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Ventricular Reshaping with Devices

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ABSTRACT

Device-based left ventricular reshaping to facilitate reverse remodeling in cases of congestive heart failure represents an innovative surgical strategy. Originating from experiences gained with partial left ventriculectomy and dynamic cardiomyoplasty, the Myocor Myosplint device and the Acorn CorCap Cardiac Support Device are intended to improve left ventricle function through left ventricular shape change by means of wall stress reduction and passive diastolic support, respectively. Encouraging experimental and early clinical results with both devices support these novel concepts. Careful patient selection and a combined approach integrating adjunct surgical and medical treatments are crucial factors for the success of ventricular reshaping.

INTRODUCTION

Despite continuous improvements in medical and surgical therapy, congestive heart failure (CHF) remains one of the leading causes of death in the Western world. Heart transplantation is a highly successful therapy for end-stage CHF. Because of the limited number of donor organs, however, alternative surgical treatment options are being sought. One strategy is to treat or interrupt the process of pathologic adaptations, ie, left ventricular (LV) dilatation. Partial left ventriculectomy improves systolic parameters by reducing the LV diameter and, hence, LV wall stress [Batista 1996]. However, as has been demonstrated by finite element analysis, any potential improvement in LV systolic function will be balanced out by the concomitant impairment of LV compliance [Ratcliffe 1998]. Because of the associated high early-failure rate as well as the poor long-term survival of these patients, this invasive procedure has been mostly abandoned [Franco-Cereceda 2001]. Importantly, the intriguing concept of wall stress reduction in the pathologically dilated LV has been brought to the attention of clinicians and researchers and has since been subject of vigorous investigation.

In this article, we review the experimental validation and clinical application of two recently developed devices that aim at the improvement of LV function through ventricular reshaping without removing viable myocardial tissue. Whereas the Myosplint (Myocor, Maple Grove, MN, USA) changes the LV geometry to reduce wall stress, the CorCap Cardiac Support Device (Acorn Cardiovascular, St. Paul, MN, USA) passively constrains the LV to provide diastolic support. The potential advantages of both devices are the reduced invasiveness of the procedure and the possibility for a beating heart surgery.

MYOSPLINT

Technical Details and Surgical Procedure

The Myocor Myosplint device was developed to change the shape of the heart and to reduce myocardial wall stress [McCarthy 2001, Takagaki 2001]. The Myosplint consists of 2 epicardial pads that are connected by a flexible transventricular tension member. The tension member is made of braided polyethylene, has a diameter of 1.4 mm, and is covered with expanded polytetrafluoroethylene. The purpose of this last feature is to encourage endothelialization and to inhibit thrombus formation. Both epicardial pads have a diameter of 19 mm, are made of a rigid polymer, and are covered with polyester. One pad is fixed to the tension member. The deployable second pad determines the individual length of the Myosplint device.

Three Myosplint devices are implanted onto the LV and draw the opposing walls together (Figure 1A). The dilated LV is divided into 2 chambers with a reduced effective radius (Figure 1B). According to the law of Laplace, a reduction in radius correlates linearly with myocardial wall stress: if the radius is reduced, wall stress reduces by the same percentage. Although the law of Laplace is a simplification of the forces that are present, it allows a good estimation of the circumferential wall stress in the shape-changed LV and correlates well with complex models and the results of computer simulation, eg, finite element modeling [McCarthy 2001]. The length of the Myosplints was chosen to reduce the effective LV radius by 20% and to reduce wall stress by 20%. This stress reduction allows for the highest possible stress reduction without hemodynamic compromise [McCarthy 2001, Fukamachi in press].

