Original Article

Epicardial Cardiac Basal Annuloplasty: Preliminary Findings on Extra-cardiac Mitral Valve Repair

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Background: **Correction of functional mitral regurgitation in ischaemic heart disease, with a better risk:benefit ratio is an unmet need. A new methodology of external approach of correcting the annulus (BACE: basal annuloplasty of the cardia externally) to repair and stabilise the mitral valve without entering the heart was used in this prospective study. This study was conducted to assess the efficacy and safety of the concept BACE device in patients with moderate functional mitral valve regurgitation as a result of symptomatic coronary artery disease and heart failure.**

Methods: **The study involved a group of patients who had complex cardiac surgery between January 2000 and December 2001 at the University of Melbourne Campus Hospitals, Melbourne, Australia. Twelve patients with ischaemic heart disease, congestive heart failure, and moderate functional mitral regurgitation (MR) (minimum 2+) underwent the BACE procedure along with coronary artery bypass grafting and/or left ventricular reconstruction.**

Results: **No peri-operative complications or deaths related to surgical procedures occurred in the study group. There were no clinically significant problems related to the BACE implantation procedure. Mean MR grade was significantly improved in BACE Group from baseline to post BACE implant (2.8 pre- and 0.3 post-surgery; $P < 0.05$). Mean left ventricular ejection fraction (LVEF) was significantly improved ($P < 0.05$) and maintained at 6, 12, and 18 months post BACE implant compared to pre-operative baseline, with a mean improvement of 20% (24% at baseline to 44% at 18 months post-operatively) ($P < 0.05$). In addition to that the patients also had a significant improvement ($P < 0.05$) in mean New York Heart Association (NYHA) functional status from pre-operative baseline to 6 and 18 months post procedure with BACE.**

Conclusions: **External stabilisation of the cardiac base with BACE was associated with significant improvement in mitral valve function with no significant intra-operative or post-operative problems in patients with moderate functional MR. These findings support further study of BACE in functional MR.**

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Keywords. Mitral regurgitation; Repair; Extra-cardiac; Heart failure

Introduction

Mitral valve reconstructive surgery is an accepted therapeutic option for the management of severe mitral regurgitation (MR) in patients with heart failure, but its use for moderate MR is controversial [1–3]. The reluctance to undertake valve repair or replacement in patients with less-than-severe mitral regurgitation is attributed primarily to the risk profile of mitral valve procedures. Mitral valve repair or replacement requires access to the mitral valve through an intra-cavitary approach, which is associated with morbidity and mortality. These procedures carry a mortality risk of 2–6% in the presence of ischaemic heart disease [4]. A mitral valve procedure with coronary artery bypass graft surgery carries a higher risk of mortality and a definite risk of stroke [5].

MR can progressively worsen, especially in patients with ischaemic heart disease and cardiomyopathy [6]. Furthermore, while prognosis worsens with increasing severity of MR, even moderate MR is associated with excess morbidity and mortality [7–9]. These observations underline the unmet need for the novel approach of mitral valve repair in moderate functional MR associated with ischaemic heart disease with better risk:benefit profile. This extra-cardiac approach by BACE (basal annuloplasty of the cardia externally) device is investigated as a potential option for meeting this need. This approach with BACE is used to repair and stabilise the mitral valve without entering the heart. It is applied epicardially to the base of the heart

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to reduce the size or to prevent the further dilation of the heart. BACE may confer the ability to correct the functional MR regardless of the concurrent use of cardiopulmonary bypass. The prospective cohort study described herein was conducted to assess the efficacy and safety of BACE in patients with moderate functional MR in the presence of symptomatic coronary artery disease and heart failure.

Methods

Cohorts

The study involved one group of patients who had complex cardiac surgery at the University of Melbourne Campus Hospitals, Melbourne, Australia. This study group comprised 12 patients with moderate MR (minimum 2+) assessed and quantified by transthoracic echocardiography (TTE), and colour Doppler. These elective patients had symptomatic triple-vessel coronary artery disease and associated congestive heart failure as assessed by coronary angiography and radionuclide ventriculography and had not previously undergone surgical revascularisation for ischaemic left ventricular dysfunction. The decision to implant the BACE device in these patients was based on the confirmation of the MR by pre-operative transthoracic or transoesophageal echocardiography (TEE). All of these patients were reviewed by a multi-disciplinary team, which included a cardiologist and a cardiac surgeon for the management of symptomatic heart failure, and were scheduled to have primary surgery in an elective setting. Each of these patients was in NYHA functional class III or IV. The predominant manifesting symptoms were shortness of breath though 8 of the 12 patients had symptoms of angina as well. The significant limiting symptom was shortness of breath.

