

Article

Surgical Ventricular Restoration: Long-Term Results in Ventricular Remodeling and Risk of Arrhythmias

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Abstract

Background: Surgical ventricular reconstruction (SVR) is performed in patients with post-infarction left ventricular remodeling with the aim of reducing ventricular volumes through the exclusion of most of the scarred tissue and to reduce the incidence of inducible ventricular tachycardia. It is not known whether SVR without concomitant anti-arrhythmic surgical procedures is sufficient for the prevention of late arrhythmias or sudden death. **Methods:** Patients who underwent SVR at our center from January 2008 to February 2021 were included in the study. All patients had complete clinical and echocardiographic evaluations before surgery, after surgery and at follow up. **Results:** Overall, 55 patients were included (mean age 61.5 ± 10 years), 45 male (82%). One patient died intraoperatively due to a massive thrombus embolization from the aneurysmal cardiac apex to the coronary ostia. Complete bypass grafting was first performed when indicated in 28 patients (51%); concomitant mitral valve treatment was performed in 5 patients (9%). A total of 19 patients underwent rescue percutaneous coronary intervention (35%). An implantable cardioverter-defibrillator (ICD) was implanted in 13 patients (24%) in the postoperative period (almost 3 months post-op). All surviving patients underwent follow-up (mean 8.5 ± 4.5 years) with complete clinical and echocardiographic examination. The Cox regression model revealed that, after accounting for confounding factors such as sex, age, smoking, hypertension, previous stroke, diabetes, ICD implantation does not significantly improve patient survival. However, a univariate analysis comparing total mortality and sudden death in patients with vs without ICD showed a significant difference. **Conclusions:** SVR is effective in improving patient symptoms and ventricular function. However, as this tech-

nique does not involve ablative treatments, the risk of sudden death remains high and patients should undergo electrophysiological re-evaluation for preventive ICD implantation.

Keywords

surgical ventricular restoration; ventricular arrhythmia; long-term outcome; revascularization

Introduction

Myocardial infarction (MI) with impaired left ventricular ejection fraction (LVEF) accounts for approximately 50% of deaths due to progressive cardiac failure and sudden death. In the pre-implantable cardioverter-defibrillator (ICD) era, several surgical techniques were developed for the treatment of ventricular tachyarrhythmias, including aneurysmectomy [1–4], mapping- or non-mapping-guided endocardial resection with or without left ventricular (LV) aneurysmectomy [5–8], catheter ablation [9], and coronary revascularization [10]. However, the reported recurrence rates, the complexity of map-guided interventions, and the high rates of sudden death recorded in post-MI patients with spontaneous and inducible ventricular tachycardia (VT), all suggested that these approaches were not adequately effective in preventing life-threatening ventricular arrhythmias (VA). Patients with ischemic heart failure (HF) show LV systolic dysfunction and progressive LV dilation, frequently accompanied by necrotic myocardial lesions, subsequent scar formation, and thinning of the infarct zone [11–14]. Surgical ventricular reconstruction (SVR) is performed in post-MI patients with LV adverse remodeling and

HF with the aim of reducing LV volumes through exclusion of the scarred tissue, thereby reshaping the LV cavity. This treatment option has been associated with improved LVEF and functional status, and reduced LV mechanical dyssynchrony [15–18]. Also, it has been speculated that SVR induces a more physiological-like alignment and contraction of the anatomically normal fibers within the residual myocardium [18–21].

SVR was first described by Dor *et al.* [22,23] and involves resection of scar, septal exclusion, and cavity reduction by endoventricular patch plasty. These authors found that extended, non-guided endocardectomy and cryosurgery at lesion borders drastically reduced the incidence of postoperative inducible VT, minimizing the need for ICD [24–26]. However, optimal treatment for VA is uncertain, and several questions remain unanswered: Should programmed ventricular stimulation be routinely performed in all patients undergoing SVR [1,4]? Should it be performed before, after, or before and after surgery? And should an ICD be used if spontaneous or inducible arrhythmias persist [3]? Other unsolved issues include: What is the anti-arrhythmic mechanism of the surgical procedure [1,4]? Is residual inducible VT caused by subtotal non-guided endocardial resection, associated cryoablation, or both? And Is the corrective factor complete coronary revascularization, volume reduction, or improved pump function [3]? A part of the answer is that SVR reduces LV size [20,27] which may therefore also reduce the incidence of late VA because myocardial stretching is thought to contribute to the development of VA [28]. However, it is not known whether SVR without concomitant anti-arrhythmic surgery provides sufficient protection from late arrhythmias or sudden death [29]. HF and surgical treatment of HF are expected to increase in frequency, therefore, the incidence of VA after SVR with or without concomitant anti-arrhythmic surgery is of interest with regard to the optimal treatment for patients with LV aneurysms. The aim of this study was to review our experience in SVR with clinical and echocardiographic follow-up, as an observational study, with a particular focus on arrhythmic events.

