Durability of epicardial ventricular restoration without ventriculotomy†

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Abstract

OBJECTIVES: We previously presented early results employing a technique designed for beating heart, ventricular volume reduction (surgical ventricular restoration, SVR) without ventriculotomy for patients with antero-septal scar and dilated ischaemic cardiomyopathy. Significant volume reduction and clinical improvement were achieved. We now report durability in the first 11 patients available for assessment at 6 and 12 months after operation.

METHODS: After the Ethics Committee approval, 31 symptomatic patients with left ventricular (LV) dilatation and antero-septal scars underwent operation. The scarred lateral LV wall was apposed to the septal scar with serial paired anchors placed through epicardial transmural catheters, excluding non-viable portions of the chamber. Patients were followed at 1, 3, 6 and 12 months postoperatively with echocardiograms. Data are presented for the first 11 patients for whom core lab echocardiographic data were available at 12 months of follow-up.

RESULTS: LV end-systolic index (LVESVI), percent decreases from baseline at 6 and 12 months were 36.2 ± 18.3 (P < 0.001) and 39.6 ± 14.8 (P < 0.001), LV end-diastolic index volume index (LVEDVI) percent decreases from baseline at 6 and 12 months were 28.6 ± 18.8 (P < 0.001) at 6 months and 32.2 ± 14.9 (P < 0.005) at 12 months. All comparisons were by one-tailed t-tests using paired data.

CONCLUSIONS: These results demonstrate the persistence of volume reduction employing a technique designed to be used on beating hearts without ventriculotomy or cardiopulmonary bypass. The extent of volume reduction was consistent with results of conventional SVR in experienced centres. These early data validate the further development of technical iterations leading to a clinical study employing a closed chest endovascular platform.

Keywords: Heart failure • Ischaemic cardiomyopathy • Surgical ventricular reconstruction

INTRODUCTION

Patients with symptomatic heart failure and large segments of scarred akinetic or dyskinetic myocardium in the distribution of the left anterior descending coronary artery benefit from surgical ventricular restoration (SVR) [1–3]. Although effective in properly selected and operated patients, referrals may be limited due to concern regarding the invasiveness of the procedure. SVR requires cardiopulmonary bypass, left ventriculotomy and often a period of cardiopletic arrest.

Lon Annest conceptualized a method for performing SVR that can be used on a beating heart without cardiopulmonary bypass or ventriculotomy. The technology was developed by Bioventrix, Inc. We assessed the durability of ventricular volume reduction using this method as determined from data acquired from the first 11 patients for whom baseline, 6- and 12-month end-systolic (ESV) and end-diastolic volumes (EDV) were available.

METHODS

All operations and studies were conducted after receiving approvals from governmental authorities and institutional ethics committees. Informed consent was obtained from each patient. The studies were conducted under good clinical practice protocols.

Eligible patients had large antero-septal scars as determined from late enhancement Gadolinium magnetic resonance cardiac images. Inclusion criteria were end-systolic index (ESVI) > 60 ml/m², ejection fraction <0.35, NYHA class II–IV, age 18–75 years, no infarction within 3 months of operation, and referral for ventricular reduction operation. Important exclusion criteria were the need for concomitant mitral valve surgery (>2+ insufficiency) or the presence of a left atrial or ventricular thrombus. Patients were

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receiving optimum heart failure therapy and had no contraindication to warfarin therapy for 3 months after the operation.

Ventricular reduction was achieved using the Bioventrix Revivent Myocardial Anchoring System. Articulating polyester covered titanium anchors (5 × 25 mm), mounted on a polyethylene-ether-ether-ketone (PEEK) tether, were delivered to the right side of the interventricular septum. Using specialized needles, dilators and catheters, the anchors were delivered through the left ventricular free wall and interventricular septum over guide wires. A unidirectional, external anchor was fitted onto the tether to allow apposition of the left ventricular free wall at the scar perimeter to the septum (Fig. 1). Positioning of anchors was achieved using fluoroscopic guidance.

The surgical procedure is demonstrated in Supplementary Video 1.

Ventricular volumes were computed by a core laboratory at Ohio State University determined from transthoracic echocardiograms using Simpson’s Rule. The majority of patients had completion ventriculography to confirm the lack of any important communication between the restored ventricular chamber and the excluded ventricular space.

RESULTS

In initial ovine studies using previously infarcted models, the anchors were tightened manually as firmly as possible. However, several post-mortem studies demonstrated erosion of the anchors into the myocardium (Fig. 2). Subsequent operations utilized a specially developed force gauge set to provide a compressive force of 4 N (Fig. 3). Ventriculographic assessment of forces of 2, 4 and 6 N showed the preservation of the restored ventricular architecture and no evidence of erosion at post-mortem examination. All anchors in the patient studies were applied with a 4 N compressive force.

