Left ventricular reconstruction in ischemic cardiomyopathy

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Chapter 11

General Discussion

Left ventricular remodeling after myocardial infarction lead to left ventricular (LV) dilatation, change in LV shape and myocardial dysfunction. Both the LV dilatation and the dysfunction (either global or regional) can additionally cause secondary or functional mitral regurgitation. In a more advanced disease state, it can cause the clinical syndrome of heart failure (HF). Furthermore, the LV remodeling is associated with malignant ventricular tachyarrhythmias and sudden cardiac death.

Surgical reconstruction of akinetic or dyskinetic segments reduces LV volume and this has two important effects. First, based on the Laplace equation, which relates wall stress inversely to wall thickness and directly to chamber radius, volume reduction diminishes wall stress and thereby reduces myocardial oxygen consumption. Minimising the mass of abnormal myocardium improves wall compliance, reduces filling pressure, and further enhances diastolic coronary flow. Second, reduction of wall stress, as a critical determinant of afterload, enhances contractile performance of the ventricle by increasing the extent and velocity of systolic fibre shortening [ref. 1].

Early and late outcome of LV reconstruction surgery

LV reconstruction surgery originates from ventricular aneurysmectomy. Secondary to extensive transmural infarction, ventricular aneurysms occur commonly anterior, less commonly inferior and rarely involving the lateral wal [ref 1]. Classically and before the widespread application of thrombolysis and later primary percutaneous intervention (PCI), the native coronary artery was totally blocked and the distal vessel filled by collaterals. Almost 50% contained an organised thrombus. There was controversy concerning the natural history of patients with ventricular aneurysms that were managed conservatively. An early report by Schlichter in 1954 reported a mere 18% survival at 5 years [ref. 2]. In contrast, analysis from the CASS trial data showed a 71% survival at 4 years [ref. 3]. Possible explanations could be differences in contractility of the remote non-infarcted myocardium, size of the aneurysm and extent of coronary disease.

Beck reported the first attempt to surgically repair a ventricular aneurysm in 1944 attaching a fascia lata graft to the external surface of the aneurysm [ref. 4]. The fascia lata graft and aneurysm were thereafter plicated with interrupted sutures. The patient died 6 weeks postoperatively from empyema and sepsis. Bailey described in 1956 the repair of four ventricular aneurysms [ref. 5]. Using a large toothed clamp across the base of the aneurysms, excision and repair of the ventricular aneurysms was possible without the use of extracorporeal circulation. In 1958, Cooley used a

pump oxygenator to excise a ventricular aneurysm and repair the ventricle with a linear closing technique [ref. 6].

Coltharp reported in 1994 on their 25-year experience in 523 patients that underwent ventricular aneurysmectomy [ref 1]. Ventricular reconstruction was performed by either the linear, septal, purse-string or patch technique. Hospital mortality was 7.5%. The most frequent complication with 22% was low cardiac output. Mortality appeared to be related to technique of repair: 8.2% for septal and linear techniques to 3.9% for purse-string technique and 4.0% for the patch technique, although the differences in these rates were not statistically significant (p=0.433). Kaplan-Meier estimates of overall survival rates were 85% at 1 year, 68% at 5 years, and 51% at 10 years. Overall median survival was 128 months. Long-term survival was best in those patients with good contractility of the nonaneurysmal LV (54%) and worst in those with impaired nonaneurysmal LV (35%) (p = 0.027).

Since Cooley's initial report on surgical aneurysm repair, new techniques have been developed and reported that attempt a more physiological and anatomical reconstruction of the residual ventricular cavity. The premise was that a more physiological reconstruction would result in a more normal ventricular function and a better long-term result. Stoney described in 1973 a repair technique in which the free lateral ventricular wall of the aneurysm is brought down and sewn to the scar along the septum [ref. 7]. With this technique, also the a- or dyskinetic septal scar could be excluded and should result in an increased LV ejection fraction. Jatene reported in 1985 a purse-string technique that incorporated a suture to close the neck of aneurysm [ref. 8]. Dor and Cooly reported - both in 1989 – the technique of using a prosthetic patch in the closure of the defect after aneurysmectomy [ref. 9, 10]. Also these techniques aimed to eliminate a- or dyskinetic scar in the interventricular septum and create a more physiologic reconstructed LV to improve postoperative hemodynamic measurement. Coltharp already discussed technical caveats that should be applied to aneurysm resection and LV reconstruction: too extensive a ventriculotomy and scar excision could encroach inadvertently on coronary arterial supply to viable muscle and extensive excision of scarred ventricles invited reconstruction of a ventricular cavity with compromised diastolic volume [ref. 1]. In patients with compromised diastolic volume, the restricted stroke volume causes cardiac output to becomes a function of pulse rate and may results in low cardiac output and pump failure.

