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Early Ventricular Restraint after Myocardial Infarction: The Extent of the Wrap Determines the Outcome of Remodeling

（心筋梗塞後早期の心室拡張予防手術：左室被覆による梗塞後心筋リモデリングの抑制効果）

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Early Ventricular Restraint after Myocardial Infarction: The Extent of the Wrap Determines the Outcome of Remodeling

Running Head: Ventricular Restraint after MI

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Abstract

Background: Early infarct expansion initiates adverse remodeling, leads to left ventricular dilatation and portends a poor long-term outcome. Early mechanical prevention of infarct expansion has been proposed as a method to improve remodeling but the extent of ventricular restraint necessary to optimize the salutary effect is not known. We tested the hypothesis that left ventricular restraint (wrap) is superior to infarct stiffening (patch).

Methods: Infarction of 20-25% of the left ventricle was induced by coronary ligation in 69 sheep. Infarcts were either anteroapical (n=33) or posterobasal (n=36). Animals with each infarct received either no treatment (anteroapical, n=26; posterobasal, n=17), infarct stiffening with a localized Marlex® mesh patch (posterobasal, n=9) or left ventricular wrapping with Merseline® mesh (anteroapical, n=7; posterobasal, n=10). End systolic volume, end diastolic volume, end systolic muscle to cavity area ratio, left ventricular sphericity, ejection fraction and degree of mitral regurgitation as determined by quantitative echocardiography were assessed before infarction and at 2, 5 and 8 weeks after infarction to evaluate the extent of left ventricular remodeling.

Results: Control animals in both groups experienced adverse remodeling. Anteroapical infarct animals developed large left ventricular aneurysms and the posterobasal infarct animals developed severe mitral regurgitation. Early infarct stiffening did not significantly improve any parameter of remodeling due to the posterobasal infarct. Early left ventricular wrapping significantly improved remodeling after both types of infarctions.

Conclusions: Early left ventricular wrapping attenuates infarct expansion and has a salutary effect on remodeling. Simple infarct stiffening alone is not effective. (245 words)

Introduction

Infarction-induced left ventricular (LV) remodeling is now responsible for almost 70% of 4.9 million cases of heart failure in the United States.[1] Early infarct expansion (i.e., stretching) has been identified as the inciting event that initiates adverse remodeling and leads to LV dilatation.[2, 3, 4] Once established, ventricular dilatation is difficult to reverse and portends a poor long-term outcome.[5] These data, in conjunction with the development of emerging devices suitable for providing LV restraint in patients,[6,7] have increased interest in this surgical strategy as a potential means of preventing rather reversing or palliating congestive heart failure (CHF) due to infarct-induced remodeling.

Recent laboratory studies have, indeed, suggested that mechanical infarct restraint initiated soon after infarction can influence outcome of remodeling.[8, 9, 10, 11] The extent of ventricular restraint required to optimally affect remodeling remains to be determined. In this study using two ovine models of infarction-induced remodeling we compared localized infarct stiffening with a Marlex® mesh patch and Merseline® mesh wrapping of the exposed LV on the outcome of remodeling.

Methods

Animals and Infarction Models

We employed two well-characterized models of infarction-induced adverse remodeling and CHF in sheep.

An anterioapical (AA) infarction involving 22 ± 3% of the LV mass was created in 33 animals by ligating the left anterior descending artery (LAD) and its second diagonal branch (D_2) 40% of the distance from the apex to the base of the heart. This infarction reproducibly results in

large LV aneurysms after 8 weeks of remodeling.[12] Twenty six of these animals acted as untreated *controls* (AAC group). These control animals were created as part of several experimental protocols over a five year period since our laboratory began performing quantitative echocardiograms in sheep in 1998. Seven animals had an appropriately sized piece of Merseline® mesh *wrap* sutured in place over the LV from base to apex and from the LAD to posterior descending coronary artery (PDA) 14 days prior to infarction (AAW group).

A posterobasal (PB) infarction involving 24 ± 4% of the LV mass was induced in 36 animals by ligating the second (OM_2) and third (OM_3) obtuse marginal branches of the circumflex artery. [13, 14] This infarction routinely results in adverse remodeling and moderate to severe ischemic mitral regurgitation after 8 weeks. Seventeen animals acted as untreated controls (PBC). Again, these control animals were created over a five year period since our laboratory began performing quantitative echocardiograms. Nine animals had infarct stiffening with a localized Marlex® mesh *patch* sutured over the infarct area 14 days prior to infarction (PBP group). Six of these animals were included in a recent report by Moainie and colleagues.[9] Ten animals had Merseline® mesh ventricular wrapping (PBW) as described for the AA infarct. These animals have been previously reported by Guy and colleagues.[10]

