Abstract: Surgical ventricular restoration (SVR) has repeatedly been suggested as a viable therapeutic strategy for ischemic heart failure (HF) patients, although the survival benefit is still debated. We investigated a real-world population treated with SVR in a single center with high case volumes. From July 2001 to June 2017, 648 patients (111 females) underwent SVR; coronary surgery was performed in 582 patients. Data were analyzed by dividing the population into two groups: Group I (371 patients operated between July 2001 and December 2007) and Group II (277 patients operated between January 2008 and June 2017). At baseline, Group I patients were more symptomatic for angina (47.4% versus 19.4%, \( p < 0.0001 \)) and less symptomatic for HF (NYHA class III/IV, 46.3% versus 57%, \( p = 0.0071 \)). The end-diastolic volume (106 mL/m\(^2\) versus 118.3 mL/m\(^2\), \( p < 0.0001 \)) and the end-systolic volume (70.5 mL/m\(^2\) versus 81.5 mL/m\(^2\), \( p < 0.0001 \)) were lower in Group I. The presence of 3-vessel coronary artery disease (CAD) was higher in Group I (73.3% versus 59.2%, \( p < 0.0001 \)). Thirty-day mortality (6.64%) was similar in the two groups (\( p = 0.4475 \)). The Kaplan–Meier estimate for all-cause mortality for the entire population was 13% at 2 years, 19.2% at 4 years and 36.6% at 8 years, and the probability was not different between groups (Log-rank = 0.11).

In a real-world ischemic HF population, SVR may be carried out with favorable results; in patients with worse LV remodeling and less extensive CAD, SVR showed a trend toward a better outcome.

Keywords: ischemic heart failure; left ventricular remodeling; surgical treatment

1. Introduction

Heart failure (HF) remains a lethal condition with a mortality rate of up to 60% within five years of diagnosis [1,2], driven mostly by the causal role of coronary artery disease (CAD) in the development of left ventricular (LV) remodeling and dysfunction. The increasing prevalence of this poor condition is related to the longevity and the improved survival after a previous myocardial infarction (MI) [3]. Coronary artery revascularization (CABG) is the first strategy in patients with chronic HF and systolic LV dysfunction (class I, level of evidence B) [4]. Surgical ventricular restoration (SVR) at the time of CABG may be performed in selected patients treated in centers with expertise (class IIb, level of evidence B) [4]. Both recommendations stem from the results of the STICH (Surgical Treatment of Ischemic Heart Failure) trial, which is more robust for the comparison of CABG versus optimal medical therapy in patients with ischemic LV dysfunction and HF [5,6]. However,
it is less evident for the additional role of SVR to CABG [7]. After more than ten years after the publication of the STICH- Hypothesis 2 results, it has been well recognized that this trial enrolled a heterogeneous population of patients with CAD and low ejection fraction (EF), with moderate symptoms of either angina and HF and relative small volumes, for which the preference between different therapeutic strategies (i.e., CABG or SVR) was not so relevant [8]. However, no effort has been made to understand which group of patients would actually benefit from this procedure in the long term, leaving uncertainties among the scientific community.

The objectives of this study were (i) to assess the clinical and imaging features, surgical treatment and prognosis of a real-world ischemic HF population referred to our center over sixteen years; and (ii) to evaluate the long-term outcome. The outcome of interest of the study was all-cause mortality, including death within 30 days.

2. Materials and Methods
2.1. Study Design

This was a retrospective study based on the database of the I.R.C.C.S. Policlinico San Donato for patients with ischemic HF undergoing cardiac surgery. The study protocol was approved by the Local Ethics Committee, according to the Italian regulatory law for observational retrospective studies. Patient consent was waived due to the processing of data in anonymized form.

2.2. Study Population

From July 2001 to June 2017, 648 patients (111 females (17%), median age 66 [IC 58–72]) with previous MI and LV remodeling were referred to our center for cardiac surgery. Follow-up continued through June 2018. All patients underwent SVR (carried out by a single surgeon—LM); CABG was performed in 582 patients (89.8%) and mitral valve surgery in 200 patients (30.1%). Indications for surgery were heart failure and/or angina.

Given changes in clinical practice over time that could have resulted in differences in the baseline profile, data were analyzed by dividing the population into two groups: Group I (patients operated between July 2001 and December 2007) and Group II (patients operated between January 2008 and June 2017). Time intervals were chosen in order to have two comparable groups by number and length of average follow-up of at least 5 years.