With the technique described by Dor, the use of a endoventricular patch instead of a large resection, both preserves epicardial vessels and adequate ventricular volume

[ref. 11]. The Dor procedure excludes akinetic or dyskinetic portions of the ventricle, reshapes the ventricle with a stitch that encircles the transitional zone between contractile and non-contractile myocardium, and uses a small patch to reestablish ventricular wall continuity at the level of the purse-string suture [ref. 12]. The Dor procedure was initially perceived as a functional amputation of the ventricle with exclusion of the entire akinetic or dyskinetic scar. This led to increased sphericity of the ventricle in some patients, but in general the volume reduction still improved function. However, a suboptimal short axis/long axis ratio may influence the development of late moderate mitral regurgitation [ref. 13]. To prevent a compromised diastolic volume, to help configure the ventricle (ensuring a more normal short axis / long axis radio and to provide the correct position of the new apex, the use of a pre-shaped elliptical balloon (Chase Medical, Dallas, Tex) has been added to the procedure.

In our systematic review of the published peer-reviewed literature (62 studies; 12,331 patients) on the early and late outcome of LV reconstruction in ischemic heart disease, we found that (weighted) average early mortality was 6.9%. Cumulative 1-year, 5-year and 10-year survival were 88.5%, 71.5% and 53.9%, respectively. The Endoventricular Reconstruction (EVR) technique showed a reduced risk for both early ($RR = 0.79$, $p < 0.005$) and late ($RR = 0.67$, $p < 0.001$) mortality compared to the linear repair (early: $RR = 1.38$, $p < 0.001$; late: $RR = 1.83$, $p < 0.001$) confirming the improved outcome with a more physiological and anatomical reconstruction of the LV. Also of influence could be that patients that underwent EVR were operated in a more recent era with improved myocardial protection, anesthesiologic techniques, and perioperative care. Another contributing factor could be that revascularization further reduced the risk for late ventricular arrhythmias. These factors probably outweigh the increase in operative and extra-corporal circulation time with EVR and thus did not result in higher early mortality. Early and late mortality were mainly cardiac in origin, with as predominant cause heart failure in respectively 49.7% and 34.5% of the cases. Ventricular arrhythmias caused 16.6% of early deaths and 17.2% of late deaths. Concomitant CABG significantly decreased late mortality ($RR = 0.28$, $p < 0.001$) without increasing early mortality ($RR = 1.018$, $p = 0.858$). This decreased late mortality could be caused by a combination of a reduction in ischaemia and improvement in function of the remote non-scarred myocardium in the patients that underwent concomitant CABG. Concomitant mitral valve surgery showed both an increased risk for early ($RR = 1.57$, $p = 0.001$) and late mortality ($RR = 4.28$, $p < 0.001$). The presence of important secondary or functional mitral regurgitation (FMR) in patients with previous large anterior myocardial infarction is a marker of a more advanced disease state. The pathological mechanism behind it is either more

advanced LV dilatation, with tethering of the mitral valve leaflets, displacement of the subvalvular apparatus and dilatation of the mitral annulus causing incompetence of the mitral valve. The other possible mechanism is that the FMR could be caused by ischaemia or infarction in the postero-inferior wall of the LV or posterior papillary muscle complex in addition to the infarcted tissue in the anterior wall. Either way, the ventricular disease state in these patients with FMR is most probably more advanced.

One third of patients included in the review analysis were operated for HF (14 studies; 4,135 patients). In this group we noted an early mortality of 11.0% with a late mortality (3-year) of 15.2%. The EVR technique showed in these patients an even more profound reduction in relative risk (RR = 0.66, p = 0.004). An explanation could be that the patients that underwent LV reconstruction for heart failure, probably have larger LV volumes with more septal scarring. The linear technique cannot exclude the septal scar and carries the risk of creating a restrictive residual LV cavity, leading to compromised volume and increased diastolic dysfunction with LV failure as a consequence.