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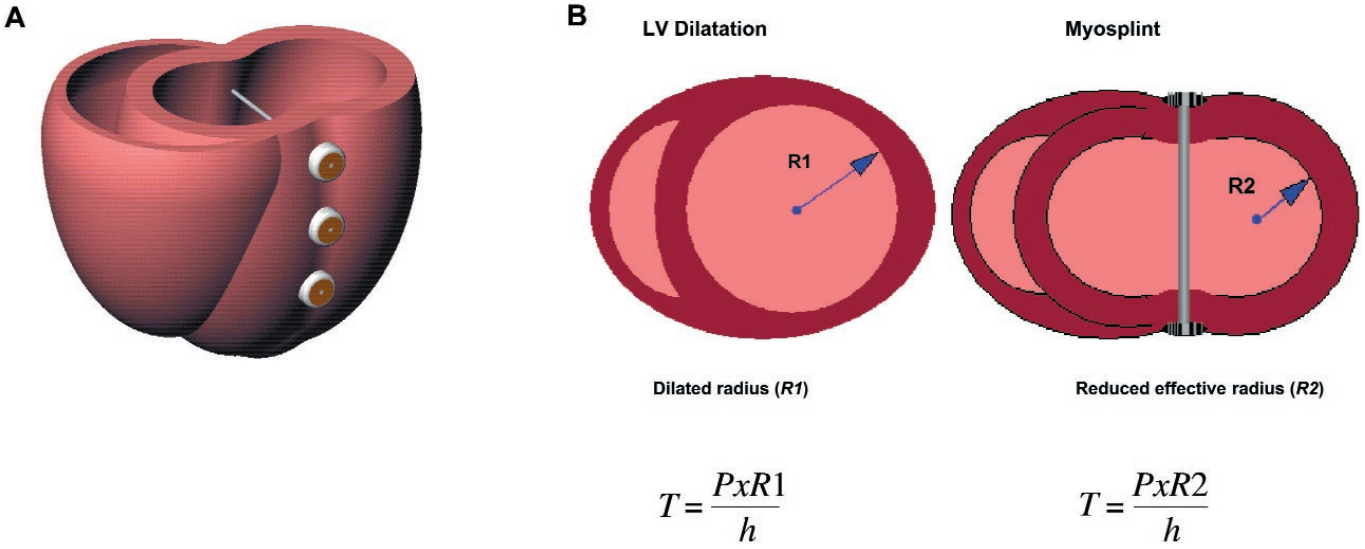

Figure 1. Myosplint concept. A, Three Myosplint devices are implanted to bisect the dilated left ventricle (LV). B, The law of Laplace predicts wall stress (*T*) in relation to ventricular radius (*R1*), intraventricular pressure (*P*), and wall thickness (*h*) (left). The Myosplint bisects the dilated LV to reduce the effective radius (*R2*) and wall stress (right).

The implantation of the Myosplint devices is performed on the beating heart without cardiopulmonary bypass [Fukamachi 2002]. The basal Myosplint is positioned medial (or lateral) to the anterolateral papillary muscle, and approximately 2 cm lateral to the posterior descending coronary artery. The middle and apical Myosplints are implanted in parallel with a distance of 3 to 5 cm from each other. The measurement and tightening device is employed to reduce wall stress by 20% (Figure 2). Epicardial echocardiography evaluates the position of the devices in relation to intracardiac structures as well as mitral valve function.

Experimental and Clinical Studies

The first animal experiments were started in June 1997 at the Cleveland Clinic to test the shape-change concept, to develop the implantation technique and all instruments, to test various locations of the Myosplint devices, and to assess the optimum level of LV wall stress reduction [Takagaki 2001, Fukamachi in press]. Several studies on the efficacy of the procedure were to follow in a pacing-induced canine heart failure model [McCarthy 2001]. In the Myosplint group (n = 8), the ejection fraction improved from 19% ± 5% to 39% ± 13% after 4 weeks of continued pacing with a simultaneous reduction in wall stress of 31%. The end-systolic pressure relationship shifted leftward with a significantly steeper slope, expressing an improved systolic function (Figure 3) [Takagaki 2002]. Furthermore, myocardial oxygen consumption was significantly lower in dogs implanted with the Myosplint devices (n = 3) than in control animals (n = 4) performing the same amount of LV work, results indicating improved myocardial energetics with the device [Inoue 2002].

The first clinical Myosplint implantations were started as an acute feasibility study in July 1999 at the Cleveland Clinic and were carried out on transplantation patients immediately before excision of their native heart and as the surgeons were waiting for the arrival of the donor organ (n = 5). The acute effects were described as a significant reduction of end-systolic wall stress by 27%. The LV end-diastolic and end-systolic volumes decreased significantly by 21% and 26%, respectively; these reductions enabled stable hemodynamic parameters to be maintained [McCarthy 2000].