Materials and Methods

Surgical Technique

Our surgical technique has been described previously [30]. In brief, after identification of the antero-apical LV aneurysm (Fig. 1A), a left ventriculotomy incision of 6–8 cm is made lateral and parallel to the left anterior descending coronary artery at the level of the akinetic/dyskinetic or aneurysmal area (Fig. 1B). Then, the LV cavity is inspected for the presence of a thrombus and to delineate the borders of the aneurysm. Finally, an endocavitary oval patch (~6–7

× 2–2.5 cm) is sutured to the borders of the scar (Fig. 1C).

According to our institutional protocol, at baseline all patients were optimally treated with aspirin, beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and statins. In cases of clopidogrel as second antiplatelet therapy, it was continued or withdrawn based on the timing of coronary angioplasty. All patients had complete clinical and echocardiographic evaluation before surgery, and underwent SVR under total cardiac arrest with antegrade cold blood cardioplegia.

All patients provided written informed consent for inclusion, data or sample collection/use and/or publication of data results.

Echocardiographic Evaluation

All ultrasound datasets (2D-3D) were stored/performed and processed live with a GE Vivid E95 ultrasound system (GE Healthcare; Vingmed Ultrasound, Horten, Norway) equipped with an M5S probe (frequency range: 1.5–4.6 Mhz). All patients were examined in the left lateral decubitus position. For each dataset, 4D LV analysis automatically provided the following global parameters: end-diastolic volume index (EDVi), end-systolic volume index (ESVi), LVEF, global longitudinal strain (GLS) and myocardial work. Volume analysis was made using a semi-automated analysis tool, 4D auto LV volume quantification (4DLVQ, EchoPAC PC version 108.1.4, GE Healthcare). The contour detection was performed at end-diastole frames by only one cardiac cycle, single beat, during end-expiration breath-hold and was automatically displayed in quad-view: apical four-, two-, three-chamber and LV short-axis views. GLS was performed with easy automated function imaging of the left ventricle. After having stored three cycles of apical four-, two- and three-chamber views, we used this tool for endocardial border detection at end-systole. The following indices of myocardial work were assessed with the EchoPAC Version 203 software: global work index (GWI), global constructive work (GCW), global wasted work (GWW), and global work efficiency (GWE). GLS is derived from speckle tracking, and it reflects the longitudinal contraction of the myocardium. This method is operator-independent, more reproducible than LVEF, easily measured and integrated to standard echocardiogram method. Speckle tracking was performed frame-by-frame throughout the LV wall during the cardiac cycle and basal, mid, and apical regions of interest were created. Segments that failed to track were manually adjusted by the operator. GLS was calculated as the mean strain of 18 segments. It is a simple parameter that expresses longitudinal shortening as a percentage (change in length as a proportion to baseline length). Using myocardial work, we can measure LV strain and pressure, overcoming GLS and LVEF limitations. Once blood pressure is inputted into