Risk stratification and predictors for mortality or poor functional outcome

Numerous studies have identified risk factors for mortality and limited survival after LV reconstruction in patients with HF, including renal insufficiency, severe mitral regurgitation, concomitant mitral valve surgery, and progressive LV dilatation, however no plain single risk variable is yet available to identify patients who would have a poor outcome and should not undergo LV reconstruction. These patients could better be referred for implantation of a left ventricular assist device (LVAD) or heart transplantation. Additionally, better patient selection and preoperative risk stratification will reduce mortality and improve outcome of LV reconstruction procedures. Colthard reported already in 1994 that hospital mortality in patients that underwent ventricular aneurysmectomy was related to the contractility grade of the remote myocardium [ref. 1] . About half of the patients he studied (231 out of 523) presented with congestive HF or angina with congestive HF. Mortality varied from 4.9% for patients with contractility Grade A (good contraction of nonaeurysmal anterior and inferior wall), 8.7% for patients with contractility Grade B (good contraction of nonaeurysmal anterior wall and hypokinesis of the inferior wall) to 15.7% for patients with contractility grade C (good contraction of nonaeurysmal anterior anterior wall and akinesis of the inferior wall; p=0.031). Five- and 10- year survival rates were 82% and 57% for patients with Grade A contractility, 72% and 38% for patients with Grade B contractility, and 60% and 42% for patients with Grade

C contractility. The difference in survival for Grade A and B approached statistical significance ($p = 0.096$), and the difference in survival between Grade A and Grade C was statistically significant ($p = 0.027$).

We tested echocardiographic wall motion score index (WMSI) as a predictor for mortality or poor functional result. WMSI was found to be the only statistically significant predictor for poor outcome (odds ratio 139, 95% confidence interval (CI) 17—1116, $p < 0.0001$). The optimal cut-off value for WMSI in predicting mortality or poor functional result was 2.19 with a sensitivity and specificity of 82% (95% CI 81.5—82.5% and 81.4—82.6%). The area under the curve was 0.94 (95% CI 0.90—0.99). We found that the echocardiographically derived WMSI has a good ability to predict outcome after SVR surgery. This was the single statistically significant predictor for poor outcome at 1-year follow-up. Other preoperative variables including age, renal insufficiency, severe pulmonary hypertension, and moderate to severe mitral regurgitation proved not to be significant predictors of outcome. Sufficient residual remote myocardium is necessary to recover from a SVR procedure and to translate the surgically induced morphological changes into a functional improvement.

We found that preoperative LVEF, LVESVI and LVEDVI were not statistically significant in predicting poor outcome after SVR surgery. This is interesting since White described already in 1987 that LV dilatation after myocardial infarction was more closely related to outcome then a decreased LVEF [ref. 14]. Di Donato and Dor confirmed that in ventricular restoration procedures, relatively irrespective of LVEF, the mortality increased in parallel to preoperative LV volumes [ref. 12]. The explantation could be that heterogeneity in the capacity for functional recovery of the residual remote myocardium might influence operative risk in patients with equally increased LV volumes. The post-infarction remodelled LV consists of heterogeneous tissue: scar (with varying degrees of transmurality), and residual myocardium with varying contractility. Volume derived indices are incapable of predicting outcome since these parameters depend on global ventricular measurements.

Our initial strategy to use the function of the basal pyramid (in line with the findings and work of Colthard on the remote myocardium) to select patients eligible for SVR surgery, proved to be insufficient: about one quarter of the patients did not benefit from the procedure (26 out of 101 patients: mortality 15 patients, NYHA class >/= III 10 patients). Indeed using the function of the basal pyramid takes into account only part of the LV and does not differentiate between normo- and hypokinesia. WMSI considers the entire LV and uses quantitative segmental function.

Quantification of scar

Cardiac magnetic resonance (CMR) is often used to assess ventricular shape, volume, and viability before a revascularization or ventricular reconstruction procedure. Hüther postulated that differences in the outcome should be reflected in the basal scar distribution, because the residual contractility of the ventricle is generated in this area and should be affected by scar tissue [ref. 15]. Patients with poor improvement of postoperative LVEF had more basal scar than those with large LVEF improvement. Of interest, they also found that only 22% of all improvements of regional function were located in segments that have received revascularization and 77% of all regional functional improvements were located in non-revascularized segments. This might indicate that the functional improvement may be more influenced by the SVR procedure than by revascularization.