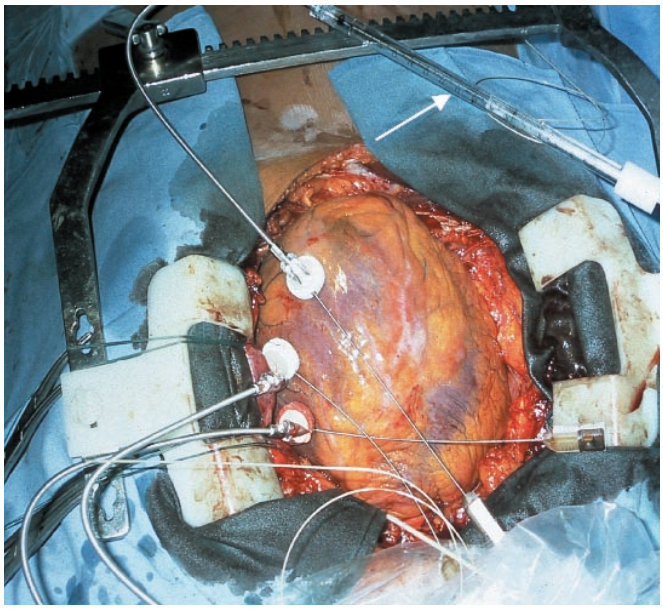

Figure 2. Myosplint implantation. Three tension members are inserted into the left ventricle. The measurement and tightening device (arrow) is applied to reduce the effective left ventricular radius by 20% and the wall stress by 20%.

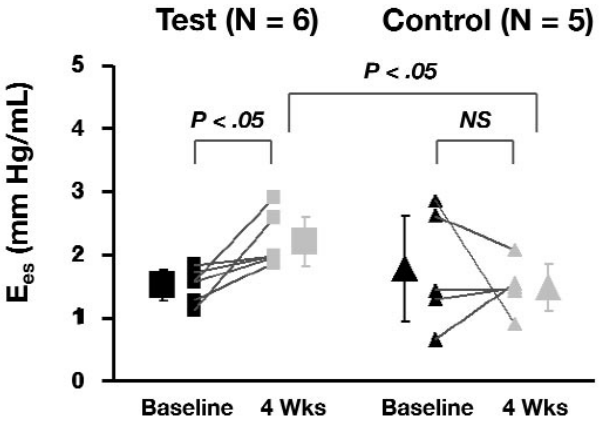

Figure 3. Myosplint effect in a pacing-induced heart failure model. Rapid ventricular pacing was done for 4 weeks before Myosplint implantation induced heart failure. Animals were instrumented with a conductance catheter before Myosplint implantation (Baseline) and after 4 weeks of continued pacing (4 Wks) to acquire the end-systolic pressure-volume relationship (ESPVR). Three-dimensional echocardiography was used for volume conversion. A significant steeper slope (Ees) of ESPVR was observed at 4 weeks after Myosplint implantation, indicating improved systolic left ventricle function compared with baseline and control animals. From [Takagaki 2002].

Since June 2000, chronic implantations have been performed in Germany and the United States as part of a phase I safety and feasibility study. Key inclusion criteria were (1) age between 18 and 80 years, (2) LV diameter between 65 mm and 120 mm, (3) LV ejection fraction of 35% or less, and (4) New York Heart Association (NYHA) functional class of III or IV. Exclusion criteria were (1) need for cardiac surgery on an emergency basis, (2) evidence of dyskinetic wall motion or LV aneurysm, (3) other mechanical support, (4) unstable or uncontrolled arrhythmias, or (5) presence of intracardiac thrombi. As of November 2002, both Myosplint implantations alone (n = 9) and Myosplint implantations in combination with mitral valve repair or replacement (MVR) (n = 12) have been performed. The first results with 7 patients indicate the safety and feasibility of the procedure [Schenk 2002]. All devices were successfully deployed, and the structural integrity of the devices was maintained throughout the follow-up period. Approximately 35 to 45 minutes were required for the Myosplint device implantation and shape-change procedure. If necessary, the devices were readily repositioned or removed. The procedure was well tolerated, and neither device-associated bleeding nor arrhythmias occurred. There was no evidence of intraoperative or postoperative thromboembolic events in any patient. In patients with mitral valve insufficiency (2+ or higher), concomitant MVR was indicated to realize the full benefit of the procedure. On the removal of the devices at the time of heart transplantation, a thin translucent layer covering the tension members was found (Figure 4). As depicted in Figure 5, the event-free survival rate (the absence of transplantation or death before transplantation) of all patients (n = 21) at 1 year after Myosplint implantation was 70% (personal communication with Myocor). Clinically, a number of patients improved, as seen by the marked decrease in patient heart size (Figure 6). The US Food and Drug Administration (FDA) has approved the device for an investigational device exemption as part of the evaluation in 20 patients at 4 centers in the United States. Only after completion of the European and US multicenter studies will one be able to comment on the true efficacy of the device.