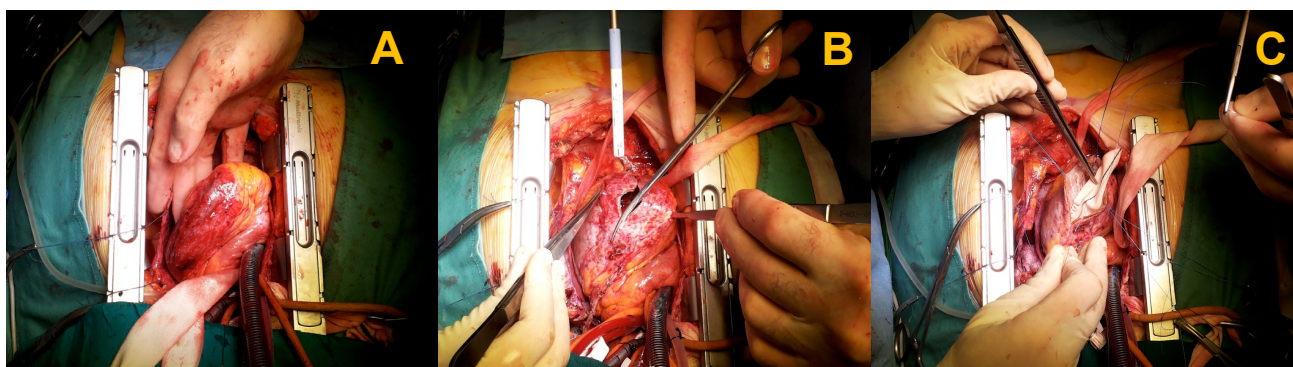


Fig. 1. Surgical ventricular restoration technique. (A) Identification of the antero-apical aneurysm. (B) Left ventriculotomy incision and inspection of the cavity for the presence of a thrombus. (C) Suture of an endocavitary oval patch.

the software, a myocardial work bull's-eye plot is created, similar to GLS (Fig. 2). Four values are calculated: GWI, GCW, GWW, and GWE.

Statistical Analysis

Continuous variables are reported as mean with standard deviation, while qualitative and categorical variables are shown as frequencies. Comparative analysis of the variables of interest between subjects before and after SVR was performed using the χ^2 test for categorical variables and the two-sample Student's *t*-test or Wilcoxon test for continuous variables. A *p*-value of 0.05 was considered statistically significant.

Cox survival regression model was used for investigating the effect of several confounding factors on the probability of patient survival from the day of the surgical intervention until the last day of follow-up. All patients were reviewed at follow-up (mean follow-up 8.5 ± 4.5 years).

Results

From January 2008 to February 2021, 55 patients (mean age 61.5 ± 10 years), 45 male (82%) with HF with previous MI and LV remodeling underwent SVR at our center. Eight patients (14.5%) presented with atrial fibrillation. Three patients (5.4%) had a biventricular pacemaker or ICD for cardiac resynchronization therapy due to a severely reduced LVEF with or without left bundle branch block. No patients underwent electrophysiological study preoperatively. Complete bypass grafting was first performed when indicated in 28 patients (51%); concomitant mitral valve treatment was performed in 5 patients (9%). A total of 19 patients underwent rescue percutaneous coronary intervention (PCI) (35%). One patient died intraoperatively due to a massive thrombus embolization from the aneurysmal cardiac apex to the coronary ostia. All surviving patients underwent follow-up with complete clinical and echocardiographic examination. Baseline clinical char-

acteristics of the study population are reported in Table 1. Patient characteristics before and after SVR are shown in Table 2. An ICD was implanted in 13 patients (24%) in the postoperative period (almost 3 months post-op). To evaluate the effect of ICD implantation, patients who received an ICD were compared with those who underwent a standard procedure. The Cox regression model showed that, after accounting for confounding factors such as sex, age, smoking, hypertension, previous stroke, diabetes, ICD implantation did not significantly improve patient survival. However, a univariate analysis comparing total mortality and sudden death in patients with vs without ICD showed a significant difference (Fig. 3). Moreover, LVEF improved more significantly in the non-ICD group ($p < 0.01$) (Fig. 4).

Discussion

Our study demonstrates the efficacy of the SVR. In fact, our population improves the follow-up LVEF and the NYHA class. However, some cases of sudden death, in patients with a good health status, impose a word of caution. The results of our study can be considered as contradictory: on the one hand, good hemodynamic and clinical results were achieved with SVR; on the other hand, the doubts about residual arrhythmic risk—already expressed by Vincent Dor who added electrical isolation surgery to his ventricular reshaping technique—are confirmed. The sudden death occurred almost one year after surgery. A high rate of sudden death was recorded, though at late follow-up, likely due to VA. In these patients, no ICD was implanted as, following surgical intervention and medical therapy, their LVEF improved over time above the reference threshold values for ICD placement. In particular we noted an improvement of the LVEF in patients without an ICD preoperatively; maybe due to a better preoperative cardiac function. The underlying mechanistic feature is that LV restoration involves scar exclusion, triggering ventricular volume expansion and leading to progressive arrhythmia responsible for sudden death [31]. Why would patients with improved