Yamazaki et al. reported that the actuarial survival rate after isolated coronary artery bypass grafting (CABG) in patients with preoperative indexed LV end-systolic volume (LVESVI) of >100 ml/m2 was significantly worse than that in patients with LVESVI of ≤100 ml/m2 [ref. 16]. They also showed that congestive HF was more common among patients with LVESVI of >100 ml/m2. Using delayed-enhancement MRI, the mean percentage of hyper-enhancement in the entire LV area was 31 ± 12 (range 13–67%). The mean number of segments where scarring was >50% of the area (non-viable) was 4.5 ± 2.4, and the mean number of segments where scarring was >25% of the area (LV segments with MI) was 8.1 ± 2.8. The infarct size was significantly correlated with the LVEDVI, LVESVI and LVEF values. Moreover, the number of LV segments with MI was correlated with the LVEDVI, LVESVI and LVEF values, although the number of non-viable segments was not correlated with these values.

With regard to Laplace's law, a larger ventricle may receive greater benefit from volume reduction surgery; however, many reports have indicated that a larger LVESV was a significant risk factor after the SVR procedure. Patel et al. demonstrated that patients with LVESVI of >100 ml/m2 had a significantly increased mortality after SVR, whereas Athanasuleas et al. (in their RESTORE registry) reported that preoperative LVESVI of ≥80 ml/m2 was a risk factor for death after SVR [ref. 17, ref. 18].

The 2017 ESC/EACTS Guidelines on myocardial revascularization defined CABG with SVR for scarred LAD territory to be a class IIb recommendation if a postoperative LVESVI of <70 ml/m2 can predictably be achieved [ref. 19]. Di Donato et al. reported that SVR for patients with a relatively low LVESVI (<73 ml/m2) leads to a poor response and may even be useless [ref. 20]. They concluded that the LVESVI at follow-up in patients without reverse remodelling was not markedly large; hence,

without reverse remodelling, they would paradoxically show good survival. Skelley et al. indicated that patients with lower preoperative LVESVI had greater preoperative LVEF; however, there was no difference in preoperative LVEF or change in LVEF, compared with patients with larger LVESVI [ref. 20]. Consistent with these reports, we observed that patients with low LVESVI had the lowest likelihood of LVEF and LVESVI improvement at follow-up, although this did not affect their good clinical outcomes due to the fairly good baseline cardiac function.

Secondary or functional mitral regurgitation

As we have found in our structured review of published literature on early and late outcome after LV reconstruction surgery, the presence of important secondary or functional mitral regurgitation (FMR) in patients with previous large anterior myocardial infarction is a marker of a more advanced disease state. The presence of chronic secondary MR is associated with an impaired prognosis [ref. 21]. The pathological mechanism behind it is either more advanced LV dilatation, with tethering of the mitral valve leaflets, displacement of the subvalvular apparatus and dilatation of the mitral annulus causing incompetence of the mitral valve. The other possible mechanism is that the MR could be caused by ischaemia or infarction in the postero-inferior wall of the LV or posterior papillary muscle complex in addition to the infarcted tissue in the anterior wall. Either way, the ventricular disease state in these patients with FMR is clearly more advanced.

The most recent 2017 ESC/EACTS Guidelines for the management of valvular heart disease state that in contrast to patients with primary mitral regurgitation, there is currently no evidence that a reduction of FMR improves survival [ref. 22]. The guidelines furthermore highlight the importance of decision making by the Heart Team and that HF and electrophysiology specialists should be involved in the decision making. Controversy still exist on optimal surgical approach. Mitral valve repair with an undersized complete ring to restore leaflet coaptation and valve competence is the preferred technique according to the ESC/EACTS guidelines. However, valve replacement should be considered in patients with echocardiographic risk factors for residual or recurrent mitral regurgitation such as a mitral diastolic annulus diameter ≥37 mm, a systolic tenting area ≥1.6 cm2, and a severe functional ischaemic MR [ref. 4, 5]. The probability of recurrence of regurgitation after mitral valve repair could be as high as 50%. Indications for surgery in secondary mitral regurgitation are particularly restrictive when concomitant revascularization is not an option, owing to significant operative mortality, high rates of recurrent mitral regurgitation and the absence of a proven survival benefit.