2.3. Echocardiography

A comprehensive echocardiographic assessment was performed using a GE Vivid 7 (GE Healthcare, Waukesha, WI, USA) instrument, and all 4-chamber, 2-chamber, long-axis and short-axis views were analyzed before and after surgery at a median time of 12 months from the operation. The following parameters were collected: LV diastolic diameter (mm), LV systolic diameter (mm), end-diastolic volume (EDV) index (mL/m²), end-systolic volume (ESV) index (mL/m²), EF (%), stroke volume (SV) index (mL/m²), LV mass index (g/m²), tricuspid annular plane systolic excursion (TAPSE) (mm), systolic pulmonary artery pressure (PAPs) (mmHg), left atrial diameter (mm), E wave velocity (cm/sec), E/A ratio, deceleration time (DT) (mm), mitral annulus dimension (mm), inter-papillary distance (IPD) (mm) at the end of diastole and systole, diastolic and systolic sphericity index (SI) (calculated as the short- to long-axis ratio in apical 4ch-view) and systolic and diastolic conicity index (CI) (calculated as the ratio between the apical and the short axis to assess the shape of the apex) [9]. All measurements were done in triplicate and displayed as an average value.

2.4. Follow-Up

The outcome of the study was considered all-cause mortality, including death within 30 days, during the follow-up period. Follow-up was 100% complete and was conducted either at the hospital during a routine clinical evaluation or by telephone contact with the
patients, their relatives or their family doctors. If a patient was not seen in the hospital or a telephone interview was not possible, the National Registry of Death was contacted.

2.5. Surgical Technique

The surgical technique has been previously reported in detail [8]. Briefly, the procedure was performed under total cardiac arrest with antegrade crystalloid cardioplegia. After completion of coronary grafting when indicated, the left ventricle was opened with an incision parallel to the left anterior descending artery, starting at the middle scarred region and ending at the apex. Surgical ventricular reconstruction was performed using a mannequin (TRISVR, Chase Medical Richardson, TX, USA) filled at 50–60 mL/m² to optimize the size and shape of the new ventricle. When needed, the mitral valve was repaired through the ventricular opening.

2.6. Statistical Analysis

Categorical variables were presented as number (%) and continuous variables as median [interquartile range]. Changes over time between preoperative and postoperative echocardiographic characteristics were compared with the McNemar paired test.

The differences in baseline demographic and clinical characteristics between Group I and Group II were compared with the Chi-square test; continuous variables were compared by the non-parametric Kruskal–Wallis test for non-normally distributed data.

The association between demographic, preoperative echocardiographic variables and the time to all-cause death was investigated by the use of a univariate and multivariable Cox proportional hazard regression analysis.

A first screening of potential predictors was performed by a univariate analysis. For this method, the model considered baseline demographic and preoperative echocardiographic characteristics significantly associated with the outcome and defined by a backward selection. The internal validity of the final models was partially assessed by the bootstrap resampling technique [10]. For each of the 200 bootstrap samples, the model was refitted and tested on the original sample to obtain estimates of predictive accuracy. The bootstrap resampling did not include the first stage of variable selection.

The proportionality and linearity of hazards were evaluated by graphic inspection and testing for Martingale residuals. Median follow-up time was calculated according to the reverse Kaplan–Meier method.

All p values were two-tailed and considered significant if <0.05. Statistical analyses were done with SAS software, version 9.4 (SAS Institute, Inc., Cary, NC, USA) and with the R program (http://CRAN.R-project.org (accessed on 28 March 2022)) with the RMS package.

3. Results

The demographics and clinical profile data of the patient population are shown in Table 1, based on the two different periods.

At baseline, although patients in Group I had less hypertension (203 [54.7%] versus 178 [64.2%], p = 0.0146), hyperlipidemia (188 [50.6%] versus 193 [69.7%], p < 0.0001) and tabagic habit (222 [59.8%] versus 217 [78.3%], p < 0.0001), they were more symptomatic for angina (176 [47.4%] versus 54 [19.5%], p < 0.0001), but less symptomatic for HF (NYHA class III/IV, 172 [46.3%] versus 54 [19.5%], p < 0.0001), but less symptomatic for HF (NYHA class III/IV, 172 [46.3%] versus 54 [19.5%], p < 0.0001). Medical treatment at the time of admission is reported in Table 1. The prescription of ACE-inhibitors was similar between Group I and Group II (83.20% versus 81.82%, p = 0.6467), while β-blockers (64.23% versus 89.09%, p < 0.0001), aspirin (72.63% versus 93.45%, p < 0.0001), diuretics (75.88% versus 93.12%, p < 0.0001), statins (47.70% versus 93.48%, p < 0.0001) and oral anticoagulants (6.79% versus 11.39, p = 0.0071). PCI prior to surgery was performed less frequently in Group I (79 [21.2%] versus 104 [37.6%], p < 0.0001), while the arrhythmogenic burden was greater in
Group II compared with Group I, with more ventricular arrhythmias (75 [27.1%] versus 31 [8.3%], p < 0.0001) and implanted ICD (25 [9%] versus 15 [4.0%], p < 0.0001), (Table 1).