CORCAP CARDIAC SUPPORT DEVICE

Technical Details and Surgical Procedure

The Acorn CorCap Cardiac Support Device provides passive diastolic constraint to the dilated LV. The concept is supported by studies on the mechanism of dynamic cardiomyoplasty, which have indicated that the passive "girdling" effect of the muscle wrap contributes prominently to any improvement in LV function [Kass 1995]. The CorCap device consists of a knitted polyester-mesh jacket designed to provide bidirectional compliance, allowing the dilated LV to return to an ellipsoid shape [Oz 2001]. The device may be supplemented with MVR or coronary artery bypass grafting (CABG) (Figure 7) [Konertz 2001c, Raman 2001]. A full sternotomy and cardiopulmonary bypass for partial unloading are used, and the device is wrapped around the heart with the hem fixed by anchoring sutures to the atrioventricular groove. The anterior edges are approximated and trimmed, and the procedure constrains the heart to a 10% reduction of the LV end-diastolic diameter [Konertz 2001c] (Figure 8).

Experimental and Clinical Studies

A number of preclinical studies have been conducted in various animal models to test the efficacy of the device. In a

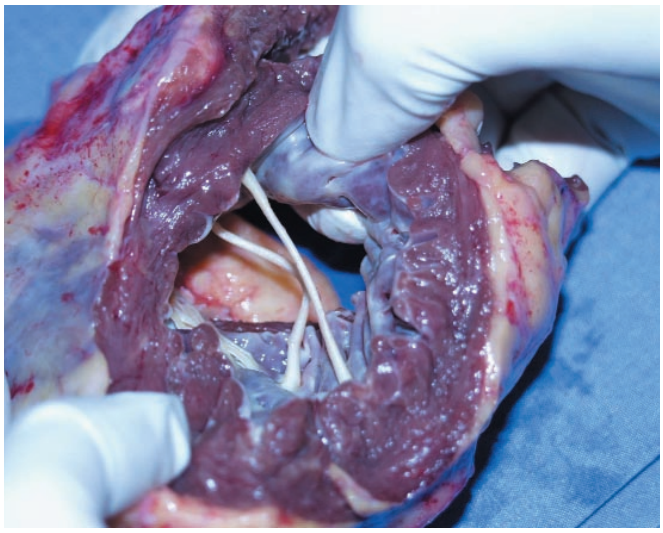

Figure 4. Myosplint blood compatibility. Removal of native heart with devices for heart transplantation was carried out 6 months after Myosplint implantation. All devices were covered by a thin, translucent layer; these observations are compatible with endothelialization of the tension members. The epicardial pads were encapsulated in fibrous tissue with no chronic reaction (not shown).

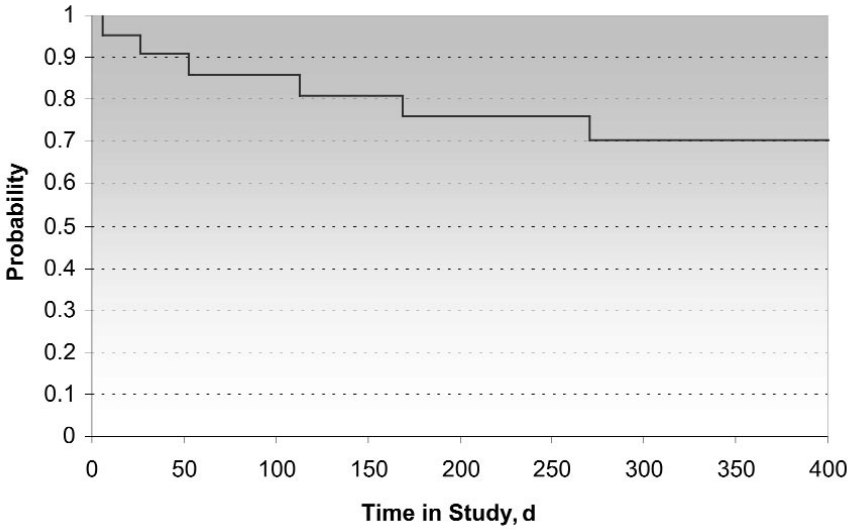

Figure 5. Event-free survival (freedom from death or heart transplantation) in 22 patients after Myosplint implantation.