The impact of LV reconstruction on FMR – both early and at late follow-up – is unclear, as is the indication for concomitant correction of FMR during LVR. On the one hand, immediate decrease of LV volumes and diameters, with the reduction of the distances between annulus and papillary muscles and between the papillary muscles, can lead to improved mitral valve leaflet coaptation [ref. 23-25]. Reduction of wall stress by the decrease in LV volumes and dimensions contributes to improvement in ventricular and papillary muscle function [ref. 8]. On the other hand, it is possible that LV reconstruction leads to a distortion of the geometry of the LV and subvalvular apparatus, causing an increase in MR. Moreover, possible further LV remodeling over time with gradual increase of LV volumes and diameters might lead to the appearance or recurrence of FMR at midterm follow-up if FMR is left untreated. Our management of FMR in patients undergoing LV reconstruction encompassed performing a restrictive mitral annuloplasty (RMA) when FMR ≥ grade 2+, established either preoperatively or immediately after LV reconstruction. Direct concomitant RMA was planned and performed in 38 out of 40 patients (95%) with preoperative MR ≥ grade 2+. In 17 out of 52 patients (33%) with FMR < grade 2+ preoperatively, FMR increased after LV reconstruction to ≥ grade 2+ leading to additional RMA during a second period of aortic cross-clamping. Early mortality in the RMA group (n = 55) was 12.7% and survival at 36 months 78.2 ± 11.2%. Early mortality in the no-RMA group (n = 37) was 5.4% and survival at 36 months 81.1 ± 12.8%. Patients in the RMA group had significantly more reduced LV function with greater LV dimensions and volumes preoperatively. As such, the presence or occurrence of at least moderate (grade 2+) FMR pre- or during surgery confirms to be marker of a more advanced disease state and translates into a higher early or in-hospital mortality. However, the combination of LV reconstruction with RMA (+/- CABG) leads to a sustained improvement in LVEF with reduction of LV volumes and equal survival in both patient groups. Also, recurrence-rate of FMR at late follow-up was low in both groups (1 patient per group).

Di Donato et al. propose to leave FMR grade 2+ untreated. They demonstrated an excellent survival; however, a substantial percentage of patients (29%) was found to have at least a moderate degree of FMR (grade 2+) at follow-up [ref. 27]. Prucz et al. demonstrated an overall reduction in FMR grade with good functional results and excellent survival in a group of patients who underwent LVR with untreated moderate MR. However, 76% of the patients still had MR > grade 2+ at follow-up [ref. 26]. As such, a conservative approach to FMR grade 2+ will leave a significant proportion of patients at risk for the potentially deleterious effects of FMR, which are further LV remodeling and increased mortality. As has been demonstrated, a moderate degree of FMR proves to be of hemodynamic importance in patients with reduced LV func-

tion and imposes significant clinical implications in post-infarction patients, even in those with minimal symptoms [ref. 29, 30]. In the setting of ischemic F .MR, even a regurgitant volume as little as 30 ml is associated with a limited 5-year survival of 47%.

We also evaluated 10-year clinical outcomes in 159 patients after an integrated approach of LV reconstruction with concomitant procedures (based on well-defined indications by the Heart team), and to assess preoperative risk factors for long-term clinical outcomes, focusing on LV geometry, LV function, and the presence of FMR. Concomitant mitral valve repair was performed in 68 of 70 patients with preoperative FMR ≥ grade 2. Mitral valve repair was not performed in 2 patients because of a completely calcified posterior mitral annulus. Preoperative FMR ≥ grade 2 was absent in 89 patients. Nonetheless, intraoperative TEE showed an increase in FMR to ≥ grade 2 immediately after LVR in 24 patients. These patients underwent additional mitral valve repair during a second period of aortic cross-clamping. Intraoperative echocardiography after mitral valve repair showed no more than mild FMR in any of the patients and a leaflet coaptation height of 8 ± 1 mm. This approach resulted in LV reverse remodeling (LVESVI –36%, improved LVEF +46%) and absence of FMR ≥ grade 2 at mid-term follow-up. Event-free survival 10 years after surgery was 46%. Increased age, higher preoperative WMSI, preoperative presence of MR ≥ grade 2 and a longer time interval after myocardial infarction were associated with worse event-free survival after surgery. Event-free survival is favourable in patients with WMSI < 2.5 and significantly worse when WMSI is ≥ 2.5. In both groups, the presence of preoperative MR grade ≥ 2 negatively affects event-free survival, despite successful correction of FMR. The presence of preoperative FMR negatively affected event-free survival in both patients with WMSI < 2.5 and WMSI ≥ 2.5 despite successful mitral valve repair. Consequently, the presence of preoperative FMR could be interpreted as a marker of LV remodeling. Advanced LV systolic dysfunction and presence of FMR provide a fatal combination. Preoperative LV volumes were not associated with adverse outcomes in the present study, in contrast to previous reports. However, the extent and function of the remote myocardium—and consequently the ability to recover after LV reconstruction surgery— may differ between patients with equally increased LV volumes. This heterogeneity in remote myocardium may explain why global ventricular measures such as LV volumes may not accurately predict event-free survival after LV reconstruction surgery.