Surgical Protocol

Dorset male sheep (Animal Biotech Industries, Doylestown, Pennsylvania) weighing 35 to 45 kg were used for this study. Animals were treated under an experimental protocol approved by the University of Pennsylvania's Institutional Animal Care and Use Committee (IACUC) and in compliance with NIH publication No. 85-23 as revised in 1985. Animals were induced with thiopental sodium (10 to 15 mg/kg intravenously [IV]) and intubated. Anesthesia was maintained with isofluorane (1.5% to 2%) and oxygen. All animals received glycopyrrolate (0.4 mg IV) and

enrofloxin (10 mg/kg IV) on induction. Under aseptic conditions, animals underwent left thoracotomy and polypropylene snares were loosely placed around the appropriate coronary arteries. Control group animals (AAC and PBC) then underwent chest closure with the coronary snares left subcutaneously. Patch treated animals (PBP) had a piece of Marlex® mesh (Ethicon, Somerset, NJ) fashioned to cover the area of intended infarction only (Figure 1). This patch was sewn in place using multiple 4-0 sutures. Wrap group animals (AAW and PBW) had a piece of Merseline® mesh (Ethicon, Somerset, NJ) appropriately tailored and sutured to the accessible LV from base to apex and from LAD to PDA (Figure 2). After placement of either restraining mechanism animals had chest closures with snares left subcutaneously.

Baseline Data and Infarction

Fourteen days after initial instrumentation, the sheep were again anesthetized. The surface electrocardiogram (ECG) and arterial blood pressure were continuously monitored. Echocardiographic data were recorded as described below. The subcutaneous snares were exposed, tightened, and tied to produce a myocardial infarction. Each animal received magnesium sulfate (1g IV), amiodarone (150mg IV), and lidocaine (3 mg/kg IV bolus, then 2 mg/min infusion) prior to infarction. Echocardiographic data were collected 30 minutes after infarction.

Echocardiography

Quantitative two-dimensional subdiaphragmatic echocardiograms were obtained before infarction and at 30 minutes, 2, 5, and 8 weeks after infarction. A sterile midline laparotomy (or a right or left subcostal incision) was made and subdiaphragmatic quantitative two-dimensional echocardiographic images were obtained using a 5 MHz probe (77020A; Hewlett Packard). Images were recorded on VHS videotape at 30 Hz (Panasonic AG-6300 VHS Recorder). LV

short axis images at three levels (the tips of the papillary muscles, the bases of the papillary muscles, and the apex) and two orthogonal long axis views were recorded. Previous reports have validated the reproducibility and effectiveness of this technique for evaluating LV remodeling in sheep.[8, 9, 10] Left ventricular volumes at end-systole (LVESV) and end-diastole (LVEDV) were calculated using Simpson's rule. Ejection fraction (EF) was calculated from LVESV and LVEDV. End-systolic muscle to cavity area ratio (ESMCAR) was also determined at each time point. Ventricular sphericity at end systole was assessed as the ratio of LVESV to the volume of a sphere with a diameter equal to the LV long axis dimension. This ratio approaches unity as the ventricle becomes more spherical. All the measured echocardiographic indexes of remodeling were normalized to their baseline values. The degree of mitral regurgitation (MR) was determined quantitatively in PB infarct animals by assessing the area of the regurgitant jet as a percentage of left atrial area in the apical four-chamber view. The following grading was used: grade 1 < 20%; grade 2 = 20% to 40%; grade 3 = 40% to 60%; and, grade 4 > 60%.[15]

Follow-up studies

Echocardiographic data were collected at 30 minutes and 2, 5, and 8 weeks after infarction. Following the 8-week study, the animals were euthanized (80 meq potassium chloride IV bolus). The heart was excised, opened, and inspected to confirm infarction size and location.

Statistics

Measurements are reported as means ± standard errors of the mean. For each dependent variable differences between groups are compared by analysis of variance (SPSS, Chicago, IL); significance was established at $p < 0.05$. Post hoc comparisons at each time point are performed with a Student's t-tests with Bonferroni correction. Differences in degree of MR were compared using the Mann-Whitney test.

Results

Echocardiographic data are summarized in Tables 1 and 2. In the AA infarct groups all animals had significant ($p < 0.05$) increases in LVESV (AAC = 2.38 ± 0.12, AAW= 1.74 ± .35) and LVEDV (AAC=1.78 ± 0.07, AAW=1.32 ± 0.13) by 8 weeks after infarction (Figure 3). However, both of these parameters of remodeling were significantly less in the AAW group ($p < 0.05$). Normalized sphericity increased and ESCMAR decreased significantly ($p < 0.05$) at 8 weeks in the AAC group (respectively; 1.20 ± 0.06 and 0.86 ± 0.06) but were maintained at baseline values in the AAW group (respectively; 1.01 ± 0.14 and 1.01 ± 0.07) at 8 weeks after infarction (Figure 4).