All 12 patients had BACE implantation along with coronary artery bypass grafting (CABG) and/or left ventricular reconstruction with out other mitral valve intervention between May 2000 and June 2001. The BACE surgical technique is described later in this section. Left ventricular reconstruction was performed in 10 patients in this group.

Informed consent was obtained from all participating patients upon clear explanation of the surgical procedures in the study and their associated risks.

Surgical Procedures

All procedures were performed through a midline sternotomy incision. Cardiac surgical procedures were performed with the aid of cardiopulmonary bypass on a heart arrested by blood cardioplegia.

BACE SURGICAL TECHNIQUE. The schematic diagram in Fig. 1 illustrates the concept.

The heart size was assessed early after chest opening. The circumference of the base of the heart was measured soon after the pericardium was opened and while the heart was beating with resting filling pressures. This was done with a piece of intravenous tubing that was slipped around the heart to encircle the heart at the atrio-ventricular groove, and then cross-referenced with a ruler. This gave a measurement of the circumference of the base of the

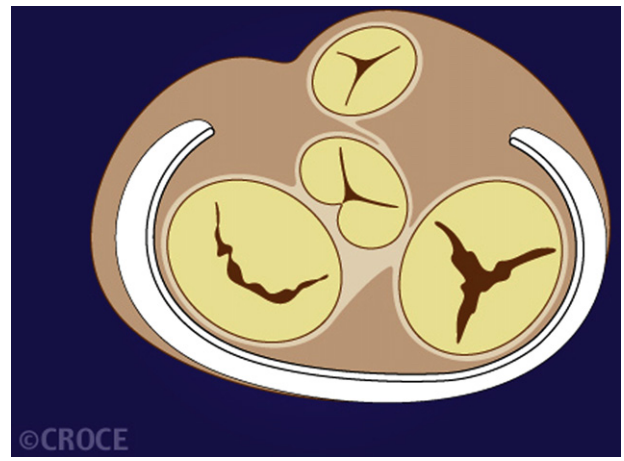


Figure 1. *Schematic showing the principle behind the BACE procedure.*

heart. The BACE device was then constructed with a strip of pliable polyester hernia mesh and tailored to the size measured on initial assessment of the base of the heart (~30 cm long, 4–5 cm wide). Once the cross clamp was applied and cardioplegia instilled, the heart was lifted. The BACE device was implanted along the atrio-ventricular groove on the posterior aspect of the heart. This is illustrated in Fig. 2 with the posterior sutures of the mesh to the a-v groove. It was then anchored on the atrial and ventricular sides of the atrio-ventricular groove with interrupted 4/0 prolene sutures, placed at 2–2.5 cm intervals. Once the BACE mesh was implanted, the distal anastomoses were constructed between the bypass grafts and coronary arteries. The coronary artery bypass grafts were then completed with the fashioning of the proximal anastomoses. Left ventricular reconstruction was performed in the presence of

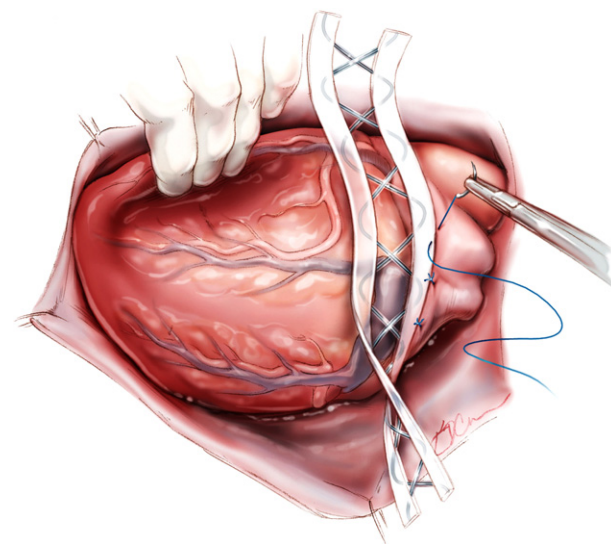


Figure 2. *Posterior implantation sutures of the mesh on atrial and ventricular side of the a-v groove. Note: the mesh here is stylised to show the underlying structures.*

haemodynamically significant confluent ventricular scars. Typically any scar that was larger than 4 cm in diameter was reconstructed using a geometric endo-ventricular repair (modified Dor procedure), with a bovine pericardial patch. The cross clamp was removed, and the heart was allowed to return to a regular rhythm. Once reasonable ventricular contraction was evident on transoesophageal echocardiography, patients were weaned from cardiopulmonary bypass. Patients were not routinely started on inotropes. No intra-aortic balloon pumps were used in the BACE Group. The typical strategy for the weaning process off CPB was as follows:

Rhythm was optimised by atrial and ventricular pacing followed by visualisation of right ventricular contraction by direct inspection and left ventricular contraction by transoesophageal echocardiography. Spontaneous recovery of cardiac function was allowed on pump gradually, then the bi-ventricular function was evaluated 30 min after removal of the cross clamp. If the functional recovery was slow, milrinone was infused at 0.5 mcg/kg/min; if bi-ventricular function had not significantly recovered after 30 min of support with milrinone, an intra-aortic balloon pump was used. The patients were then weaned off cardiopulmonary bypass with filling pressures similar to pre-bypass values.

At this stage, the degree of MR was dynamically assessed with transoesophageal echocardiography (TEE). The posterior aspects of the BACE device had been secured earlier. This left the free edges of the mesh on either side for additional tensioning and traction to literally tighten the base of the heart. Fig. 3 illustrates this, with the free edges of the mesh on either side of the RVOT ready to be tensioned. Once the appropriate degree of tension was achieved, the anterior edges of the mesh were secured in the "tensioned" position over the atrio-ventricular groove anteriorly on either side of the right ventricular outflow tract. The BACE device was adjusted and tightened just enough to eliminate MR. Fig. 4 shows the mesh edges secured on either side after the appropriate tensioning.

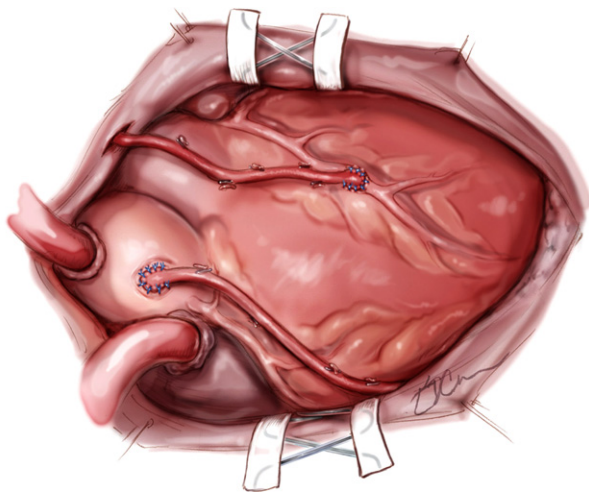


Figure 3. *The free edges of the mesh on either side of the RVOT, after completion of the grafting: awaiting final tensioning.*

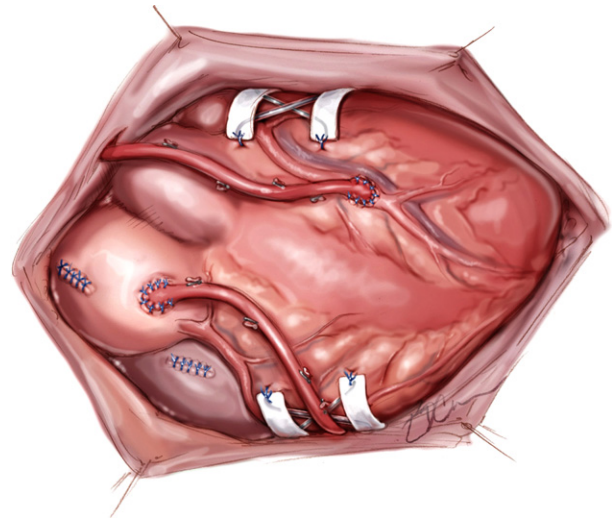


Figure 4. *The sutures on either side securing the BACE device with appropriate tension. Note sparing of the RVOT.*

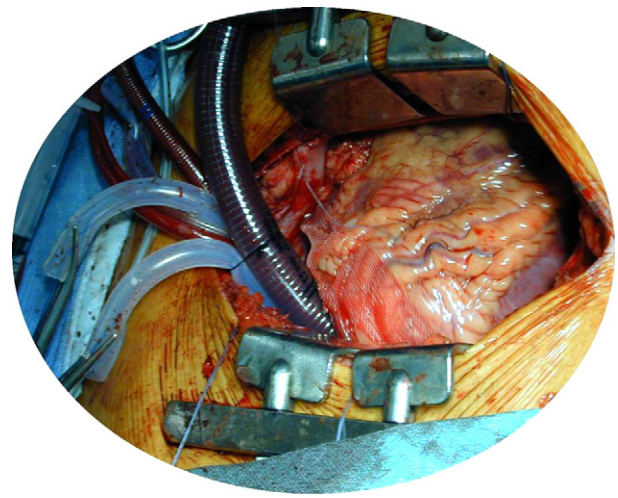


Figure 5. *Basal cardiac annuloplasty procedure. BACE device constructed from polyester mesh.*

This mesh typically did not cover the right ventricular outflow tract. Fig. 5 shows an operative photograph of the completed procedure.