Table 1. Baseline characteristics of the total study cohort and by period.

|                         | n  | Total        | n  | 2001–2007 (n = 371) | n  | 2008–2017 | p-Value  |
|-------------------------|----|--------------|----|---------------------|----|-----------|----------|
| Age, years              | 648| 66 [58–72]   | 371| 67 [58–72]          | 277| 64 [58–71]| 0.1365   |
| BSA                     | 648| 1.83 [1.74–1.92] | 371| 1.83 [1.73–1.94]   | 277| 1.85 [1.75–1.94] | 0.0689   |
| Creatinine              | 648| 1.10 [0.91–1.39] | 371| 1.14 [0.96–1.44]   | 277| 1.05 [0.88–1.30] | 0.0020   |
| Family history of CAD   | 648| 132 (35.58)  | 135 (35.88)| 130 (34.68) | 1.39 (30.18) | 0.0002   |
| Smokers or ex-smokers   | 648| 439 (67.75)  | 222 (59.84)| 217 (58.34) | 0.0001   |
| Hypertension            | 648| 203 (54.72)  | 178 (46.26)| 0.0146   |
| Atrial fibrillation     | 648| 49 (13.21)   | 42 (11.56)| 0.0027   |
| Stroke                  | 648| 42 (11.32)   | 13 (4.69)| 0.0027   |
| Angina                  | 648| 176 (47.44)  | 54 (15.16)| 0.0001   |
| Ventricular arrhythmias | 648| 31 (8.36)    | 75 (20.78)| <0.0001  |
| Chronic renal failure   | 648| 24 (6.47)    | 23 (6.30)| 0.3731   |
| Diabetes mellitus       | 648| 97 (26.15)   | 69 (20.00)| 0.7414   |
| Hypercholesterolemia    | 648| 188 (50.67)  | 193 (69.68)| <0.0001  |
| NYHA class III/IV       | 648| 172 (46.36)  | 158 (57.04)| 0.0071   |
| Previous PCI            | 648| 79 (21.29)   | 104 (35.55)| <0.0001  |
| PCI + ICD               | 648| 3 (0.81)     | 34 (12.27)| <0.0001  |
| ACE inhibitor           | 644| 304 (83.20)  | 225 (81.82)| <0.0001  |
| β-blockers              | 644| 237 (64.23)  | 257 (93.48)| <0.0001  |
| Aspirin                 | 644| 268 (72.63)  | 257 (93.45)| <0.0001  |
| Digoxin                 | 644| 37 (10.03)   | 48 (11.39)| <0.0001  |
| Statins                 | 645| 176 (47.70)  | 257 (93.12)| <0.0001  |
| Diuretic                | 645| 250 (73.98)  | 257 (93.12)| <0.0001  |
| Oral anticoagulant      | 644| 48 (11.39)   | 48 (11.39)| <0.0001  |
| Amiodarone              | 644| 85 (23.04)   | 61 (22.18)| 0.7981   |
| Nitrates                | 644| 158 (48.22)  | 47 (17.09)| <0.0001   |

Data are median [Q1–Q3] or number (%); BSA = body surface area; CAD = coronary artery disease; PCI = percutaneous coronary intervention; NYHA = New York Heart Association.

At baseline echocardiography (Table 2), the EDV index (106 [88.8–128.1] mL/m² versus 118.3 [88.7–140.8] mL/m², p < 0.0001) and the ESV index (70.5 [55.7–92.0] mL/m² versus 81.5 [65.8–101.9] mL/m², p < 0.0001) were lower in Group I, but not the EF (33 [26–38] % versus 31 [25–36] %, p = 0.010). Group I patients had a higher LV mass (168.26 [141.9–203.8] g/m² versus 160.5 [131.2–193.7] g/m², p = 0.0060), a lower left atrial dimension (46 [40.5–50] mm versus 47 [43–52] mm, p = 0.0083), a lower E/A ratio (0.82 [0.64–1.40] versus 1.15 [0.72–2.09], p = 0.0003) and more anterior remodeling (316 [85.2%] versus 210 [75.8%], p = 0.0100), while the rate of posterior remodeling was higher (44 [18.7%] versus 52 [11.8%], p = 0.0100) in Group II. Grade 3/4 of mitral regurgitation was higher in Group II (40.4% versus 28.2%, p < 0.0001), which showed a higher SI. The presence of 3-vessel CAD was higher in Group I (272 [73.3%] versus 164 [59.2%], p < 0.0001), resulting in more coronary grafts combined with SVR (347 [93.53%] versus 235 [84.84%], p = 0.0003) as well as a higher percentage of two or more distal anastomosis (278 [74.9%] versus 160 [57.7%], p < 0.0001) (Table 2). Figure 1 shows the changes after surgery in echocardiographic parameters in Group I and Group II in respect to baseline differences.

