and function and it accurately rules out the presence of intracardiac thrombus. If a thrombus is detected, the recommendation is to anticoagulate patient with vitamin-K antagonizing agents, for example, warfarin, for 3 months and repeat the LGE CMR. Figure 3 summarizes key aspects in LGE CMR screening for the LIVE procedure.

### 3.3 | Cardiac computed tomography

Alternatively to LGE CMR, in patients with intracardiac devices not compatible with it, LV wall motion and scar assessment is done using contrast enhanced multiphasic 4D computed tomography (CT). Even in patients with MRI conditional devices, 4D CT may be better for regional motion assessment of the interventricular septum, mainly in patients with pacemaker/implantable cardioverter defibrillator/cardiac resynchronization therapy leads placed in the right side of

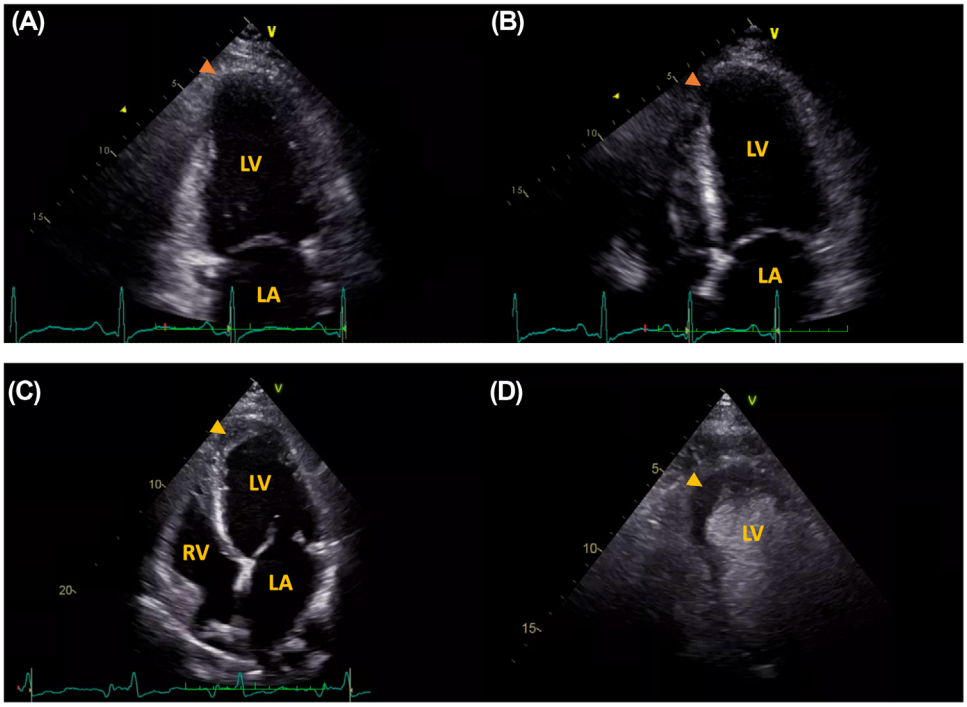


**FIGURE 2** (A,B) Apical 2- and 4-chamber views, respectively, showing LV dilatation and bulbous apex, with apical, distal anterior, and septal wall thinning (orange arrowheads); (C,D) apical 4-chamber view showing apical thrombus (arrowheads) without (C) and with contrast-enhancement (D). LA, left atrium; LV, left ventricle; RV, right ventricle