In the PB infarct groups all animals underwent remodeling as demonstrated by significant changes in LVESV (PBC = 2.09 ± 0.17, PBP = 2.09 ± 0.18, PBW = 1.73 ± 0.17), LVEDV (PBC = 1.74 ± 0.12, PBP = 1.52 ± 0.14, PBW = 1.52 ± 0.19), sphericity (PBC = 1.44 ± 0.12, PBP = 1.55 ± 0.17, PBW = 1.33 ± 0.17) and ESMCAR (PBC = 0.67 ± 0.04, PBP = 0.67 ± 0.05, PBW = 0.91 ± 0.12) by 8 weeks after infarction (Figures 3 and 4, $p < 0.05$). However, LVESV, LVEDV, ESMCAR were all significantly improved by ventricular wrapping when compared to the control and patch groups ($p < 0.05$). The PBP group was not significantly different from PBC group with respect to any parameter of remodeling. MR was significantly reduced in both the PBP and PBW groups as compared to the PBC group (Figure 5, $p < 0.05$).

Discussion

All animals in this study experienced adverse remodeling as demonstrated by increased ventricular volumes and changes in ventricular shape. These data indicate the powerful stimulus for remodeling that a 20-25% transmural infarct imposes on the LV. In spite of this stimulus to

remodel, extensive LV mesh wrapping significantly attenuated the remodeling process in both anteroapical and posterobasal infarcts. Patch infarct stiffening, however, did not produce a significant improvement in remodeling when compared to controls. Moainie and colleagues had previously reported a non-significant trend toward improved remodeling with mesh infarct stiffening in the posterobasal infarct model.[9] This trend was, however, lost in the current study with the addition of three additional animals to the treatment group and subsequent comparison of these treatment animals to a larger historical control group.

The results of the current experiment confirm and extend the findings of Guy and colleagues which demonstrated a benefit on remodeling of ventricular wrapping in the posterobasal ovine infarct model.[10] Pilla and colleagues have reported a beneficial effect of early postinfarction circumferential heart wrapping (i.e. including the right ventricle) in an ovine model of dilated ischemic cardiomyopathy not associated with LV aneurysm or IMR.[11] All these studies considered together suggest that extensive ventricular wrapping can significantly reduce infarction-induced remodeling, but that simple infarct stiffening is insufficient.

The etiologic importance of infarct expansion in the initiation and progression of infarct-induced LV remodeling is confirmed by the results of this study. Laboratory and clinical data have shown that *expansion* (stretching) of a transmural myocardial infarction initiates a progressive myopathic process in normally perfused myocardium.[2, 3, 4] This phenomenon is initially localized to myocardium immediately adjacent to the infarct but *extends* during the remodeling process to convert contiguous normally perfused myocardium into hypocontractile, *remodeled myocardium*.[3,16] The stretch-induced myopathic process has been associated with myocyte apoptosis[17] and disruption of the extracellular matrix secondary to activation of matrix metalloproteinases.[18] The failure of surgical reshaping operations and interventions for IMR to

improve survival in ischemic cardiomyopathy patients strongly suggests that infarct-induced myopathy is very difficult to reverse once established. [19, 20, 21, 22]

Using contrast echocardiography, Jackson has demonstrated that geometric changes consistent with increased regional wall stress occur in the borderzone region adjacent to infarcts undergoing early expansion and subsequent remodeling.[23] A finite element analysis by Guccione and colleagues[24] confirms these findings and also demonstrates that once the myopathic process is fully developed, contractile function in non-ischemic myocardium is impaired beyond what would be expected due to changes in LV geometry and stress distribution. The salutary effect of ventricular wrapping demonstrated in this study is likely due to its ability to attenuate early infarct expansion thereby reducing adverse remodeling.

A secondary result of the analysis performed here has to do with contribution of ischemic MR (IMR) to the remodeling process. It is interesting to note that the significant reduction in IMR seen in the PBP group was not associated with a significant improvement in remodeling. These data suggest that IMR is not an important component of the stimulus that drives postinfarction ventricular remodeling. Careful review of the echocardiographic data from the control groups provides further evidence that IMR has a minimal effect on post-infarction remodeling. Both control groups (AAC and PBC) had similar-size infarcts and even though the PBC group developed severe IMR, the outcome of remodeling as assessed by echocardiographic parameters was very similar (Figure 6). These data strongly suggest that IMR is a manifestation rather than a contributing factor to post-infarction remodeling.[10]

The pre-emptive and prophylactic surgical interventions used in this study cannot, obviously, be directly applied clinically. They were employed to simplify the experiment by

eliminating the need for a second operation after infarction had been induced. The results of the study do, however, have important clinical implications. Our findings provide further support for infarct restraint as an early intervention intended to prevent rather than reverse infarction-induced remodeling. Because of the theoretical risk of constrictive pericarditis and the potential difficultly with reoperative surgery associated with ventricular wrapping we had hoped that simple infarct stiffening would be sufficient. However, this work strongly suggests that extensive ventricular wrapping is necessary to significantly influence remodeling.

A great deal of work is still required to optimize the implementation this preventative strategy before it can be clinically applied. Future experiments will need to determine the best timing for restraint placement and if complete heart wrapping (including the right ventricle) adds any benefit. In addition, the effect of infarct location and the material properties of the wrap material on remodeling will also need to be studied. Finally, it will be important to develop an imaging modality to assess the risk of adverse remodeling early after infarction to permit intervention only in high risk patients.