Postoperative variables by period: diastolic diameter (mm) n total = 454, n = 230 in [2001–2007] and n = 224 in [2008–2017]—EF (%) n total = 478, n = 239 in [2001–2007] and n = 239 in [2008–2017]—EDV index (mL/m²) n total = 466, n = 227 in [2001–2007] and n = 239 in [2008–2017]—ESV index (mL/m²) n total = 466, n = 227 in [2001–2007] and n = 239 in [2008–2017]—E/A ratio n total = 359, n = 173 in [2001–2007] and n = 186 in [2008–2017]—MR grade n total = 495, n = 252 in [2001–2007] and n = 243 in [2008–2017]—sphericity index, diastole n total = 397, n = 175 in [2001–2007] and n = 222 in [2008–2017]—sphericity index, systole n total = 396, n = 174 in [2001–2007] and n = 222 in [2008–2017].
Table 2. Baseline echocardiographic, angiographic and operative variables of the total study cohort and by period.

| Variable                  | Total          | 2001–2007 (n = 371) | 2008–2017 (n = 277) | p-Value |
|---------------------------|----------------|---------------------|---------------------|---------|
| Diastolic diameter (mm)   | 630 65 [58–71] | 356 65 [58–70.50]   | 274 64 [59–71]     | 0.8698  |
| Systolic diameter (mm)    | 625 51 [44–59] | 355 51 [44–59]      | 270 51 [45–59]     | 0.6611  |
| EDV index (mL/m²)         | 645 112.12 [92.34–134.30] | 368 106.68 [88.77–128.06] | 277 118.27 [98.86–140.83] | <0.0001 |
| ESV index (mL/m²)         | 646 76.08 [59.17–95.81] | 369 70.47 [55.65–92.02] | 277 81.48 [65.79–101.85] | <0.0001 |
| EF (%)                    | 648 32 [26–37]  | 371 33 [26–38]      | 277 31 [25–36]     | 0.0100  |
| SV index (mL/m²)          | 644 35.20 [29.38–41.69] | 367 34.69 [24.14–40.61] | 277 36.57 [29.63–42.55] | 0.1186  |
| TAPSE (mm)                | 609 20 [18–23]  | 335 20 [17–23]      | 274 21 [18–24]     | 0.0158  |
| PAPs (mmHg)               | 556 38 [30.5–48] | 282 38 [32–46]      | 274 38 [30–49]     | 0.4370  |
| LVMI (g/m²)               | 561 164.29 [137.88–199.48] | 336 168.26 [141.93–203.81] | 225 160.51 [131.22–193.68] | 0.0060  |
| RWT                       | 597 0.32 [0.27–0.38] | 347 0.33 [0.28–0.40] | 250 0.29 [0.25–0.36] | <0.0001 |
| Left atrial diameter (mm) | 594 46 [41–51]  | 340 46 [40.50–50]   | 254 47 [43–52]     | 0.0083  |
| E/A ratio                 | 458 0.96 [0.66–1.71] | 220 0.82 [0.64–1.40] | 238 1.15 [0.72–2.09] | 0.0003  |
| DT (cm)                   | 435 1.85 [1.49–2.39] | 197 1.90 [1.55–2.31] | 238 1.82 [1.44–2.54] | 0.9478  |
| Mitral annulus (mm)       | 367 34 [30–37]  | 162 35 [31–39]      | 205 32 [29–37]     | 0.0017  |
| IPD, diastole (mm)        | 254 3 [2.5–3.5]  | 124 2.60 [2.20–3.1] | 132 3.20 [2.8–3.6] | <0.0001 |
| IPD, systole (mm)         | 254 2.10 [1.7–2.6] | 124 1.77 [1.4–2.6]  | 132 2.30 [2.00–2.7] | <0.0001 |
| Sphericity index, diastole| 395 0.60 [0.50–0.68] | 152 0.60 [0.50–0.68] | 243 0.64 [0.57–0.72] | <0.0001 |
| Sphericity index, systole | 394 0.53 [0.43–0.62] | 152 0.45 [0.37–0.54] | 243 0.58 [0.49–0.65] | <0.0001 |
| Conicity index, diastole  | 385 0.88 [0.80–0.96] | 142 0.81 [0.73–0.95] | 243 0.89 [0.83–0.97] | <0.0001 |
| Conicity index, systole   | 385 0.94 [0.83–1.09] | 142 0.95 [0.80–1.11] | 243 0.93 [0.84–1.08] | 0.8379  |
| MR grade                  |               |                     |                     |         |
| 0                         | 80 (12.35)    | 74 (19.95)          | 6 (2.17)            |         |
| 1                         | 209 (32.25)   | 126 (33.96)         | 83 (29.96)          |         |
| 2                         | 142 (21.91)   | 66 (17.79)          | 76 (27.44)          | <0.0001 |
| 3                         | 119 (18.36)   | 58 (15.63)          | 61 (22.02)          |         |
| 4                         | 98 (15.12)    | 47 (12.67)          | 51 (18.41)          |         |
| Site of remodeling        |               |                     |                     |         |
| Posterior                 | 96 (14.81)    | 44 (11.86)          | 52 (18.77)          |         |
| Anterior                  | 526 (81.17)   | 316 (85.18)         | 210 (75.81)         | 0.0100  |
| Anterior & posterior      | 26 (4.01)     | 11 (2.96)           | 15 (5.42)           |         |
| Coronary angiography      |               |                     |                     |         |
| Single vessel disease     | 159 (24.54)   | 85 (22.91)          | 74 (26.71)          |         |
### Table 2. Cont.