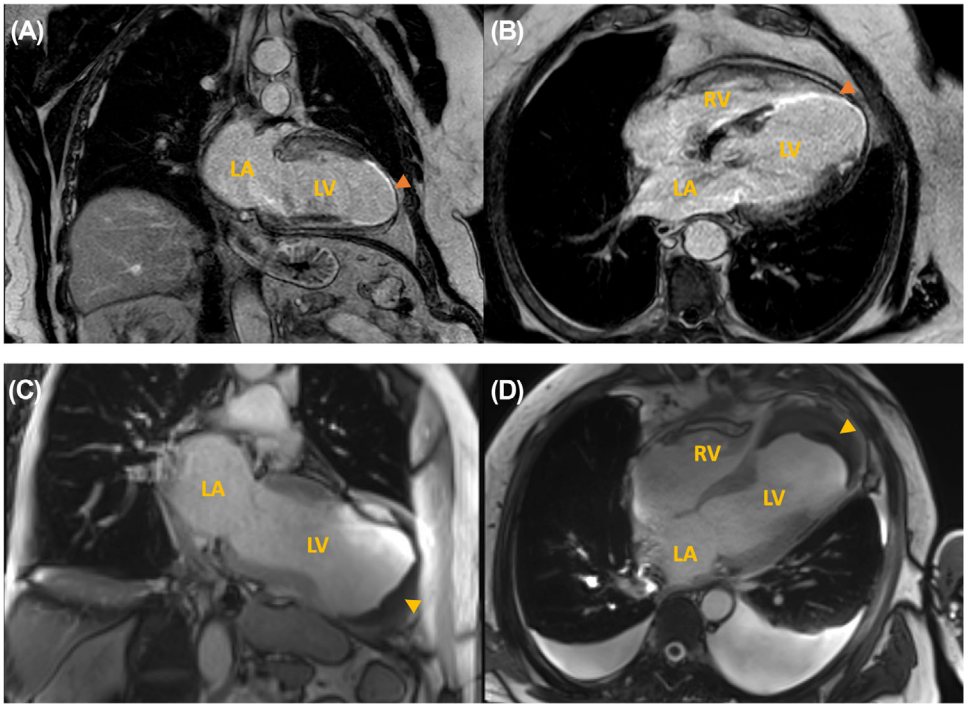


**FIGURE 3** (A,B) 2 and 4 chamber LGE views showing LV dilatation and transmural scar in distal antero-septal walls and apex (orange arrowheads); (C,D) large LV apical thrombus (yellow arrowheads). LA, left atrium; LV, left ventricle; RV, right ventricle

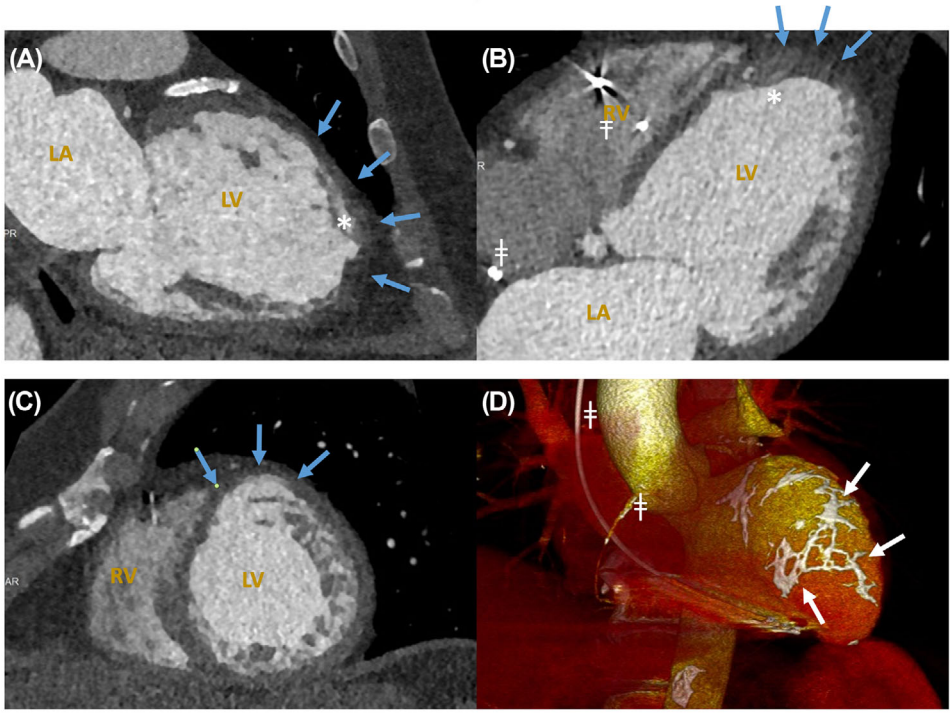


**FIGURE 4** Contrast-enhanced multiphasic CT scan: 2- (A) and 4-chamber view (B), demonstrating LV dilatation, anterior and apical wall thinning (blue arrows), and LV apical thrombus (*); (C) short axis view of the same patient, demonstrating antero-septal wall thinning (blue arrows); (D) 3D volume rendering contrast-enhanced CT scan of a patient with extensive LV antero-lateral scar and wall calcification (white arrows). Pacemaker leads are illustrated in (B) and (D) (‡). LA, left atrium; LV, left ventricle; RV, right ventricle