At this state of tension, the BACE device was anchored anteriorly and laterally along the atrio-ventricular groove and degree of MR checked again. The sizing and implantation of the BACE device took an average of 20 min.

Choice of inotropic support was based on recovery of ventricular function.

Assessments

Short- and long-term outcomes were defined prospectively for BACE Group. Patients were followed postoperatively for a minimum of 18 months for assessment of long-term outcomes.

The primary long-term outcome, was the improvement in the degree of MR graded on a scale from 1 (mild) to 4 (severe) [10,11]. Other long-term outcomes included

left ventricular ejection fraction measured by radionuclide ventriculography and New York Heart Association (NYHA) functional status determined by a cardiologist. Echocardiographic assessments were done by echocardiologists and echocardiographers blinded to the surgical treatment of the patients.

Peri-operative deaths and surgical complications were defined as short-term outcomes. These data were summarised descriptively.

The primary long-term outcome, the degree of MR was summarised. Left ventricular ejection fraction at 6, 12 and 18 months and New York Heart Association functional status were summarised at 6 and 18 months for BACE Group. Improvement from pre-operative values was tested using the *t*-test for mean MR grade, mean LVEF (%), and mean NYHA functional status score in the BACE Group.

Results

Demographics and Baseline Clinical Characteristics

The number of patients in the BACE Group was 12. Mean age was 61 years. There were 11 males and 1 female.

Surgical Outcomes

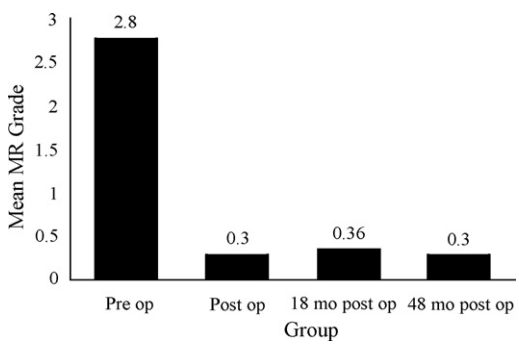
The mean number of coronary artery bypass grafts was 3.5 in the BACE Group. Left ventricular reconstruction was performed in 10 of 12 patients.

No intra- or peri-operative deaths or complications related to surgical procedures occurred in either group. No clinically significant problems related to the implantation procedure with BACE arose.

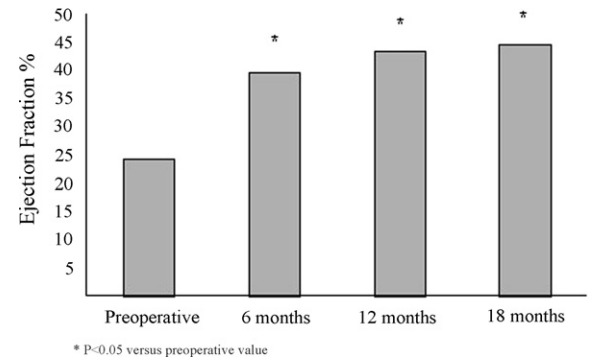
MR Grade

Mean MR grade significantly improved from baseline to post-surgery in the BACE Group (2.8 pre- and 0.3 post-surgery; $P < 0.05$); there is no change in the control group (2.0 pre- and 2.2 post-surgery).

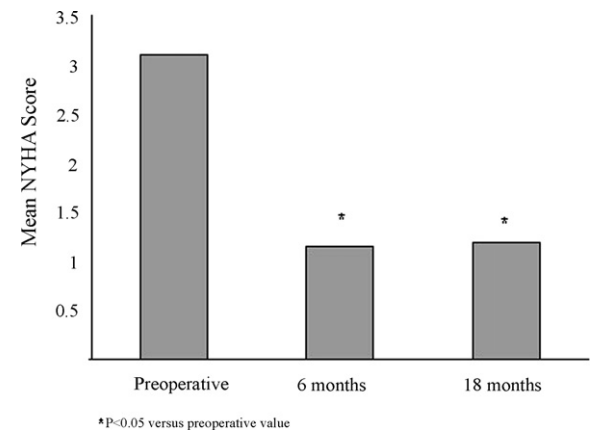
Patients in this group were followed beyond the initial 18-month post-operative follow-up period. At 48 months follow-up, 10 of the original 12 patients in BACE Group did not show any significant changes in their cardiac function and the degree of MR (Graph 1). The other two patients died due to causes unrelated to BACE procedure (emphysema and malignancy). In addition none of these patients required any other cardiac procedures during the 48-month follow-up period.