| N                  | Total  | n  | 2001–2007 (n = 371) | n  | 2008–2017 (n = 277) | p-Value |
|--------------------|--------|----|---------------------|----|---------------------|---------|
| Multivessel disease| 436 (67.28) | 272 (73.32) | 164 (59.21) | <0.0001 |
| No residual stenosis| 53 (8.18) | 14 (3.77) | 39 (14.08) | 0.0015 |
| Mitral valve surgery| 200 (30.86) | 96 (25.88) | 104 (37.55) | 0.0003 |
| CABG + SVR         | 582 (89.81) | 347 (93.53) | 235 (84.84) | 0.0003 |
| SVR                | 66 (10.19) | 24 (6.47) | 42 (15.16) | 0.0001 |
| Number of distal anastomosis |       |     |                    |    |                    |         |
| 0                  | 66 (10.19) | 24 (6.47) | 42 (15.16) | 0.0001 |
| 1                  | 144 (22.22) | 69 (18.60) | 75 (27.08) | 0.0001 |
| >=2                | 438 (67.59) | 278 (74.93) | 160 (57.76) | <0.0001 |

Data are median [Q1–Q3] or number (%). EDV = end-diastolic volume; ESV = end-systolic volume; EF = ejection fraction; SV = stroke volume; TAPSE = tricuspid annular plane systolic excursion; PAPs = systolic pulmonary artery pressure; LVMI = left ventricular mass index; RWT = relative wall thickness; DT = deceleration time; IPM = inter-papillary distance; MR = mitral regurgitation.
Overall, operative mortality defined as mortality within 30 days from surgery was 6.6%, corresponding to 43 patients. Of these, 27 (7.3%) were in Group 1 and 16 (5.7%) in Group 2 ($p = 0.4475$).

Figure 1. Boxplot for baseline and postoperative echocardiographic variables by period. *, $p < 0.05$; **, $p < 0.001$.

The mean follow-up time was 10 years (range, 0 days to 16 years) for the entire cohort; 13 years (range, 0 days to 16 years) in Group I and 5 years (range, 0 days to 10 years) in Group II.

The Kaplan–Meier estimate for all-cause mortality of the entire population was 13% (10.5–15.8%) at 2 years, 19.2% (16.2–22.5%) at 4 years and 36.6% (32.4–40.9%) at 8 years (Figure 2).
diastole total = 397, n = 175 in [2001–2007] and n = 222 in [2008–2017].

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The Kaplan–Meier estimate for all-cause mortality of the entire population was 13% (10.5%–15.8%) at 2 years, 19.2% (16.2%–22.5%) at 4 years and 36.6% (32.4%–40.9%) at 8 years (Figure 2).

There was no evidence of a difference in all-cause death between the two groups (Log-rank = 0.11).