it. Despite not having direct scar determination capabilities, 4D multiphasic CT scan is a powerful tool in regional wall thickness and motion assessment as well as LV volume assessment.[9] Thinned, akinetic, or dyskinetic regions are considered non-viable, and as such, suitable for exclusion with the LIVE technique. Although sensitivity and specificity are lower than LGE CMR, existence of an apical thrombus can also be assessed by CT.[10] Extensive LV wall calcification is an absolute contraindication for the procedure and can be easily depicted from CT, and not from CMR. Additionally, 3D multiphasic volume rendering is an important tool in determining scar location, assessing basal wall contractility, and precise planning of anchor placement. Finally, 4D CT is useful in assessing graft positioning in postcoronary artery bypass graft patients. Figure 4 summarizes key aspects in 4D multiphasic CT screening for the LIVE procedure.

## 4 | CASE PLANNING

LIVE therapy with Revivent TC encompasses two main techniques: RV-LV and LV-LV approaches. The first one, RV-LV, includes an internal anchor deployment, through the RIJV, bringing the interventricular septum together with the antero-lateral LV wall (Figure 1). The more distal apex is also excluded with external, surgically applied anchor pairs.[11] When the septal component is not significant or transmural enough, antero-lateral and apical scar is excluded with external, surgically applied, LV-LV anchor pairs.

### 4.1 | RV-LV

RV-LV approach is used when there is a significant septal distribution of the myocardial scar. To evaluate the scar location and to plan the procedure, short axis stacks of LGE CMR or 4D multiphasic CT scan are used. Both location and extension of the scar are assessed in order to plan anchor placement and the number of needed devices. The internal anchor and the corresponding external anchor pair are the first ones to be implanted. Then, if more scar is identified basally to this pair, a second external anchor pair is applied in this location. This anchor pair can exclude a portion of septal scar as well, sacrificing a small portion of the RV—this is nicknamed the "Antonius stitch," after the development of this modification at the St. Antonius Hospital, Nieuwegein, The Netherlands (a hospital with extensive experience with the LIVE procedure) (Figure 5). Finally, the apical component is treated with LV-LV anchor pairs. If the scar does not affect the entire apical circumference, anchor placement can be tailored to exclude only the non-viable segments.

### 4.2 | LV-LV

LV-LV scar exclusion can be applied when there is LV scar limited to the antero-lateral and apical walls, without septal involvement. Consequently, the reconstruction does not include the septum in the exclusion. As such, the procedure is carried out in a purely surgical fashion.

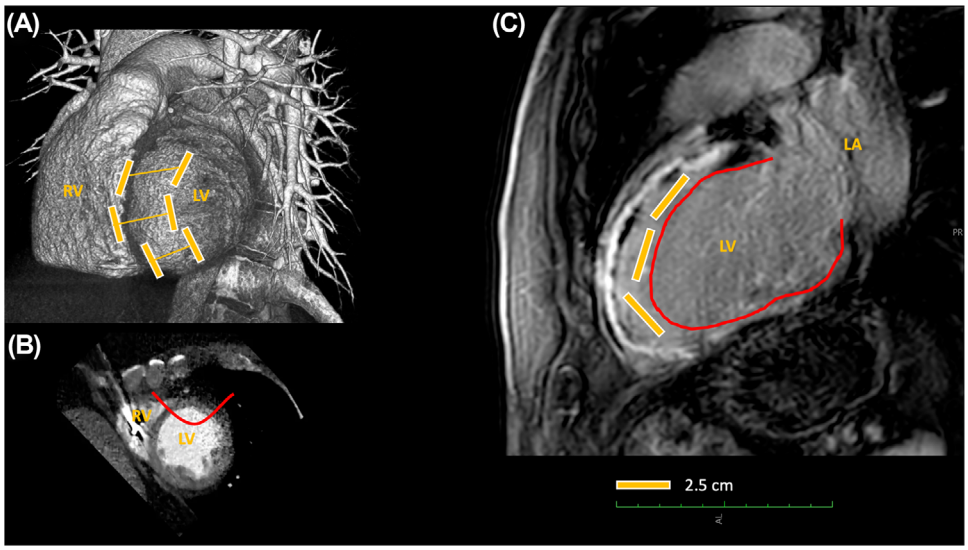


**FIGURE 5** CT scan: (A) case planning according to scar location on 3D volume rendering; (B) RV-LV basal "Antonius" stitch, addressing additional antero-lateral and septal components of the scar; (C) expected result of preoperative LGE CMR (red line). Anchors are represented by yellow rectangles. LA, left atrium; LV, left ventricle; RV, right ventricle