All values are given as the mean ± standard deviation. Significance was calculated using a paired t-test. Although 31 patients underwent operation, this study reports the first 11 patients to have core laboratory volume data at baseline, 6 and 12 months, with such data not yet being available on the remaining patients.

At 6-month follow-up evaluation, ESV (Fig. 4) was reduced from a baseline of 72.6 ± 26.9 to 46.2 ± 22 ml/m² (P < 0.0003) and to 43.9 ± 22 ml/m² at 12 months (P < 0.0001), with no significant difference between ESV at 6 and 12 months. The percent reduction from baseline was 36.2 ± 18.3 (P < 0.001) and 39.6 ± 14.8 (P < 0.001) at 6 and 12 months, respectively.

At 6-month follow-up evaluation, EDV (Fig. 5) was reduced from a baseline of 102.5 ± 27.3 to 73.2 ± 28.7 ml/m² (P < 0.0001) and to 69.5 ± 27.2 ml/m² (P < 0.0002) at 12 months with no significant difference between EDV at 6 and 12 months. The percent reduction from baseline was 28.6 ± 18.8 (P < 0.001) and 32.2 ± 32.2 ± 14.9 (P < 0.001) at 6 and 12 months, respectively.

DISCUSSION

Many effective surgical procedures are limited in their application when physicians are reluctant to refer patients due to perceived invasiveness and risks. New technology frequently mitigates both
risk and perception of risk. Examples include the successful development of minimally invasive valve surgery, percutaneous valves, ventricular support devices and percutaneous coronary intervention as an alternative to coronary bypass grafting. We have developed and applied a patented technique that allows ventricular restoration to be performed without cardiopulmonary bypass or ventriculotomy on a beating heart. This preliminary study is presented to demonstrate that a method has been devised that produces stable ventricular reduction over a 1-year period. The manuscript is submitted as a method paper rather than to advocate the use of this procedure. Like in all new methods, problems arise, and subsequent technical developments may mitigate adverse outcomes. In this instance, we focus on a solution to eliminate anchor erosion due to excessive compressive forces and argue that success was achieved initially in ovine models and subsequently in our early experience with patients. The data available to date are incomplete for suggesting routine application to patients.

During the developmental phase, in an ovine model, erosion of the anchors into the myocardium was observed as early as 6 weeks after operation. Erosion of the anchors into the left ventricular cavity would potentially result in expansion of the cavity volume. This has been avoided in patients at 1-year follow-up echocardiographic evaluation by applying a controlled compressive force of 4 N.

The procedure is not applicable as sole therapy to patients with mitral regurgitation severe enough to require concomitant repair or replacement. However, it can be used for the SVR portion of the operation as a method for shortening bypass time or cardioplegic arrest time. The presence of ventricular or left atrial thrombus is a relative contraindication, but several patients have been operated on following a period of anticoagulation and echocardiographic demonstration of thrombus resolution. Additionally, the presence of cardiac resynchronization therapy devices or internal defibrillators does not preclude its use.

The extent of volume reduction achieved using this novel technology is comparable with multiple observational studies of ventricular restoration surgery and exceeds the volume reduction achieved in the STICH trial [4–6].

SUPPLEMENTARY MATERIAL

Supplementary material (Video 1) is available at EJCTS online.

Video 1: Animation illustrating the catheter based left ventricular volume reduction. Scarred myocardium is eliminated from the contractile chamber by anchors placed at the periphery of the scar on the right side of the interventricular septum and the left ventricular free wall. These are then drawn together under carefully controlled conditions.

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Conflict of interest: Lon Annest is medical director of Bioventrix and salaried by Bioventrix as well as having stock options. Andrew Wechsler is a paid consultant to Bioventrix and has stock options.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr H. Reichenspurner (Hamburg, Germany): I have a few questions regarding where you put anchors, particularly the anchors at the interventricular septum, because we know from surgery that it differs a lot from case to case where you put your patch. It is usually at the border of viable myocardium to the scar. So how do you determine where to actually put your anchors?

And then it was not really clear to me how you determine the actual residual left ventricular volume. We use different devices, and Dor has taught us for many years that you have somehow to calculate the residual left ventricular volume. There actually are even devices for that.

And the last question is whether in your animal experience or in your human experience there was any generation of a ventricular septal defect in any of your cases.

Dr Wechsler: The first answer is that the operation is planned based on the gadolinium-enhanced magnetic resonance image, and it is possible to measure very carefully along the length of the interventricular septum the depth of the scar at each level. Time did not really allow going into this, but there is actually a series of needles, and there is a guide on the needle. So it is possible to align the tip of the needle with the guide of the needle and you can predict the depth of the needle insertion on the left ventricular septum. On the external left ventricular free wall, it is done manually or by taking a needle and just touching the wall and being sure there is scar tissue where you put it in.