In the multivariable Cox regression analysis, age (HR 1.069, 95% CI: 1.046–1.093, p < 0.0001), baseline EF (HR 0.97, 95% CI: 0.95–0.99, p = 0.0151) and E/A ratio (HR 1.61, 95% CI: 1.31–1.99, p < 0.0001) were significantly associated with mortality in Group I. Conversely, baseline NYHA class (HR 4.282, 95% CI: 1.474–12.441, p = 0.0075) and diastolic sphericity index (HR 1.03, 95% CI: 1.00–1.07, p = 0.0379) were found to be independent predictors of mortality in Group II (Table 3).
| Risk Category                        | 2001–2007 (n = 371) | 2008–2017 (n = 277) |
|-------------------------------------|---------------------|---------------------|
|                                     | Univariate          | Multivariate        | Univariate          | Multivariate        |
|                                     | Death (n = 212)     | Death (n = 57)      | Death (n = 277)     | Death (n = 57)      |
|                                     | Hazard Ratio (95% IC) | p-Value            | Hazard Ratio (95% IC) | p-Value            |
|                                     | p-Value            | Hazard Ratio (95% IC) | p-Value            | Hazard Ratio (95% IC) | p-Value |
| Sex                                 | M vs. F            | 0.83 [0.60–1.17]    | 0.2899              | 0.94 [0.44–1.99]    | 0.8688 |
| Site of remodeling                  | Ant/post vs. Ant   | 1.82 [0.89–3.71]    | 0.0991              | 2.61 [1.17–5.85]    | 0.0194 |
|                                     | Post vs. Ant       | 1.52 [1.03–2.24]    | 0.0359              | 1.56 [0.79–3.07]    | 0.1996 |
|                                     | Yes vs. No         | 1.10 [0.76–1.59]    | 0.5986              | 1.48 [0.73–3.03]    | 0.2761 |
|                                     | Yes vs. No         | 1.04 [0.79–1.36]    | 0.7783              | 1.01 [0.60–1.73]    | 0.9739 |
|                                     | Yes vs. No         | 0.66 [0.50–0.86]    | 0.0024              | 1.06 [0.60–1.87]    | 0.8449 |
|                                     | Yes vs. No         | 1.24 [0.92–1.66]    | 0.1578              | 1.96 [1.15–3.34]    | 0.0136 |
|                                     | Yes vs. No         | 1.18 [0.90–1.56]    | 0.2340              | 0.92 [0.50–1.71]    | 0.7928 |
| Previous procedures                 | PCI vs. No         | 0.87 [0.61–1.24]    | 0.4436              | 0.57 [0.30–1.09]    | 0.0908 |
|                                     | PCI + ICD vs. No   | 2.27 [0.56–9.20]    | 0.2493              | 1.33 [0.62–2.96]    | 0.4868 |
|                                     | ICD vs. No         | 1.01 [0.49–2.05]    | 0.9849              | 1.79 [0.81–3.99]    | 0.1516 |
|                                     | Other vs. No       | 1.48 [0.92–2.40]    | 0.1071              | 0.98 [0.14–7.22]    | 0.9831 |
| Ventricular arrhythmias            | Yes vs. No         | 1.29 [0.81–2.04]    | 0.2842              | 0.758 [0.40–1.43]   | 0.3858 |
| Attrial fibrillation               | Yes vs. No         | 1.47 [1.02–2.11]    | 0.0384              | 3.14 [1.79–5.49]    | <0.0001 |
| Stroke                              | Yes vs. No         | 1.32 [0.88–1.99]    | 0.1864              | 1.63 [0.59–4.50]    | 0.3496 |
| Chronic renal failure              | Yes vs. No         | 2.92 [1.18–7.46]    | <0.0001             | 3.36 [1.74–6.50]    | 0.0003 |
| Angiography                         | Single vessels     | 0.67 [0.33–1.37]    | 0.2750              | 0.96 [0.35–2.59]    | 0.9317 |
|                                     | No significant stenosis | 0.95 [0.48–1.86]    | 0.8761              | 1.63 [0.62–4.28]    | 0.3219 |
|                                     | No significant stenosis | 0.95 [0.48–1.86]    | 0.8761              | 1.63 [0.62–4.28]    | 0.3219 |
| Angina                              | Yes vs. No         | 1.20 [0.91–1.57]    | 0.1885              | 0.83 [0.44–1.58]    | 0.5709 |
| NYHA                                | III-IV vs. I-II    | 1.82 [1.38–2.39]    | <0.0001             | 3.12 [1.65–5.90]    | 0.0005 |
| MR grade                            | >= 2 vs. <2        | 1.41 [1.08–1.85]    | 0.0126              | 2.48 [1.25–4.92]    | 0.0092 |
| Age                                 | 1 unit             | 1.06 [1.04–1.07]    | <0.0001             | 1.07 [1.05–1.09]    | <0.0001 |
|                                     | 2 unit             | 1.00 [1.00–1.00]    | 0.1126              | 1.07 [1.03–1.10]    | <0.0001 |
| BSA                                 | 1 unit             | 0.96 [0.43–2.14]    | 0.9241              | 0.07 [0.01–0.54]    | 0.0099 |
| Haemoglobin                         | 1 unit             | 0.86 [0.78–0.94]    | 0.0005              | 0.83 [0.70–0.97]    | 0.0205 |
| Creatinine                          | 1 unit             | 2.15 [1.78–2.59]    | <0.0001             | 1.62 [1.21–2.18]    | 0.0012 |
| Diastolic diameter (mm)             | 1 unit             | 1.02 [1.00–1.04]    | 0.1266              | 1.03 [1.00–1.06]    | 0.0511 |
| Systolic diameter (mm)              | 1 unit             | 1.02 [1.00–1.03]    | 0.1122              | 1.03 [1.00–1.06]    | 0.0173 |
| EDV index (mL/m²)                   | 1 unit             | 1.00 [1.00–1.01]    | 0.0906              | 1.00 [1.00–1.01]    | 0.4235 |
| ESV index (mL/m²)                   | 1 unit             | 1.00 [1.00–1.01]    | 0.0670              | 1.00 [1.00–1.01]    | 0.1935 |
| EF                                  | 1 unit             | 0.96 [0.94–0.98]    | <0.0001             | 0.97 [0.95–0.99]    | 0.0151 |
| SV index (mL/m²)                    | 1 unit             | 0.98 [0.97–0.99]    | 0.0421              | 0.98 [0.95–1.01]    | 0.2228 |
| RVT                                 | 1 unit             | 0.11 [0.03–0.53]    | 0.0054              | 0.09 [0.01–0.29]    | 0.0765 |
| Risk Category | 2001–2007 (n = 371) | | 2008–2017 (n = 277) | |
|---|---|---|---|---|
| LVMI (g/m²) | 1 unit | 1.00 [1.00–1.00] | 0.2207 | 1.00 [1.00–1.01] | 0.1060 |
| Left atrial diameter (mm) | 1 unit | 1.04 [1.02–1.06] | <0.0001 | 1.05 [1.01–1.09] | 0.0146 |
| E/A ratio | 1 unit | 1.50 [1.23–1.84] | <0.0001 | 1.61 [1.31–1.99] | <0.0001 |
| DT (m sec) | 1 unit | 0.99 [0.99–1.00] | 0.0604 | 1.00 [0.99–1.00] | 0.2290 |
| TAPSE | 1 unit | 0.94 [0.91–0.98] | 0.0027 | 0.91 [0.84–0.97] | 0.0053 |
| PAPs (mmHg) | 1 unit | 1.02 [1.01–1.03] | 0.0006 | 1.02 [1.01–1.04] | 0.0082 |
| Mitral annulus (mm) | 1 unit | 1.05 [1.02–1.09] | 0.0051 | 1.05 [0.99–1.11] | 0.0800 |
| IPD, diastole (mm) | 1 unit | 1.36 [1.09–1.68] | 0.0058 | 1.34 [0.65–2.77] | 0.4312 |
| IPD, systole (mm) | 1 unit | 1.47 [1.18–1.84] | 0.0007 | 1.68 [0.89–3.17] | 0.1061 |
| MR Yes vs. No | 1.73 [1.30–2.30] | 0.0002 | 2.64 [1.36–4.47] | 0.0003 |
| Diastolic sphericity index | 1 unit | 1.01 [0.99–1.03] | 0.4265 | 1.04 [1.01–1.07] | 0.0104 |
| Systolic sphericity index | 1 unit | 1.02 [1.00–1.03] | 0.0931 | 1.04 [1.01–1.07] | 0.0041 |
| Diastolic conicity index | 1 unit | 0.99 [0.98–1.00] | 0.1062 | 0.98 [0.96–1.01] | 0.1311 |
| Systolic conicity index | 1 unit | 0.99 [0.99–1.00] | 0.1099 | 0.99 [0.97–1.00] | 0.0552 |