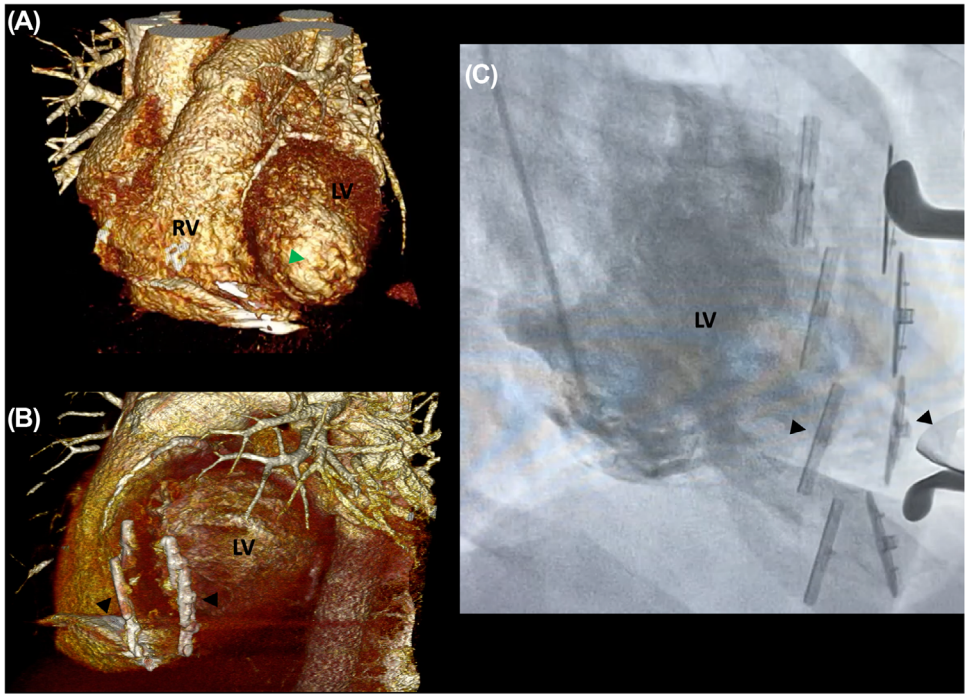


**FIGURE 6** (A) Preoperative 3D volume rendering CT of a patient with distal antero-lateral and apical scar (green arrowhead); (B) postoperative 3D volume rendering CT of the same patient with three LV-LV anchor pairs deployed, demonstrating full scar exclusion; (C) postoperative LV ventriculography of patient with lateral LV scar, treated with four linear LV-LV anchor pairs (black arrowheads pointing to an anchor pair). LV, left ventricle; RV, right ventricle

Case planning follows the same principles of multimodality imaging. Anchor deployment and orientation can be tailored to the scar location and full scar exclusion should be feasible in most patients (Figure 6B). The patients treated with this therapy have suffered from a LAD MI and the consequent scar tissue is located in anterior, antero-septal, antero-lateral, and apical segments. However, different scar locations can be addressed with this technique as it is essentially based on plicating scarred segments, using the same surgical approach. In fact, manipulation of the heart from an apical skin incision by the liberal use of "myocardial leashes"—temporary "U" stitches in the scarred

myocardium, snugged and fixed with a hemostatic clamp, enabling direct manipulation of the heart without hemodynamic disturbance—allows the surgeon to expose the lateral and inferior walls as well. Figure 6C shows an example of a postoperative left ventriculography of patient with an extensive lateral scar due to a previous left circumflex MI.