We identified risk factors that can easily be determined and may help the Heart team to decide on which intervention to choose for patients with refractory HF with reduced Ejection Fraction (HFrEF). LV reconstruction surgery with concomitant

procedures is favourable for patients with a preoperative WMSI < 2.5— both with and without FMR, provided that the mitral valve is successfully repaired. In patients with WMSI ≥ 2.5 without MR, LVR may still be considered a viable option, however with slightly worse outcomes at longer follow-up. For patients with WMSI ≥ 2.5 and presence of FMR, event-free survival is extremely poor despite durable correction of MR. For these patients, the Heart team might first consider alternatives such as LVAD implantation or HTx. LV reconstruction surgery might still have a place in patients with contraindications for these alternatives, and in those for whom it might be warranted to defer LVAD implantation or HTx. Given that a longer interval between myocardial infarction and surgery was associated with adverse event-free survival, LV reconstruction surgery should preferably be considered in an early stage if patients develop symptoms of HF.

Incidence of ventricular arrhythmias and sudden cardiac death and the indication for ICD after LV reconstruction surgery

Sudden cardiac death (SCD) is an important cause of mortality in patients with both ischemic and non-ischemic heart failure. The Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) randomised 1,232 post-myocardial infarction patients with systolic dysfunction (LVEF ≤30%) to prophylactic ICD or conventional medical therapy [ref 31]. Unlike the earlier MADIT-I (1996) and MUSTT (1999) trials, MADIT-II did not require electrophysiologic testing for inducible ventricular tachyarrhytmia prior to enrolment [ref 32, 33]. After a mean follow-up of 20 months, the trial was terminated early because prophylactic ICD reduced all-cause mortality (14.2% vs. 19.8%; P=0.016; NNT=18). A post-hoc analysis demonstrated that the mortality reduction appeared to be entirely attributed to a reduction in SCD (3.8% vs. 10.0%; P<0.01). Interesting, ICD implantation was also found to be associated with a higher rate of new or worsened HF (20% vs. 15%). More recent, the SCD-HeFT trial demonstrated the mortality benefit of ICD's in patients with either ischemic or nonischemic cardiomyopathy (LVEF ≤ 35%) also in comparison to medical treatment with amiodarone and to placebo [ref. 34].

Since LVEF is used a selection criterium in patient with ischemic cardiomyopathy to qualify for prophylactic ICD implantation and SVR improves LVEF routinely to values above the selection criterium, the value of LVEF as criterium for ICD implantation in HF patients undergoing SVR was examined in a study. There is some theoretic or indirect evidence that SVR promotes electrical stability in the heart by different mechanisms [ref 35]. Thirty-seven consecutive patients with end-stage HF who underwent ICD implantation and SVR were evaluated. During admission, two-dimensional (2D) echocardiography (LV volumes and LVEF) was performed before

surgery and was repeated at 3 months after surgery. During 18-month follow-up, 12 (32%) patients had ventricular arrhythmias, resulting in appropriate ICD therapy. No significant relations existed between baseline LVEF (P = 0.77), LVEF at 3-month follow-up (P = 0.34), change in LVEF from baseline to 3-month follow-up (P = 0.28), and the occurrence of ICD therapy during 18-month follow-up. Hence, we concluded that LVEF before and after SVR is of limited use as criterium for ICD implantation in patients with end-stage HF since these patients remain at risk for malignant ventricular arrhythmias and hence may benefit from prophylactic ICD implantation. O'Neill et al. confirmed this finding in their study prospectively evaluating 217 consecutive patients with left ventricular ejection fractions less than 40% undergoing SVR [ref. 36]. They found an high early event rate of ICD-therapy (occurring in the first 90 days after SVR) that supports the use of pre-discharge electrophysiologic studies, implantation of ICD before discharge from the hospital, or both. A major limitation of the O'Neill study is that ventricular volumes are not measured before and after SVR. Ventricular volume before and after surgical intervention is crucial for arrhythmia development based on the following considerations. A large ventricular volume brings high wall stress and stretch, and stretch is arrhythmogenic [ref 37, 38]. Patients with ventricular arrhythmias (spontaneous or inducible) have end-diastolic and end-systolic volumes significantly larger than those seen in non-inducible patients and that patients who die at follow-up have the largest ventricular volumes[ref 39, 40]. The antiarrhythmic effect of SVR has been demonstrated by several groups and is related to volume reduction (less tension and stretch) and to the exclusion of the myocardial scar, which constitutes the trigger for electrical instability, but also to complete revascularization, which relieves ischaemia (another important component of electrical instability), and to mechanical resynchronisation which brings a more homogeneous distribution of wall tension and reduces regional pre-stretch [ref. 37, 41-42].