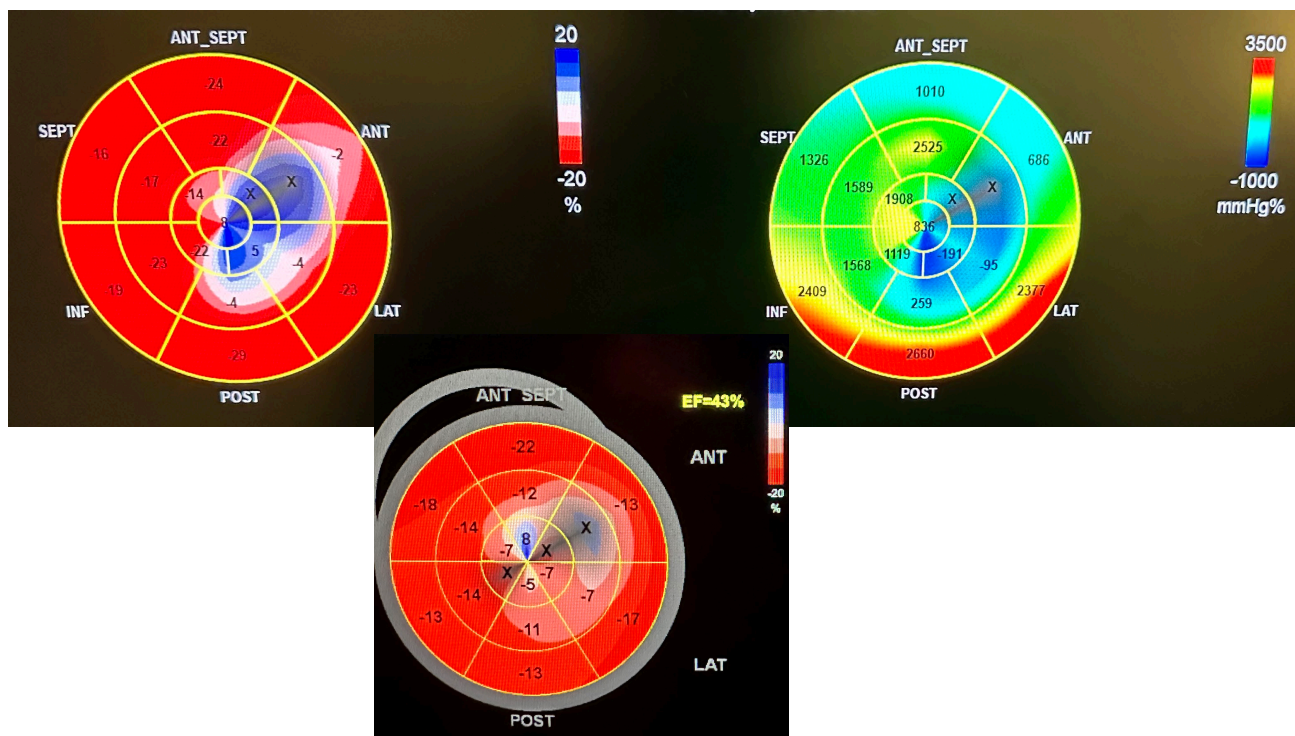


Fig. 2. Myocardial work bull's-eye plot. SEPT, Septal; INF, Inferior; POST, Posterior; LAT, Lateral; ANT, Anterior.