## 5 | FUTURE PERSPECTIVES

As any other structural heart intervention, LIVE therapy is based on multimodality imaging for procedural guidance and planning. A full 3D understanding of the LV is needed to precisely plan this unique intervention. New technologies such as augmented reality and 3D printing may further improve screening and case planning, by providing a more detailed and realistic view of the diseased LV.[12]

Regarding intraoperative monitoring, the combination of TEE with fluoroscopy is the foundation of interventional imaging. However, these two modalities are displayed on different screens, and are handled by different operators, which adds complexity for the interventional team. Fusion echocardiographic-fluoroscopic imaging combines, in a single view, the accurate visualization of catheter and devices provided by fluoroscopy with the continuous soft tissue information provided by TEE, which may further simplify the intraprocedural guidance.[13]

## 6 | CONCLUSION

LIVE procedure is a hybrid and minimally-invasive procedure to treat a negatively remodeled LV by plication of myocardial scar tissue in the context of ICM after an anterior MI. Its indications are specific and patient selection is crucial to achieve an optimal result. After clinical assessment, multimodality imaging is essential to confirm indication, rule-out contraindications, and to plan the procedure. Since the procedure is highly customizable by the combination of its different technical options, it allows for a true patient tailored approach to achieve the optimal results in improving ventricular performance.

### AUTHOR CONTRIBUTIONS

Paulo Neves and Thasee Pillay did paper drafting. All other authors did critical revision of the article and approved the article.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, PN, upon reasonable request.

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### REFERENCES

1. Roth GA, Mensah GA, Johnson CO, et al.; GBD-NHLBI-JACC Global Burden of Cardiovascular Diseases Writing Group. Global burden of cardiovascular diseases and risk factors, 1990-2019: update from the GBD 2019 study. *J Am Coll Cardiol*. 2020;76(25):2982-3021.
2. Stone GW, Selker HP, Thiele H, et al. Relationship between infarct size and outcomes following primary PCI: patient-level analysis from 10 randomized trials. *J Am Coll Cardiol*. 2016;67(14):1674-1683.
3. Savoye C, Equine O, Tricot O, et al. Left ventricular remodeling after anterior wall acute myocardial infarction in modern clinical practice (from the REmodelage VEntriculaire [REVE] study group). *Am J Cardiol*. 2006;98(9):1144-1149.
4. Bolognese L, Neskovic AN, Parodi G, et al. Left ventricular remodeling after primary coronary angioplasty: patterns of left ventricular dilation and long-term prognostic implications. *Circulation*. 2002;106(18):2351-2357.
5. Ruzza A, Czer LSC, Arabia F, et al. Left ventricular reconstruction for postinfarction left ventricular aneurysm: review of surgical techniques. *Tex Heart Inst J*. 2017;44(5):326-335.
6. Zivelonghi C, Klein P, Swaans MJ, Agostoni P. Hybrid transcatheter left ventricular reconstruction for the treatment of ischaemic cardiomyopathy. *EuroIntervention*. 2018;13(16):1899-1901.
7. Neves P, Pillay T, Van Bladel K, Annest A. LIVE procedure for ischemic heart failure: the evolution of an unique technique. *Eur Heart J*. 2020;41(Supplement_2):ehaa946.1132.
8. Klein P, van Kuijk JP, Swaans M. Update on mid-term results of hybrid transcatheter and minimally invasive left ventricular reconstruction for the treatment of ischemic cardiomyopathy. *EuroPCR*. 2021. 18-20 May 2021, online event.
9. Rizvi A, Deaño RC, Bachman DP, Xiong G, Min JK, Truong QA. Analysis of ventricular function by CT. *J Cardiovasc Comput Tomogr*. 2015;9(1):1-12.
10. McCarthy CP, Vaduganathan M, McCarthy KJ, Januzzi JL Jr, Bhatt DL, McEvoy JW. Left ventricular thrombus after acute myocardial infarction: screening, prevention, and treatment. *JAMA Cardiol*. 2018;3(7):642-649.
11. Pillay T, Neves P, Benetti F, Van Bladel K, Wechsler A, Annest L. Minimal access left ventricular reconstruction. *J Card Surg*. 2020;36(1):300-306.
12. Harb SC, Rodriguez LL, Vukicevic M, Kapadia SR, Little SH. Three-dimensional printing applications in percutaneous structural heart interventions. *Circ Cardiovasc Imaging*. 2019;12(10):e009014.
13. Ternacle J, Gallet R, Nguyen A, et al. Usefulness of echocardiographic-fluoroscopic fusion imaging in adult structural heart disease. *Arch Cardiovasc Dis*. 2018;111(6-7):441-448.

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