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References

[1] Gheorghiade M, Bonow RO. Chronic heart failure in the United States: A manifestation of coronary artery disease. Circulation 1998; 97: 282-289.

[2] Aweisman HF, Healy B. Myocardial infarct expansion, infarct extension, and reinfarction: pathophysiologic concepts. Prog Cardiovasc Dis 1987; 30:73–109.

[3] Jackson BM, Gorman III JH, Moainie S, et al. Extension of borderzone myocardium in postinfarction dilated cardiomyopathy. J Am Coll Cardiol 2002; 40: 1160-1167.

[4] Pfeffer MA, Braunwald E. Ventricular remodeling after myocardial infarction: experimental observations and clinical implications. Circulation 1990; 81:1161-1172.

[5] St John Sutton MG, Pfeffer MA, Plappert T, et al. Quantitative two-dimensional echocardiographic measurements are major predictors of adverse cardiovascular events after acute myocardial infarction: The protective effects of captopril. Circulation 1994; 89: 68–75.

[6] Raman JS, Hata M, Storer M, et al. The mid-term results of ventricular containment (ACORN WRAP) for end-stage ischemic cardiomyopathy. Ann Thorac Cardiovasc Surg 2001; 7:278-281.

[7] Oz MC, Konertz WF, Kleber FX, et al. Global surgical experience with the Acorn cardiac support device. J Thorac Cardiovasc Surg 2003; 126: 983-991.

[8] Kelley ST, Malekan R, Gorman III JH, et al. Restraining infarct expansion preserves left ventricular geometry and function after acute anteroapical infarction. Circulation 1999; 99: 135-142.

[9] Moainie SL, Guy TS, Gorman III JH, et al. Infarct restraint attenuates remodeling and reduces chronic ischemic mitral regurgitation after posterolateral infarction. Ann of Thorac Surg 2002; 74: 444-449.

[10] Guy IV TS, Moainie SL, Gorman III JH, et al. Prevention of ischemic mitral regurgitation does not influence the outcome of remodeling after posterolateral myocardial infarction. J Am Coll Cardiol 2004; 43:377-383.

[11] Pilla JJ, Blom AS, Brockman DJ, et al. Ventricular constraint using the acorn cardiac support device reduces myocardial akinetic area in an ovine model of acute infarction. Circulation 2002; 106 (Supplement 1):I207-I211.

[12] Markovitz LJ, Savage EB, Ratcliffe MB, et al. Large animal model of left ventricular aneurysm. Ann Thorac Surg 1989; 48:838-845.

[13] Llaneras MR, Nance ML, Streicher JT, et al. Large animal model of ischemic mitral regurgitation. Ann Thorac Surg 1994; 57: 432-439.

[14]Gorman III JH, Gorman RC, Jackson BM, Enomoto Y, St John-Sutton MG, Edmunds LH Jr. Annuloplasty ring selection for chronic ischemic mitral regurgitation: Lessons from the ovine model. Ann Thorac Surg 2003; 76:1556-1563.

[15] Miyatake K, Izumi S, Okamoto M, et al. Semiquantitative grading of severity of mitral regurgitation by real-time two-dimensional Doppler flow imaging technique. J Am Coll Cardiol 1986; 7: 82–88.

[16] Narula J, Dawson MS, Singh BK, et al. Noninvasive characterization of stunned, hibernating, remodeled and nonviable myocardium in ischemic cardiomyopathy. J Am Coll Cardiol 2000; 36:1913-1919.

[17] Cheng W, Li B, Kajstura J, et al. Stretch-induced programmed myocyte cell death. J Clin Invest. 1995; 96: 2247-2259.

[18] Wilson EM, Moainie SL, Baskin JM, et al. Region- and type- specific induction of matrix metalloproteinases in post-myocardial infarction remodeling. Circulation 2003; 107: 2857-2863.

[19] Couper GS, Bunton RW, Birjiniuk V, et al. Relative risks of left ventricular aneurysmectomy in patients with akinetic scars versus true dyskinetic aneurysms. Circulation. 1990; 82(Suppl IV): IV248-56

[20] Batista RJV, Verde J, Nery P, Bocchino L, et. al. Partial left ventriculectomy to treat end-stage heart disease. Ann Thorac Surg 1997;64:634-8.

[21] Dor V, Sabatier M, DiDonato M, et al. Efficacy of endoventricular patch plasty in large post infarction akinetic scar and severe left ventricular dysfunction: comparison with a series of large dyskinetic scars. J Thorac Cardiovasc Surg 1998;116:50-59

[22] Gillinov AM, Wierup PN, Blackstone EH, et al. Is repair preferable to replacement for ischemic mitral regurgitation? J Thor Cardiovasc Surg. 2001;122:1125-41

[23] Jackson BM, Gorman III JH, Salgo I, et al. Altered borderzone geometry increases wall stress after anteroapical myocardial infarction: A contrast echocardiographic assessment. Am J Physiol Heart Circ Physiol 2003; 284: H475-H479.