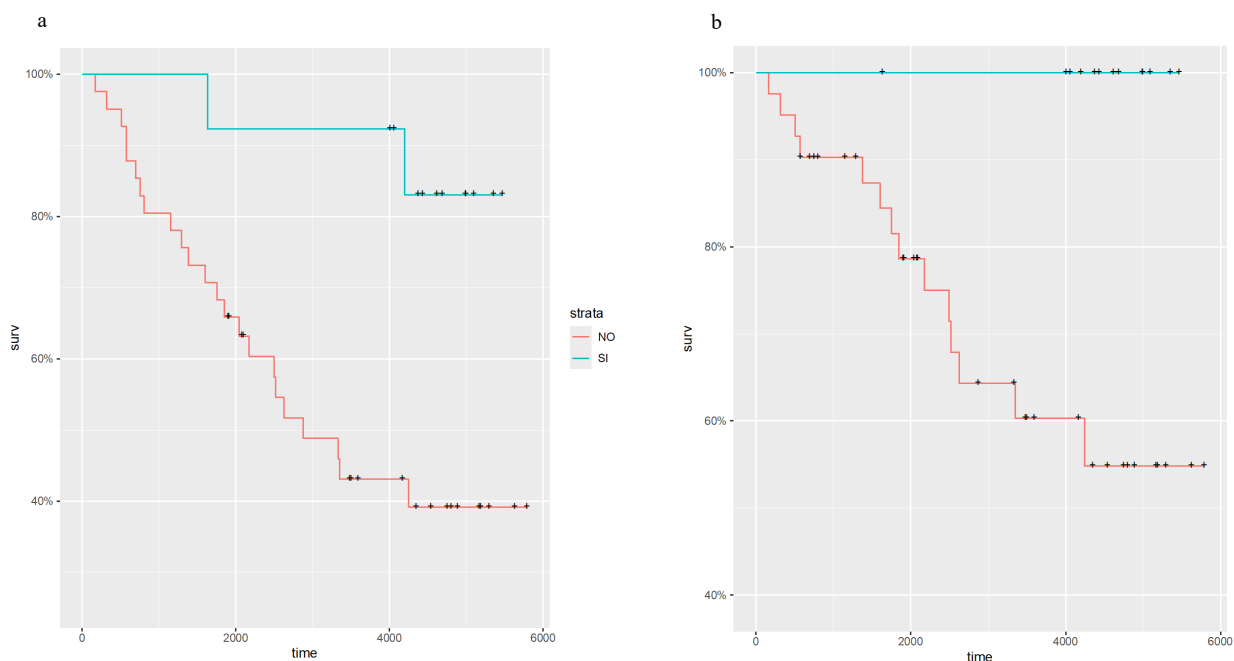


Fig. 3. Total mortality (a) and sudden death (b) in patients with and without an implantable cardioverter-defibrillator. SURV, Survival.

LV function and no signs of ischemia be at risk of developing arrhythmias? The potential arrhythmogenic risk of a dilated and hypokinetic ventricle was posed by Babuty and Lab [32] who applied the Occam's Razor principle, or central hypothesis for VA. In contrast, LV size and shape are addressed during SVR as described by Dor *et al.* [22,24] and

Sabatier *et al.* [24], in that the procedure involves scar resection, septal exclusion, and cavity reduction by endoventricular patch plasty, while supplementing coronary bypass grafting and mitral valve repair if needed. As a result, the risk for arrhythmias should almost disappear. However, Dor also added extended, non-guided endocardectomy and