MI = myocardial infarction; PCI = percutaneous coronary intervention; NYHA = New York Heart Association; MR = mitral regurgitation; BSA = body surface area; EDV = end-diastolic volume; ESV = end-systolic volume; EF = ejection fraction; SV = stroke volume; RWT = relative wall thickness; LVMI = left ventricular mass index; DT = deceleration time; TAPSE = tricuspid annular plane systolic excursion; PAPs = systolic pulmonary artery pressure; IPM = inter-papillary distance.
4. Discussion

This study reports the largest single-center experience on SVR over 16 years of observation. The major findings of this study include: (1) SVR, mostly combined with CABG in patients with ischemic systolic LV dysfunction, was carried out with a risk of death acceptably low at long-term follow-up; (2) in a real world ischemic HF population, the volume reduction was feasible even in patients with more extensive CAD (Group I); (3) in patients with worse LV remodeling and less extensive CAD (Group II), SVR showed a trend toward a better outcome, though not statistically significant.

Although the comparison between populations of different studies is always hazardous because of differences in baseline characteristics or study design, our results portend an excellent prognosis for patients with ischemic HF and systolic LV dysfunction in terms of all-cause mortality, with a 4-year risk of death of 19.2% in the overall population, lower than other rates reported in the literature, including the STICH trial [5,7].

The surgical treatment of patients with ischemic HF has been a challenge for many years because of the paucity of data from randomized clinical trials mainly regarding patients with angina and significant CAD. The landmark STICH trial was designed to determine the benefit of CABG plus SVR in patients with ischemic LV dysfunction (Hypothesis 2 [7]). The primary outcome analysis failed to show a superiority of the combined procedure compared with CABG alone, calling into question the role of SVR in this high-risk population. Indeed, the STICH trial enrolled only a small percentage (about 20%) of the eligible population, limiting the generalizability of the results, especially in the absence of a concomitant registry. Furthermore, few non-pre-specified retrospective analyses of the STICH trial –Hypothesis 2 have been conducted due to the poor confidence of many surgeons with this procedure [11].