Graph 1. *Mean MR at pre, and up to 48-month follow-up in BACE Group.*



Graph 2. *Mean LVEF at pre, 6, 12 and 18 months post-surgery in BACE Group.*



Graph 3. *Mean NYHA score in the BACE Group (n = 12).*

Left Ventricular Ejection Fraction (LVEF)

Mean LVEF in BACE Group was significantly improved ($P < 0.05$) and maintained at 6, 12, and 18 months post BACE implant compared to pre-operative baseline, with a mean improvement of 20% (25% at baseline to 44% at 18 months post-operatively) ($P < 0.05$) (Graph 2). The mean improvement of LVEF in BACE Group was 18% (from 25% to 43%).

NYHA Functional Status

The patients in BACE Group had a significant improvement ($P < 0.05$) in mean NYHA functional status from pre-operative baseline to 6 and 18 months post BACE procedure (Graph 3).

Discussion

Intra-cavitary operative procedures that either repair the annulus of the mitral valve or replace the mitral valve with a prosthetic valve are the main definitive methods of managing MR. These major cardiac procedures, performed with the aid of cardiopulmonary bypass and cardioplegic arrest, are associated with significant complications and risks. Consequently, mitral valve repair is

primarily reserved for patients with severe MR. As moderate MR is likely to progress and is associated with adverse outcomes, particularly in the context of ischaemic heart disease, [7–9,12] a means of mitral valve repair with a risk:benefit ratio that is suitable for use in moderate MR is needed.

In this prospectively selected cohort study, external stabilisation of the cardiac base with the prototype of BACE device, a new approach in repairing and stabilising the mitral valve without entering the heart was associated with significant improvement in mitral valve function in patients with moderate functional MR. Improvement during the 18-month post-operative follow-up period was observed across several functional measures that include MR grade, LVEF, and NYHA functional status. The improvement in MR grade was better, and sustained in patients who had BACE implant than that of the patients in the control group, who had CABG and/or left ventricular reconstruction with no mitral valve intervention.

No safety issues related to the BACE procedure emerged in this study, which enrolled high-risk patients with triple-vessel coronary artery disease and congestive heart failure. The BACE implant procedure was not associated with any peri-operative deaths or complications. Furthermore, no post-operative complications related to BACE were reported over the 18-month post-operative follow-up period.

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There are important caveats about this study and report, that need to be highlighted:

1. Despite the study cohort being prospectively studied, the control group was selected in a retrospective manner. The control group was made up of a similar group of patients undergoing surgical procedures in the same time period and were similar in risk profile, pathophysiology, heart failure stage and functional status.
2. The study group is small because this is the first clinical report of a new procedure in a subset of complex and high-risk patients undergoing procedures over the period of 18 months. This is akin to a phase I study report in that respect in terms of safety and efficacy of the procedure.
3. Specific echocardiographic parameters such as mitral annular dimensions, LV volumes, ERO, etc. were not routinely measured as part of the standard echocardiographic studies in either the control or study group. This maybe partly because these parameters are newly accepted and were not in widespread use at the time of the study period.
4. A significant number of patients in both groups underwent ventricular reconstructive procedures, and this may have contributed to some improvement in mitral regurgitation.
5. Finally, this report is a real world experience of a complex group of patients that were not part of a formal trial, which may account for some of the deficiencies in data.

The results of this study should be interpreted in the context of these and other limitations. First, the sample size was too small to support definitive conclusions about effectiveness. Second, the effect of potentially confounding variables such as the concomitant medications, presence of arrhythmias, use of defibrillators, etc. on study outcomes were not assessed or accounted for. Our major reason for not including a control group was that this would be a comparison with a retrospectively derived patient cohort and that the size of the cohorts would be too small to make meaningful comparisons. These shortcomings notwithstanding, the findings constitute important preliminary observations that support further study of BACE implant. All patients that received the BACE implant had improvement in MR.

The major advantages of the BACE implantation are that:

1. It is less invasive; applied to the exterior or epicardial surface of the heart, which avoids intra-cavitatory approach related complications, such as embolism, coagulopathy, infection and prolonged cross clamp times due to intra-cavitary surgery within the heart.
2. The opportunity exists with this approach to assess the functionality of the mitral valve dynamically with the adjustment of the BACE device.
3. There is provision of support to the ventricular myocardium below the annulus as well as the annulus.
4. The ability to implant the device off-pump or on a beating heart.

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