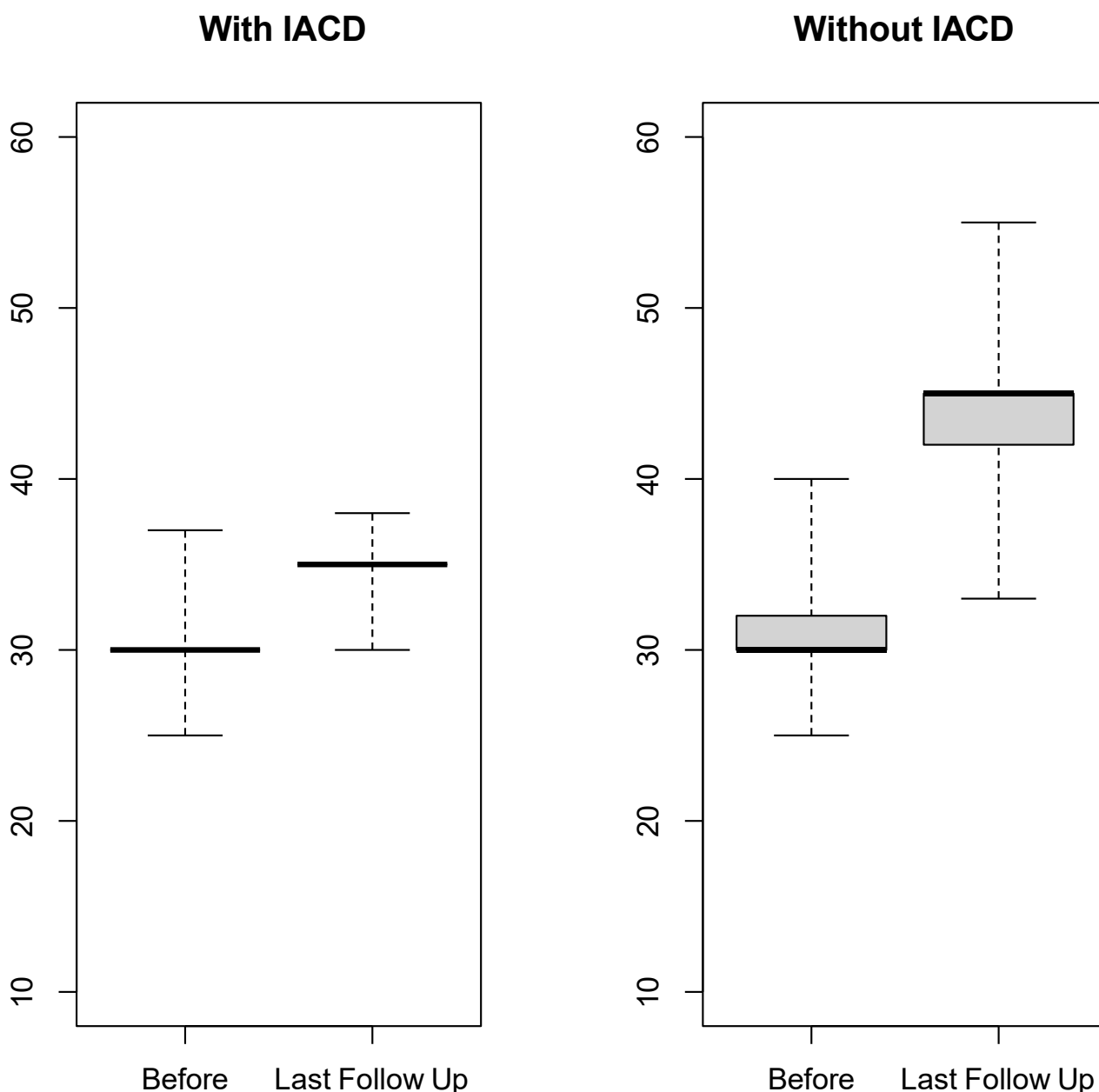


Fig. 4. Left ventricular ejection fraction (LVEF) before surgery and at last follow-up in patients with and without an automated implantable cardioverter-defibrillator (IACD).

cryosurgery at lesion borders, achieving a considerable reduction in the incidence of postoperative inducible VT, prolonged early survival without chronic HF progression [33], and no need for ICD implantation [25]. Dor's success in anti-arrhythmic management has been confirmed by others [34].

Since then, however, several questions on pro- and anti-arrhythmogenic mechanisms have remained unanswered: is a surgical procedure that reduces ventricular stretch anti-arrhythmic? Furthermore, are procedures such as endocardial resection and cryoablation able to reduce the risk of inducible VT? And finally, what is the impact of

complete revascularization in these patients? Our limited and heterogeneous sample size does not allow us to provide a thorough evaluation of these issues: approximately half of the patients underwent surgical revascularization associated with SVR, whilst others did not undergo coronary revascularization, or underwent PCI or rescue PCI. During follow-up, the family members of patients who died suddenly reported that their relatives had a good quality of life before the fatal event also under effort conditions, but remote analysis of the coronary anatomy (e.g., coronary angiography or coronary computed tomography scan) was performed in none of them because LVEF improvement did not prompt

Table 1. Preoperative characteristics (n = 55).

Age, years	61.5 ± 10
Female sex	10 (18)
Hypertension	44 (80)
Diabetes	29 (53) ^a
Dyslipidemia	27 (49)
Previous myocardial infarction	22 (40)
Previous PCI	15 (27)
Smoking	19 (34)
COPD	7 (13)
Renal insufficiency	12 (22) ^b
CCS class	1.8 ± 0.7
NYHA class	2.6 ± 0.6
Rescue PCI	19 (35)
Surgery	
SVR	22 (40)
SVR + CABG	28 (51)
SVR + Mitral	5 (9)

Values are given as mean ± standard deviation, or n (%). CABG, coronary artery bypass graft; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; PCI, percutaneous coronary angioplasty; SD, standard deviation; SVR, surgical ventricular restoration. ^a12 patients with insulin-dependent diabetes. ^b2 patients were in dialysis.