The results of our study share some insights with the STICH trial and, at the same time, focus attention on the selection of patients that could best benefit from this procedure. Firstly, the Group I population had very similar results to the STICH population (enrollment period 2002–2005). As most patients were more symptomatic for angina and less for HF, they received less PCI before surgery and had more CAD that required a higher number of coronary grafts combined with SVR (Figure 3), resulting in a favorable post-surgical volume (median $\Delta$ ESVI equal to 28.7%). Although we cannot discern the weight of the individual procedures on the percentage of volume reduction, it is noteworthy that in this population the decrease in LV size was more important than that reported in the STICH trial [7] (ranging between 6% in the CABG group and 19% in the CABG plus SVR group), supporting a major role of SVR in inducing LV reverse remodeling compared to medical therapy and/or devices [12]. On the other side, despite the evident benefit in all-cause death at 2, 4 and 8 years, the complex ischemic burden related to the presence of extensive CAD and angina in this group of patients might have been the driver for the negative impact of the diastolic dysfunction on the outcome. This implies that an increased E/A ratio along with a low EF may confer a higher risk of death at follow-up, in agreement with previous observations [13,14].

Conversely, the Group II population presented more symptoms of HF, a higher arrhythmogenic burden likely driven by the LV dilatation and a less ischemic profile, apart from the aetiology, with a more extensive LV remodeling and more secondary mitral regurgitation causing a less favorable geometry (Figures 3 and 4).

In this group, a higher baseline LV diastolic SI, with the ventricle being even more spherical after surgery, was associated with worse survival (Figure 1). This observation is in agreement with the results from the STICH trial reported by Oh et al. [15]. However, the link between baseline SI, changes after surgery and survival is not completely clear because the STICH investigators ascribed the worsening of diastolic dysfunction and/or mitral regurgitation to an increase in SI. Conversely, our results show that, although SI increases after surgery, there is a significant improvement in mitral regurgitation (Figure 1). Moreover, changes in E/A ratio do not necessarily indicate a deterioration in diastolic function, meaning that the degree of dysfunction can be the same (grade II) beyond the
statistical significance (Figure 1) [16]. Moreover, although the survival was not statistically
different between groups, a trend toward a better outcome was observed in Group II,
supporting a more robust role of SVR in patients with greater remodeling. Therefore,
to better understand the link between changes in LV remodeling phenotypes, surgical
technique and outcomes, a new analysis is needed.

This study has several limitations. First, the observation time was extremely long
and included changes in patients’ profile, medical and percutaneous therapies; surgical
techniques; and length of follow-up. The division used in this study, partially arbitrary,
was an attempt to take into account, in some way, how the population has changed over the
years. Although our center has a large amount of experience in this field, data collection
suffered from missing information, including the total number of previous PCI, which
could have affected changes in LV remodeling as well as the presentation of the patients.
On the other side, the released STICH results in March 2009 have undoubtedly affected
the decision to refer a patient for SVR, but the same results pushed expert surgeons to
reconsider the indications [17].

However, despite these potential confounders, the overall number of patients and the
length of the follow-up make the survival analysis fairly consistent.

Lastly, our findings should be applied to other populations with ischemic HF with caution
because of many differences in baseline characteristics, data collection and surgical expertise.

5. Conclusions

The patient population has consistently changed over time, making a shift from pa-
tients mainly symptomatic for angina and suitable for CABG to patients with prevalent
symptoms of HF and worse LV remodeling. In the latter group, the therapeutic target

Figure 4. Temporal changes in clinical, angiographic and echocardiographic characteristics which
may have influenced the decision for favoring SVR plus more or less coronary grafts.
might be the ventricle rather than coronary arteries. Suggested indications for SVR include: a previous anterior or posterior MI; a preoperative LV ESV index > 60 mL/m²; regional LV asynergy, either dyskinetic or akinetic; predominant HF symptoms [NYHA functional class III/IV] or in the presence of ventricular arrhythmias and/or angina needing surgical revascularization if the previous conditions are present. The procedure is contraindicated in the presence of severe dysfunction of the right ventricle and/or severe diastolic dysfunction [8]. These criteria should guide the patient selection, making SVR still a possible therapeutic strategy for ischemic HF, along with the operator experience and the volume of treated patients [18]. Of course, further studies are required in order to establish the real benefits of SVR at the time of CABG.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to the “Restricted Access” policy, as stated by Zenodo (the multi-disciplinary open repository maintained by CERN).

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