[24]Guccione JM, Moonly SM, Moustakidis P, et al. Mechanism underlying mechanical dysfunction in the borderzone of left ventricular aneurysm: A finite element model study. Ann Thorac Surg 2001; 71:654- 662

Table of Abbreviations	
LV	Left Ventricle, Left Ventricular
CHF	Congestive Heart Failure
AA	Anteroapical
AAC	Anteroapical Infarct Control Group
AAW	Anteroapical Infarct Wrap Group
PB	Posterobasal
LAD	Left Anterior Descending Artery
D_2	Second Diagonal Branch of the Left Anterior Descending Artery
PDA	Posterior Descending Coronary Artery
OM_2	Second Obtuse Marginal Branch of the Circumflex Artery
OM_3	Third Obtuse Marginal Branch of the Circumflex Artery
PBC	Posterobasal Infarct Control Group
PBP	Posterobasal Infarct Patch Group
PBW	Posterobasal Infarct Wrap Group
IV	Intravenous, Intravenously
ECG	Echocardiogram
LVESV	Left Ventricular End Systolic Volume
LVEDV	Left Ventricular End Diastolic Volume
EF	Ejection Fraction
ESMCAR	End-Systolic Muscle to Cavity Area Ratio
MR	Mitral Regurgitation
IMR	Ischemic Mitral Regurgitation

Table 1 Anterior Apical Infarct

	LVEDV	LVESV	EF	Sphericity	ESMCAR
Control group					
Preinfarction	1.00	1.00	1.00	1.00	1.00
Postinfarction	1.16 ± .05	1.30 ± .07	1.29 ± .41	.89 ± .05	1.17 ± .05
2 weeks	1.42 ± .11	1.87 ± .18	.98 ± .33	1.03 ± .07	.90 ± .05
5 weeks	1.56 ± .11	2.06 ± .16	.97 ± .36	1.17 ± .08	.88 ± .07
8 weeks	1.78 ± .07	2.38 ± .12	.93 ± .32	1.20 ± .06	.86 ± .06
Apical wrap					
Preinfarction	1.00	1.00	1.00	1.00	1.00
Postinfarction	1.10 ± .06	1.27 ± .12	.88 ± .08	.87 ± .09	1.16 ± .11
2 weeks	1.18 ± .09*	1.47 ± .21	.84 ± .08	1.00 ± .10	1.03 ± .11*
5 weeks	1.30 ± .14*	1.67 ± .28	.80 ± .07	.97 ± .12*	1.06 ± .08*
8 weeks	1.32 ± .13*	1.74 ± .35*	.83 ± .10	1.01 ± .14*	1.01 ± .07*

Echocardiographic ventricular remodeling parameters for anteroapical groups: Left Ventricular End Diastolic Volume (LVEDV), Left Ventricular End Systolic Volume (LVESV), Ejection Fraction (EF), Sphericity (see text for definition), End Systolic Muscle to Cavity Area Ratio (ESMCAR). All values are normalized to preinfarction values. Statistically significant changes from control are marked (*) for $p \leq 0.05$.

Table 2 Posterobasal Infarct Echocardiographic Data

	MR	LVEDV	LVESV	EF	Sphericity	ESMCAR
Control group						
Preinfarction	.4 ± .13	1.00	1.00	1.00	1.00	1.00
Postinfarction	2.0 ± .22	1.20 ± .05	1.04 ± .10	1.08 ± .09	.92 ± .09	.86 ± .07
2 weeks	2.4 ± .17	1.36 ± .07	1.51 ± .13	.92 ± .06	1.19 ± .11	.78 ± .05
5 weeks	2.4 ± .27	1.45 ± .10	1.57 ± .15	.64 ± .08	1.17 ± .14	.72 ± .07
8 weeks	2.8 ± .24	1.74 ± .12	2.09 ± .17	.79 ± .07	1.44 ± .12	.67 ± .04
Posterior patch						
Preinfarction	.4 ± .16	1.00	1.00	1.00	1.00	1.00
Postinfarction	1.6 ± .38	1.21 ± .11	1.19 ± .14	1.05 ± .07	1.05 ± .09	.86 ± .03
2 weeks	1.7 ± .28*	1.41 ± .13	1.80 ± .16	.74 ± .07	1.35 ± .14	.71 ± .06
5 weeks	1.7 ± .15*	1.45 ± .11	1.98 ± .17	.66 ± .07	1.43 ± .14	.73 ± .09
8 weeks	2.0 ± .13*	1.52 ± .14	2.09 ± .18	.72 ± .11	1.55 ± .17	.67 ± .05
Posterior wrap						
Preinfarction	0.8 ± 0.2	1.00	1.00	1.00	1.00	1.00
Postinfarction	1.1 ± 0.2	1.17 ± .10	1.03 ± .11	1.29 ± .12	.99 ± .06	1.07 ± .06
2 weeks	1.1 ± 0.2*‡	1.29 ± .11	1.34 ± .14‡	1.04 ± .11*‡	1.26 ± .11	.90 ± .10
5 weeks	1.3 ± 0.2*‡	1.43 ± .18	1.52 ± .15‡	1.02 ± .10*‡	1.26 ± .10	.86 ± .09
8 weeks	1.2 ± 0.2*‡	1.52 ± .19	1.73 ± .17*‡	.96 ± .11*‡	1.33 ± .17	.91 ± .12*‡