pacing-induced ovine heart failure model, the animals with CorCap implantation (n = 6) had a higher fractional shortening, less mitral valve regurgitation, and smaller LV dimensions than control animals (n = 6) [Power 1999]. Similar results were obtained in a canine model of ischemic cardiomyopathy. Control animals (n = 6) progressed to further LV dilation during a follow-up period of 3 months, but CorCap-treated dogs (n = 6) did not [Chaudry 2000]. The latter investigation showed an improvement of LV function, as demonstrated by an increased fractional shortening, compared with control animals. Both studies have documented a high biocompatibility of the CorCap with observations of thin encapsulation of the device by surrounding tissue and only minor fibrosis. Furthermore, in an ovine model of acute myocardial infarction, CorCap implantation attenuated infarct development by alleviating pathologic wall stress and the subsequent reduction of the akinetic area [Pilla 2002]. These investigators hypothesized a positive effect of the CorCap on ventricular remodeling, which is further supported by studies that show an improvement of adrenergic signaling and calcium homeostasis as well as a reduction of myocyte hypertrophy and apoptosis after CorCap implantation [Sabbah 2000, Gupta 2001, Saavedra 2002].

The first clinical study involving 34 patients was initiated in April 1999 in Germany and Australia to test the safety and feasibility of the CorCap implantation [Konertz 2001c, Raman 2001]. In patients with dilated or ischemic cardiomyopathy, both CorCap implantations alone (n = 12) and CorCap implantations carried out in conjunction with MVR (n = 15), CABG (n = 1), CABG with infarct exclusion surgery (n = 4), or left ventricular assist device placement (n = 1) have been performed. The device was found to be safe as well as a feasi-

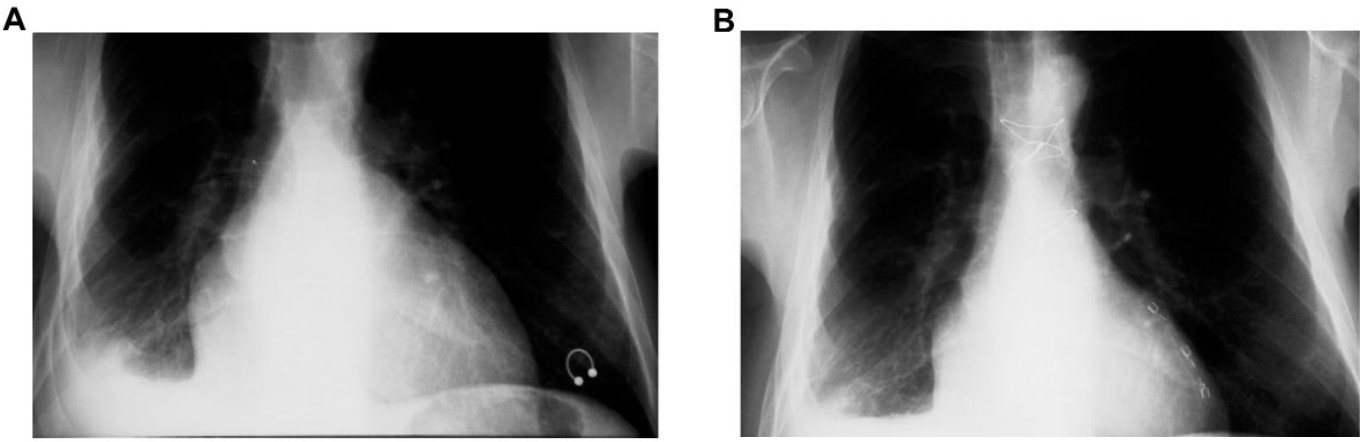

Figure 6. Myosplint implantation alone in a patient with dilative cardiomyopathy at the Department of Cardiac Surgery, Heart Center Leipzig, Germany. Radiographs at baseline (A) and 6 months postoperatively (B). Improved lung-to-heart ratio accompanied with an improvement in the ejection fraction and a reduction in the left ventricular end-diastolic volume (14% to 37% and 334 mL to 145 mL, respectively). Radiographs and data provided by courtesy of Prof. F. Mohr, Heart Center Leipzig, Germany.