Size is an interesting question because we have not experienced a case of diastolic dysfunction which would imply that we had overly reduced the ventricular volume. I think the reason for it is that when we do a traditional Dor procedure, we usually base the Fontan stitch on the endocardial appearance of the ventricle. I think oftentimes, even if you put the stitch at the junction between healthy and not healthy myocardium, it may not be a transmural scar at that point. It may only be an endocardial scar. So I think there is a greater tendency to over-reduce the ventricle. As you see, we got pretty respectable amounts of ventricular reduction, but I cannot swear that the anchors are placed exactly at the perimeter of the scar.

And the last question was? I am sorry.

Dr Reichenspurner: The volume calculation of the left ventricle.

Dr Wechsler: Yes. We did not do it as in traditional Dor procedures. In those, I always used an intracavitary balloon to try and set the end diastolic volume. We did not do that. You cannot do it here. But we have not overly reduced any of the ventricles. So I think it seems to be a good approximation. I think the idea is to try and find a way to do what we do less invasively and still get good results so that our cardiologists will be a little more willing to send patients earlier in the course of their disease, and that is where this is heading.

Dr A. Calafio (Riyadh, Saudi Arabia): I would like just to ask you a question about this procedure. This procedure is designed for patients with isolated ventricular aneurysms because these are very rare. If you have a CABG, a mitral or tricuspid, or other procedure to do, what is the role for the procedure that basically avoids CPB? In cases where you are already using CPB, it is not very important at this stage.

And the second question, are these 11 patients the only ones in whom the procedure was performed? There was morbidity and mortality, and are these just the patients that survived, or is this only a selected part of the experience; I ask just to have the procedure in the clinical context?

Dr Wechsler: There have been 32 patients operated on with one mortality early in our experience, but these 11 were selected because they are the first 11 patients for whom one-year echocardiographic data is available.

As regards concomitant procedures, of course you can do an OPCAB plus this procedure and still maintain the entire beating-heart concept in the absence of cardiopulmonary bypass. Alternatively, if you are going to do a mitral valve repair or some associated procedure, what it can do is shorten your ischemic time and shorten the period of time on cardiopulmonary bypass.

Dr C. Knosalla (Berlin, Germany): Your technique that you showed resembled more the standard linear resection introduced by Cooley than a real ventricular restoration in reconstructing the geometry of the ventricle. Reducing the volume is one thing, but the other thing is really reconstructing the geometry. Do you have any data available proving that your technique is really effective in restoration terms?

Dr Wechsler: Sure. One major difference between this approach and Dr Cooley’s approach, of course, is the fact that you are able to include the septum in the repair, so it is not purely an LV-LV procedure. There is an important reduction in the short axis radius of the ventricle, which is the goal of the procedure. It is rather linear in the long axis and, although it is beyond the scope of this presentation, I could have shown you angiograms of postoperative patients, and you would see that the ventricle is in fact reconstructed and a neoapex formed. It looks like a normal ventricle again.

Dr L. Menicanti (Milan, Italy): During your presentation, you said this procedure is good for type 1 dilatation. Nowadays we are faced with less and less dilatation type 1, and more frequently we see dilatation type 2 or type 3 where the septum is deeply involved and also the inferior portion of the apex is involved.

So I completely agree with you that these procedures can be really good for type 1, but for the other types, I have some doubt because the involvement of the left ventricle is really important. So what are your thoughts about that?

Dr Wechsler: In this procedure almost invariably the akinetic or dyskinetic left ventricle extends beyond the confines of the right ventricle. So the final stages of the procedure involve placing anchors and bringing free left ventricular wall together. Thus, we do manage the inferior component of the aneurysm. I think even in type 2 and type 3 ventricles, if there is enough of an anteroseptal component, this less invasive procedure is applicable.

Dr N. Trehan (Noida, India): One of the things that we do find very often are clots adherent to the wall. Is there any way of being sure that by doing this procedure blindly we will not embolize?

Dr Wechsler: The answer is that we do not operate on patients in whom the MRI or echo shows either left atrial or left ventricular clot. That would be a contraindication to the procedure.

Dr Trehan: So the MRI imaging would actually show us quite accurately?

Dr Wechsler: Yes, it does. It is very helpful. And, in fact, we have had a few patients whom we have placed on anticoagulation for two or three months and then brought them back and operated on them when repeat imaging showed resolution of the thrombus.

Dr R. Lorusso (Brescia, Italy): Last question, if I may. Is this cavity excluded? I mean, do you have proof that this is completely excluded, and if not, do you anticoagulate the patient for a while?

Dr Wechsler: Perfect question. We do anticoagulate the patients for three months. It is empiric. In our one patient that succumbed after the procedure, we were able to obtain an autopsy, and you can see that the walls of the ventricle are perfectly aligned and occlusive. We injected dye into the excluded cavity in the early cases, and there was no communication with the left ventricular cavity.

And, of course, we have the sheep model. We have probably operated on 90 sheep, and were satisfied that the aneurysm was completely excluded.