Echocardiographic ventricular remodeling parameters for posterobasal groups: Left Ventricular End Diastolic Volume (LVEDV), Left Ventricular End Systolic Volume (LVESV), Ejection Fraction (EF), Sphericity (see text for definition), End Systolic Muscle to Cavity Area Ratio (ESMCAR). All values are normalized to preinfarction values. The degree of mitral regurgitation (MR) was assessed by color flow Doppler echocardiography and quantified as described in the text. Statistically significant changes are marked for $p \leq 0.05$: (*) significantly different from control, (‡) significantly different from patch.

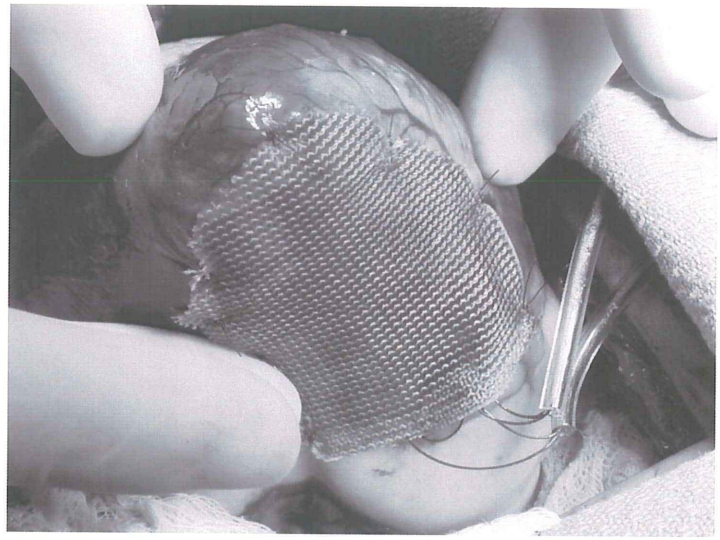

Figure 1 Intra-operative photograph demonstrating placement of Marlex® mesh restraint patch over posterolateral infarct territory. The base of the heart is at the bottom of the photograph, the posterior descending artery is at the left and the apex is at the top.

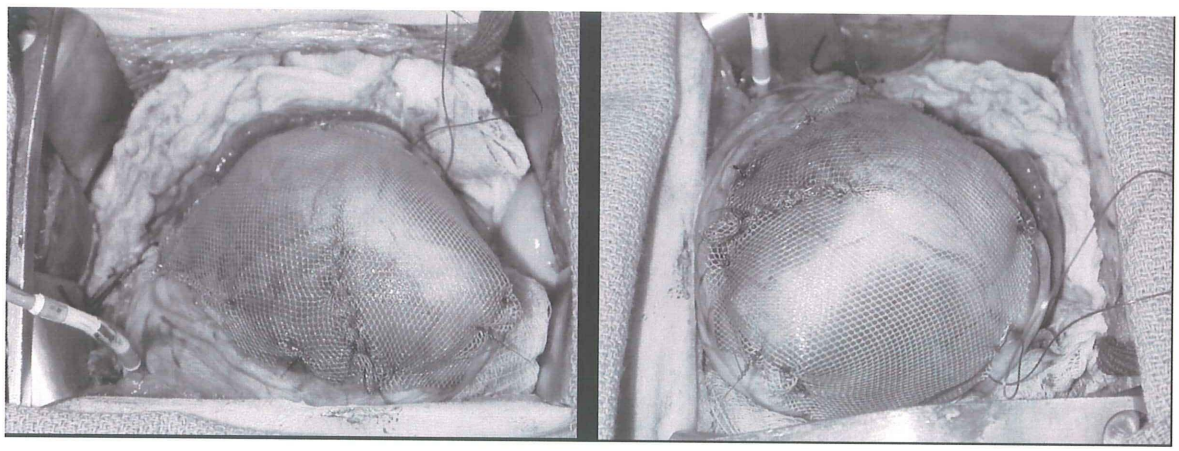

Figure 2 Intra-operative photograph demonstrating placement of the Merseline® mesh ventricular wrap. Wrap extends from base to apex and from left anterior descending artery to the posterior descending artery. The right ventricle is not covered by the wrap.