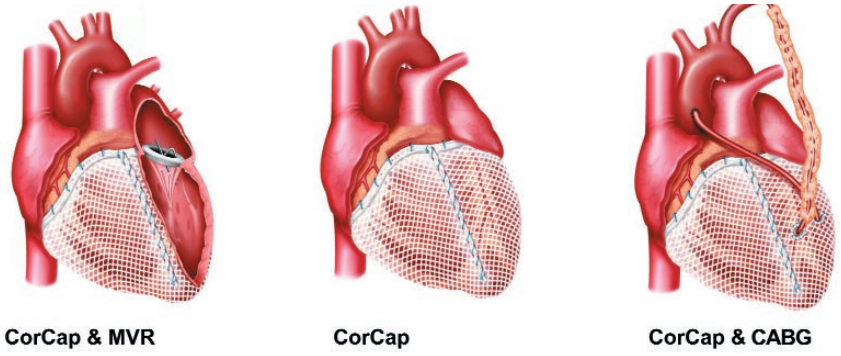

Figure 7. CorCap implantation with mitral valve replacement (MVR, left) or coronary artery bypass grafting (CABG, right) or as the sole implant (middle).

ble treatment, as demonstrated by the absence of any serious device-related adverse event and a straightforward implantation procedure (duration of skin-to-skin CorCap implantation and cardiopulmonary bypass: 2.2 ± 0.6 hours and 25 ± 4 minutes, respectively) [Konertz 2001a]. In a substudy of patients with and without MVR (n = 18), the LV end-diastolic diameter significantly decreased from 74 ± 6.3 mm at baseline to 66.1 ± 7.2 mm at 12 months after CorCap implantation, and this decrease was concomitant with a significant increase in LV ejection fraction from 22.8% ± 8.6% to 31.4% ± 12.6% [Konertz 2001b]. Similar results were obtained when patients with only the CorCap implantation (n = 10) were analyzed, indicating the efficacy of the device in the absence of confounding factors, ie, mitral valve insufficiency. Accompanied by an improvement in quality of life as perceived by the patients, the NYHA functional class of the patients significantly improved from 2.5 ± 0.5 at baseline to 1.6 ± 0.7 at 12 months after surgery. In addition, sequential pressure-volume analyses have shown a leftward shift of the pressure-volume loop without adverse changes in LV compliance up to 12 months after surgery (Figure 9) [Kleber 2000]. The device is currently being tested in a randomized clinical trial involving multiple centers in the United States, Germany, and Australia, and more than 150 patients are already enrolled. Pending the completion of this trial, approval by the FDA is being sought. Limited market release approval has already been given for CorCap implantations in 13 patients.

DISCUSSION

In view of the short supply of donor organs for heart transplantation, which is never expected to meet the overwhelming demand to treat patients with CHF, new surgical treatment options are increasingly being investigated. An intriguing strategy is to have an impact on ventricular remodeling by reshaping the dilated LV. Based on experiences gained with partial left ventriculectomy and dynamic cardiomyoplasty, investigators have developed two novel devices. One changes the shape of the dilated LV to reduce wall stress (Myocor Myosplint), and the other provides passive diastolic support to prevent further LV dilation (Acorn CorCap Cardiac Support Device). Results from experimental studies in various heart failure models have demonstrated that these devices improve LV function and contribute to reverse ventricular remodeling in CHF cases. Furthermore, both devices have been recently introduced into clinical trials, indicating that they can be safely applied and promote improvement of LV function in patients with end-stage CHF.

Several considerations must be taken into account when applying these new devices to treat patients. First, careful patient selection and patient preconditioning are imperative for optimal results. Neither procedure is intended as a salvage treatment in an emergency. Although all patients with CHF and dilated LV may potentially benefit from either Myosplint or CorCap implantation, these patients should not be dependent on inotropes and/or other circulatory support to maintain adequate hemodynamics. The indication to use either device may be rather a given in patients with end-stage, yet compensated CHF and may be likely in NYHA class II or III (or possibly "early" class IV) patients, who receive stable drug therapy for heart failure. In addition, despite the fact that neither preclinical nor clinical studies have indicated that Myosplint or CorCap implantation worsens diastolic parameter