Table 2. Patients parameters before and after surgical ventricular restoration.

	Before SVR	After SVR	p-value
NYHA class	2 (42)/3 (63)/4 (5)	1 (55)/2 (45)	<0.001
LVEF	30.91 (3.26)	41.8 (5.78)	<0.001
EDD	60.84 (2.63)	51.36 (3.27)	<0.001
ESD	50.22 (3.11)	39.24 (3.68)	<0.001
EDV	160.82 (3.94)	120.64 (3.61)	<0.001
ESV	70.73 (3.52)	52.11 (3.63)	<0.001
EDVi	120.71 (5.13)	87.56 (4.76)	<0.001
ESVi	56.76 (4.55)	46.44 (1.88)	<0.001

Values are given as n (%), or mean (standard deviation). EDD, end-diastolic diameter; EDV, end-diastolic volume; EDVi, end-diastolic volume index; ESD, end-systolic diameter; ESV, end-systolic volume; ESVi, end-systolic volume index; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SVR, surgical ventricular restoration.

the referring cardiologist to advise more in-depth diagnostic investigations. Takano and colleagues [35] evaluated the importance of complete revascularization on ventricular measurements and function. It was seen that in the majority of patients who were not completely revascularized there

was an effect on ventricular function. The impact of ventricular size and function with incomplete revascularization is independent of the risk of VT recurrence/ventricular fibrillation and may indicate ICD implantation. However, it has also been seen that in cases of severely reduced ventricular function, even complete revascularization cannot allow a good recovery of cardiac function.

In the study of Dor *et al.* [25], patients with VT episodes were treated with the original surgical technique [22] associated with anti-arrhythmic therapy, achieving a success rate of >90% in suppressing VA. In contrast, in our study population, patients did not experience any arrhythmic episodes before the procedure. Other centers have reported similar results using a map-guided approach and the Dor procedure [7]. Conversely, our study results are more similar to those recorded by Bechtel and colleagues [36], showing a high incidence of sudden death (37% of deaths at a median follow-up of 3.7 years) late after SVR when concomitant anti-arrhythmic surgery was not performed.

In the DAPA trial, 10-year all-cause mortality was significantly lower in patients receiving ICD therapy after MI [37], suggesting that ICD implantation should be considered in all patients with a history of MI. However, these studies are focused on the effects of the revascularization procedure rather than hemodynamics or the presence of scarring. In summary: promptly revascularizing the coronary arteries with PCI or bypass [38,39] is the first step and only after clinical re-evaluation will it be established as to whether it is appropriate to implant an ICD. In our study, patients suffering from sudden death underwent close clinical and echocardiographic re-assessment. In addition, early reflow volume reduction was obtained, lowering the risk for early sudden death and delaying LV remodeling, despite the failure of enhanced perfusion to improve regional contractile function. This concept of volume reduction concept was expanded in the study of DiDonato and colleagues [40] where the sudden death rate at 5-year follow-up was reduced from 50% to only 19% of all deaths in 382 patients undergoing LV restoration, a procedure that simultaneously reduces HF symptoms and improves New York Heart Association (NYHA) class [20,40–42]. In this registry, 115 NYHA class IV and 106 NYHA class III patients were included. Only one ICD was placed, and bypass surgery, mitral repair, endocardectomy and cryoablation were performed when needed [40].

It should also be remembered that even a successful revascularization after an infarction can lead to 50% of patients not being optimally reperfused. This is called the “no-reflow phenomenon” linked to coronary microvascular dysfunction [43]. We also know the importance and the difference between stunned and hibernated myocardium [44]. In fact, hibernated myocardium recovers later than stunned myocardium despite revascularization [45]. Moreover, the extent of myocardial viability is important. In fact, several studies have shown that at least a

quarter of the dysfunctional myocardium must be viable for LVEF improvement after revascularization [43–46]. According to current guidelines, optimal medical therapy can reduce the arrhythmogenic risk, with an effective hemodynamic effect demonstrated by improved diameters and increased LVEF. Although none of our patients received sacubitril/valsartan, most of them were treated with the recommended therapy, including angiotensin-converting enzyme inhibitor/type 1 angiotensin II receptor blockers, beta-adrenergic receptor blockers, and mineralocorticoid receptor antagonists [47,48].