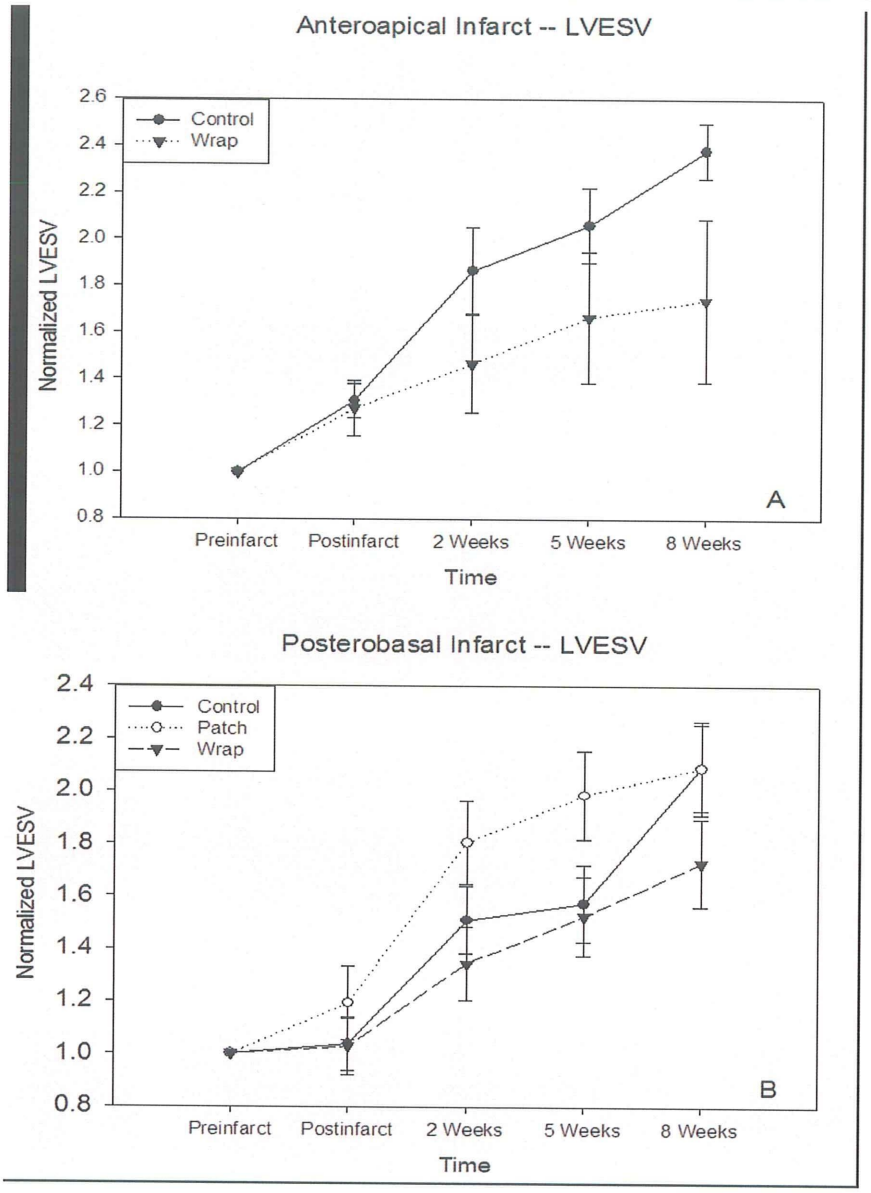

Figure 3A Normalized left ventricular end systolic volume (LVESV) during remodeling in anteroapical infarct animals: control group (*closed circle*) and ventricular wrap group (*closed triangle*). **3B** Normalized left ventricular end systolic volume (LVESV) during remodeling in posterobasal infarct animals: control group (*closed circle*), patch group (*open circle*) and ventricular wrap group (*closed triangle*).