SVR procedure while reducing volume and wall stress and hence pre-stretch, leaves a large part of the substrate (myocardial scar) for ventricular arrhythmias in place. The question remains whether or not adding specific anti-arrhythmic surgical procedures, such as endocardectomy and cryoablation to patients undergoing SVR, will provide us with potentially curative treatment option for potentially fatal ventricular tachyarrhythmias. Furthermore, EP studies could be used after SVR when surgical intervention for ventricular tachyarrhythmias has been included to identify surgical failures in which ICD therapy is warranted. Sartipy et al. recently reported their experience with such a treatment in a series of 53 consecutive patients undergoing SVR and surgical intervention for ventricular tachyarrhythmias. The success

rate in terms of ventricular tachyarrhythmias-control in their experience proved to be 90% [ref 43].

More studies (randomised) and larger experience are needed to provide a correct indication for ICD in patients with dilated ischemic cardiomyopathy and symptomatic HF submitted to LV volume reduction and reshaping surgery.

Minimal-invasive / hybrid LV reconstruction (the future?)

SVR reduces the LV volume and reconstructs the shape of the remodelled LV leading to improvement in systolic function. Consensus from expert centres for SVR is that appropriately selected patients could benefit from a well-conducted procedure sufficiently reducing the LV end-systolic volume (LVESV) and reconstructing the elliptical shape of a normal LV. Conventional SVR relies on full median sternotomy, the use of extracorporeal circulation, cardioplegic arrest and ventriculotomy, which inflicts a considerable physical burden on often vulnerable patients with ischaemic heart failure. A less invasive procedure able to achieve the same results as conventional SVR is appealing and is a logic strategy to explore.

We evaluated the use of a novel hybrid transcatheter technique to reconstruct the remodelled LV by plication of the anteroseptal LV scar tissue which relies on the micro-anchoring technology of the Revivent TC Ventricular System (BioVentrix Inc. San Ramon, CA, USA). This system consists of a number of paired anchors connected by a poly-ether-ether-ketone (PEEK) tether that, once properly positioned, are pulled together with a controlled force by means of a specialised force gauge and finally released. The Revivent TC System represents the evolution of its previous fully surgical version. The Revivent system offers a minimally invasive strategy for LV reconstruction in HF patients with LV antero-apical scar and/or aneurysm. The procedural concept is similar to SVR, except that it utilises titanium anchor pairs on the beating heart. The decrease in the radius of the LV cavity reduces the myocardial wall stress (according to Laplace's law), thus leading to more efficient contractile function. This hybrid procedure is performed off-pump, under general anesthesia with fluoroscopic and echocardiographic guidance. The Revivent TC system implantation has several advantages compared to surgical LV aneurysm repair, as it does not require a median sternotomy, ventriculotomy, cardioplegia, extracorporeal circulation or aortic clamping, therefore it may result in reduced bleeding and air embolism risk, shorter recovery time and hospital stay.

The preliminarily experience regarding the early outcome of 9 patients that underwent implantation of the Revivent TC system between October 2016 and April

2017 by 2 Dutch Heart Centers (the Academic Medical Center Amsterdam, currently Amsterdam University Medical Center and the St. Antonius Hospital in Nieuwegein) were evaluated. Procedural success was 100%. On average, 2.6 anchor pairs were used to reconstruct the LV. Comparing echocardiographic data preoperatively and directly postoperatively, LV ejection fraction increased from 28 ± 8% to 40 ± 10% (change +43%, P < 0.001) and LV volumes decreased: LV end-systolic volume index (LVESVI) 53 ± 8 ml/m2 to 30 ± 11 ml/m2 (change -43%, P < 0.001) and LVEDVI 75 ± 23 ml/m2 to 45 ± 6 ml/m2 (change -40%, P = 0.001). Hospital mortality was 0%. The median duration of intensive care unit stay was 2 days [interquartile range (IQR) 1–46 days], and the median length of hospital stay was 9 days (IQR 3–57 days).

SVR procedures have demonstrated—in selected patients—that the dysfunctional myocardium can be favourably remodelled. When these preliminary results of the Revivent TC procedure are compared to (open) SVR, the efficacy of the LV reconstruction appears to be similar. Safety profile of the procedure and impact on the patient (median length of hospital stay 9 days) seem to be favourable. However, it must be stated that these preliminary results of the Revivent TC procedure in patients with ischemic HF, are observational and describe only the short term outcome. However, apart from a case report and an experimental paper of the technique in an ovine model, this was the first report describing the clinical results of this novel technique.