In our study, what is most surprising is not the relevance of medical therapy or the revascularization procedure but the occurrence of arrhythmic episodes in patients with an almost normal LVEF. The risk of arrhythmias due to ischemic conditions, particularly in the first few months after MI, was high in patients with a reduced LVEF [49–51]. Current guidelines [47,48,52,53] recommend routine ICD implantation for primary prevention of VA in patients with LVEF $\leq 35\%$. However, in our study, sudden death occurred in patients with LVEF $>35\%$ showing a significant improvement of LVEF at the last follow-up compared to preoperative values. It cannot be postulated that the underlying arrhythmic episodes were related to the acute surgical phase. The immediate risk is higher in surgical revascularization which could be reduced with an “off-pump” approach [54,55]. Subsequently, patients undergoing bypass had improved ventricular function one year after surgery [56,57]. However, a left ventriculotomy was used in our patients requiring cardioplegic arrest, and the arrhythmic episodes likely underlying sudden death were recorded late after the operation, excluding confounding factors such as cardiopulmonary bypass and sternotomy.

Based on the above and on our study results, it can be concluded that ICD implantation should be considered in all patients for prevention of sudden death. The debate is always open on the indication for the implantation of an ICD; with health and economic factors that come into play [18,58–60]. Therefore, the ICD is able to save lives [18,60], but revascularization must be better evaluated and integrated into the decision for implantation. In fact, the role of revascularization still remains to be fully understood especially for the type of approach to be preferred and in which patient [61,62]. Moreover, the presence of a chronic total occlusion (CTO) is associated with an increased risk of sudden cardiac death [63–66]. This seems to be mainly driven by a higher risk of VA [63,66–70]. There is emerging clinical evidence that the presence of a CTO has a proarrhythmic effect [70–73]. Considering the current knowledge on the increased risk of VA in patients with CTO, further clinical studies are warranted to confirm this relationship. van Dongen *et al.* [74] performed an interesting systematic review to identify electrophysiological parameters associated with increased VA risk which could be used for future research. Suggested parameters were fragmented

QRS, late potentials, QT interval, QT dispersion, T-wave peak-to-end interval and T-wave alternans [74]. The condition of our patients, in whom a closed vessel resulted in scar formation, resembles that of a patient with CTO.

Conclusions

Our results do not allow any definite conclusions to be drawn on the role of SVR in the long-term risk of sudden death. We confirm that an adequate indication for this intervention is key for long-term hemodynamic results and for improving the patient’s quality of life. In contrast, the use of ventricular reconstructive techniques in patients with non-aneurysmal akinetic or dyskinetic ventricles is still under evaluation. It should not go unnoticed that these patients are affected by end-stage disease, and treatment success depends upon procedural complexity and complete accomplishment of SVR by adequately addressing the different components of the “triple V” concept (i.e., vessel, valve, and ventricle) [75]. The satisfactory results obtained in our series suggest that the modified SVR technique, by restoring an elliptical normal cardiac shape and creating a neo-apex, still represents a valuable option in the surgeon’s armamentarium for appropriately selected patients. An electrophysiological evaluation, even remotely and even in asymptomatic patients with improved LVEF, for ventricular arrhythmogenic risk is in our opinion a prudent tool to adopt for the possible implantation of an ICD, creating a new prophylactic indication for this device.

Availability of Data and Materials

Datasets used and/or analyzed for this study are available from the corresponding author upon appropriate request

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by GS, GT, LA and SA. The first draft of the manuscript was written by GS and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Internal board (Protocol No. 11/24). All patients provided written informed consent for inclusion, data or sample collection/use and/or publication of data results. The clinical ethical board has approved the use of patient's clinical data, according to privacy rules.

Acknowledgment

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Conflict of Interest

The authors declare no conflict of interest. GS serves as the Editor-in-Chief of this journal. GS declares that he had no involvement in the processing of this article and had no access to information about the processing of this article.

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