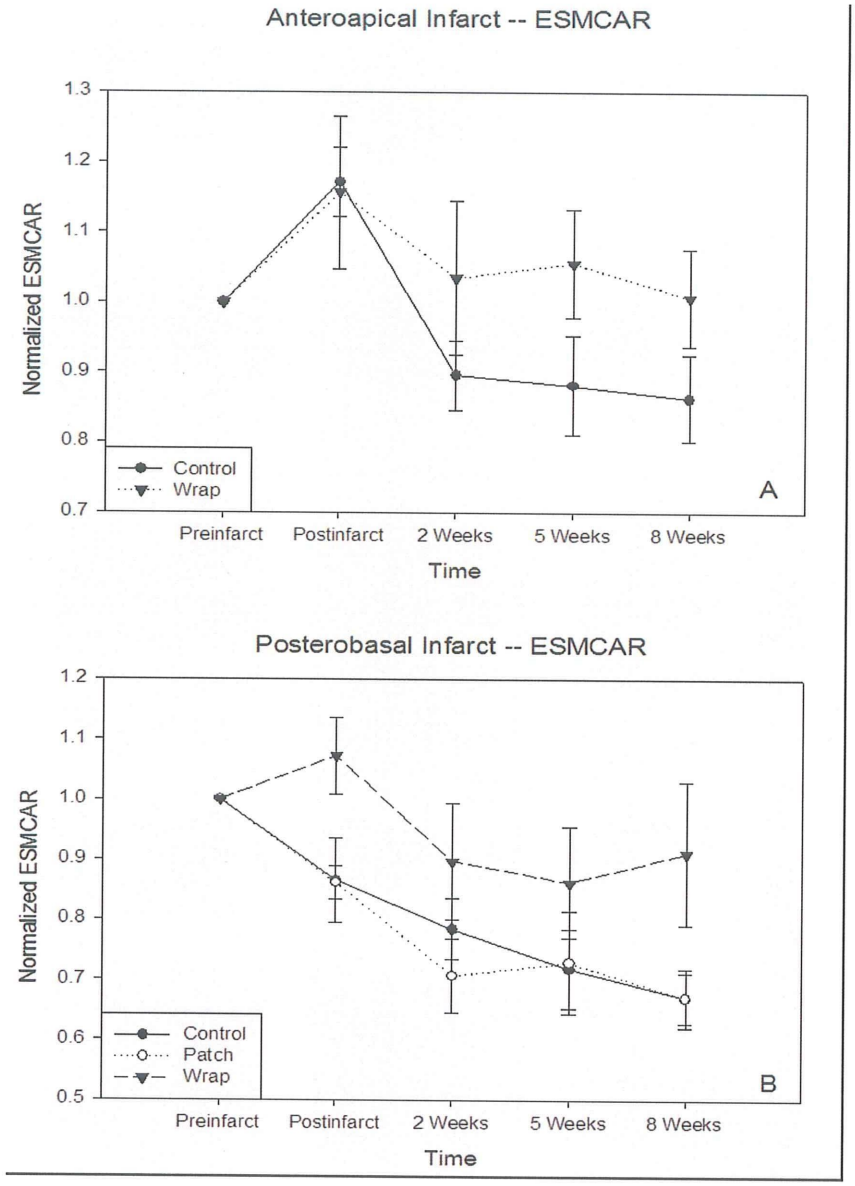

Figure 4A Normalized end systolic muscle to cavity area ratio (ESMCAR) during remodeling in anteroapical infarct animals: control group (*closed circle*) and ventricular wrap group (*closed triangle*). **4B** Normalized end systolic muscle to cavity area ratio (ESMCAR) during remodeling in posterobasal infarct animals: control group (*closed circle*), patch group (*open circle*) and ventricular wrap group (*closed triangle*)

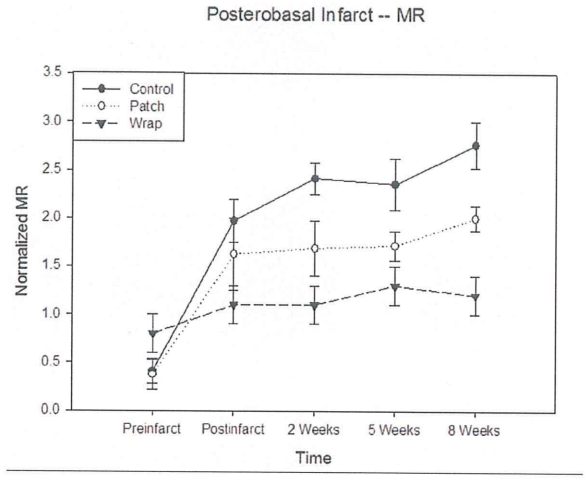

Figure 5 Degree of mitral regurgitation (MR) graded on a scale of 0 to 4 (0 = no MR, 4 = severe MR) in posterobasal infarct animals: control group (*closed circle*), patch group (*open circle*) and ventricular wrap group (*closed triangle*).

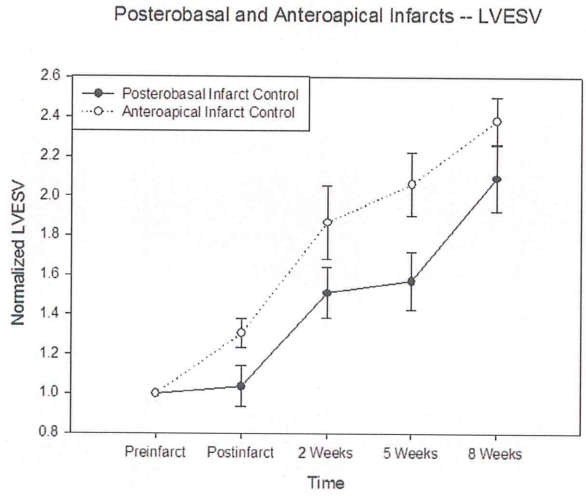

Figure 6 Comparison of normalized left ventricular end systolic volume (LVESV) between anteroapical and posterobasal infarct control groups during remodeling. Even though the posterobasal animals developed moderate to severe mitral regurgitation there was no statistical difference between the groups in the extent of ventricular dilatation 8 weeks after infarction.