A larger and more thorough evaluation was done by reporting the first multicenter and multinational European experience with the Revivent TC system in a total of 86 patients, 51 of whom had the first-generation delivery system through median sternotomy and 35 had the procedure through the hybrid approach of mini-thoracotomy and internal jugular access. Eligible patients had LVEF 25-45%, LVESVi 60-120 mL/m2, NYHA class II-IV symptoms and an akinetic or dyskinetic scar in the anteroseptal, anterolateral and/or apical regions as a result of MI more than 90 days prior to enrolment. Patients with severe (4+) FMR were excluded. 30-day in-hospital mortality after Revivent TC System implantation was 4.5%, overall lower than the reported range of 3-14% 30-day mortality in SVR cohorts [ref. 48]. Furthermore, the estimated survival rate at 12 months post-procedure was very good (90.6%). At baseline, 59% of HF patients were in NYHA class III compared with 22% at 12-month follow-up. Improvements in quality of life measures (Minnesota Living with Heart Failure Questionnaire 39 vs. 26 points, P <0.001) and 6-min walking test distance (363 m vs. 416 m, P = <0.001) were also significant. Besides the substantial improvement in clinical and LV parameters, a significant FMR reduction of about 1 grade was also observed. Based on the above safety and efficacy data, CE marking was awarded, and the Revivent TC System has been available in Europe since 2016. To further as-

sess the clinical benefit of the Revivent TC System, the Randomized Evaluation and Verification of Ventricular Enhancement (REVIVE-HF) randomized-controlled trial is currently being conducted in Europe, comparing the Revivent TC System plus GDMT to GDMT alone in patients with HF and previous MI. 126 patients will receive the investigational device and 60 will remain on GDMT. The primary outcome is improvement in 6-minute walk test (6MWT) distance. Secondary outcomes include changes in Minnesota Living with Heart Failure Questionnaire (MLHFQ) score, New York Heart Association (NYHA) class, LV volumes, and LVEF by CMR. Preliminary data in a small cohort of patients has demonstrated a significant reduction in LVESVI and LVEDVI along with improvements in LVEF and cardiac output measured with CMR at 12 months.

The American Less Invasive Ventricular Enhancement (ALIVE) is a prospective, multi-center, dual-arm pivotal trial of the Revivent TC system, being conducted in US and UK sites. 126 patients will be allocated in 2:1 fashion to the study device and GDMT groups respectively. The key qualifying criteria for Revivent TC implantation are LV dysfunction (LVEF<45%) and dilatation (LVESVi >50 mL/m2), NYHA III-IVa symptoms despite GDMT, and presence of contiguous, akinetic scar involving the septum, anterior, apical or anterolateral LV walls. The control group will consist of patients on GDMT who meet all the inclusion criteria, except that the LV aneurysm/scar location does not permit treatment with the study device or the patient had previous open-heart surgery, pericardiotomy or left thoracotomy. Key exclusion criteria include the presence of a calcified LV wall near anchor targets, thrombus/mass in LA or LV, more than moderate SMR or degenerative MR, recent MI or stroke, need for coronary revascularization, significant pulmonary hypertension, renal dysfunction, and prior open-heart surgery or pericardiotomy. Safety data from patients treated with the Revivent TC system will be compared with surgical outcomes from the Society of Thoracic Surgeons database on LV aneurysm repair. The primary endpoint is freedom from device-related major adverse events including all-cause death, myocardial infarction, stroke, non-elective cardiac surgery and worsening HF requiring mechanical support more than 24 hours. Secondary endpoints to be assessed include improvement in quality of life and clinical parameters (NYHA class, 6MWT distance and MLHF score) and reduction in HF-related hospitalization rates.

The question still remains of whether patients with ischemic receiving optimal GDMT who have already undergone complete (functional) revascularization but continue to demonstrate symptomatic HF with LV dilatation (with or without FMR), benefit from an isolated structural intervention specifically targeting the LV. Because of the overall high surgical risk of these patients, as well as the complexity and

highly invasive nature of SVR, percutaneous ventricular remodeling devices may appear more attractive, and enhance our ability to answer this question due to easier patient selection and identification of independent device related effects. However, it needs to be stressed that most of our surgical patients underwent concomitant procedure (ventricular arrhythmia surgery, mitral and tricuspid repair, CABG) and it is likely that these procedures accounted to some extent to the succes of the procedure.

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