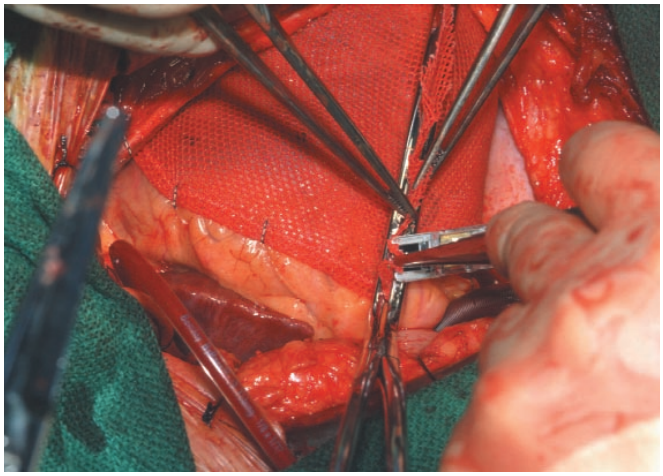

Figure 8. CorCap implantation. The CorCap is wrapped around the heart and anchored at the atrioventricular groove. The device is trimmed, and excessive material is removed. Photograph provided by courtesy of Dr. Smedira, Department of Cardiovascular Surgery, The Cleveland Clinic Foundation, Cleveland, OH, USA.

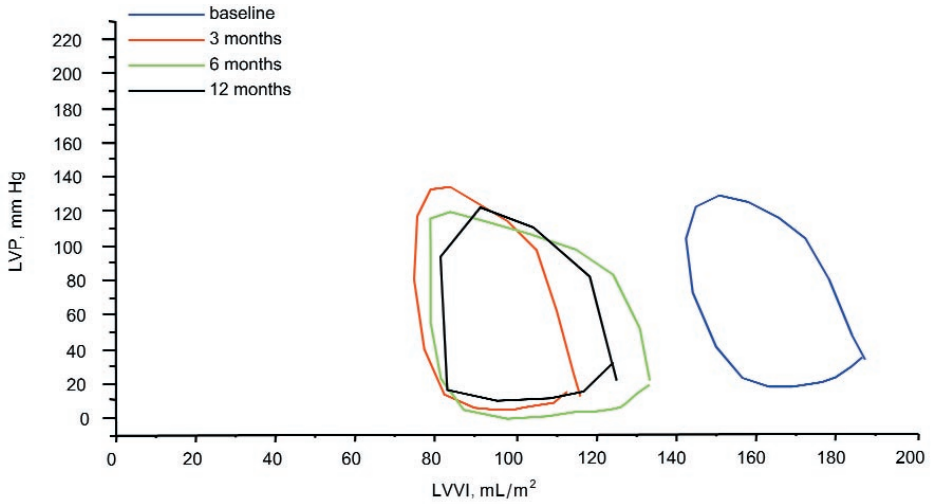

Figure 9. Pressure-volume relationship in patients with Acorn CorCap implantation. Left ventricular relaxation and late diastolic function are preserved, and systolic function is improved. Data provided by courtesy of Prof. Kleber, Department of Internal Medicine, Unfallkrankenhaus, Berlin, Germany. LVP indicates left ventricular pressure; LVVI, left ventricular volume index.

values, some attention should be paid to any preexisting impairment of diastolic function, such as in cases of restrictive or hypertrophic cardiomyopathy. Furthermore, concomitant lesions, ie, mitral valve insufficiency or coronary artery disease, should prompt the consideration of simultaneous procedures. The lessons learned from the initial clinical studies have been that adjunct procedures, such as MVR, CABG, and infarct inclusion surgery, may be readily performed in combination with Myosplint or CorCap implantation. Although it is still the subject of investigation, such combined treatment may add up to additional improvement in LV function. Therefore, based on a thorough preoperative workup with sufficient cardiovascular imaging results, an individual strategy is to be established that addresses each patient's unique needs. Finally, neither device should be regarded as an alternative to medical treatment. The severity of end-stage CHF requires multidisciplinary efforts, including intensive drug treatment with β-blockers and angiotensin converting enzyme (or "ACE") inhibitors, to complement heart failure therapy with Myosplint or CorCap implantation. This integrated medical and surgical approach may ultimately lead to a better prognosis and quality of life for these patients.

In summary, both Myosplint and CorCap represent new surgical strategies for treating patients with CHF by reducing LV wall stress and by providing diastolic support, respectively. Encouraging experimental and clinical results indicate that both devices may live up to their expectations. The efficacy of each procedure in the treatment of heart failure will be determined by future experience gained and in the lessons learned in the current European and US multicenter studies.

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