THE MITRAL VALVE AND THE LEFT VENTRICLE

IT TAKES TWO TO TANGO

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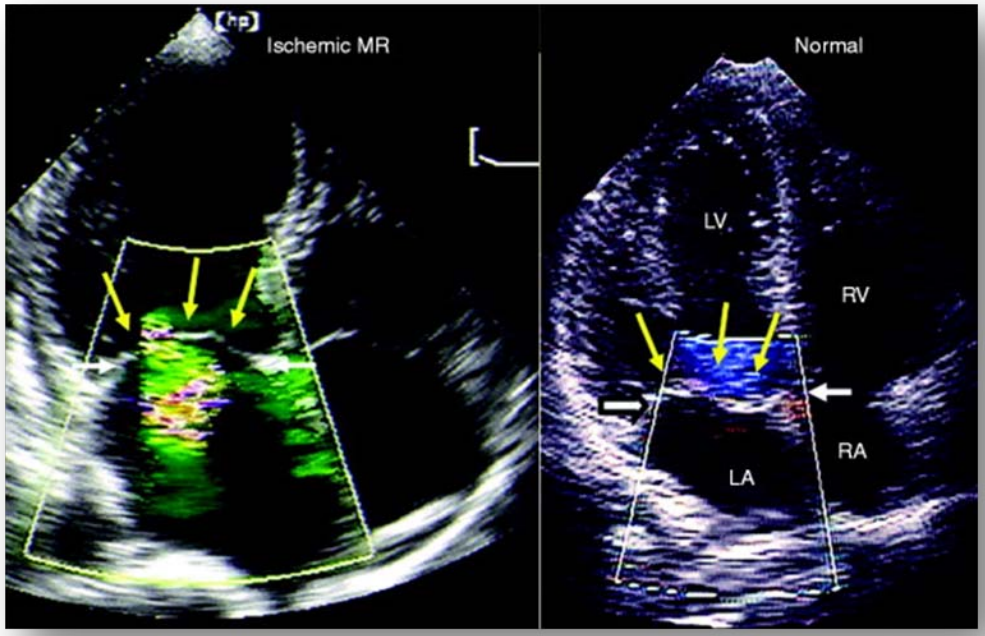
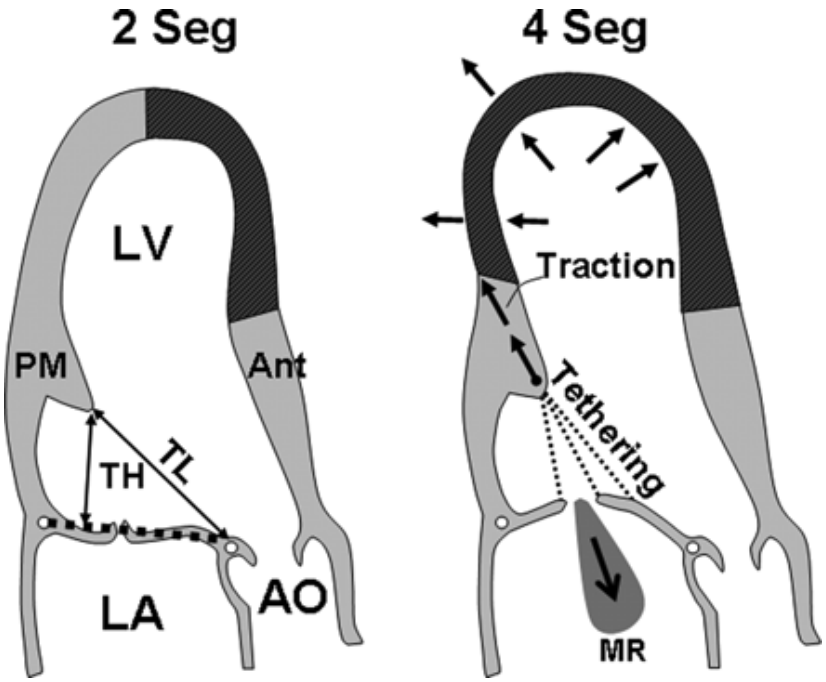
Mechanism- Infero-Posterior MI

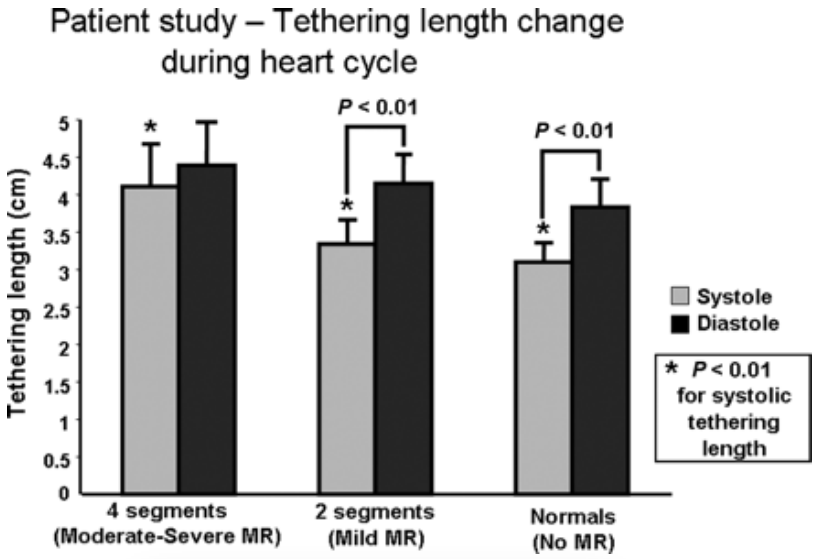


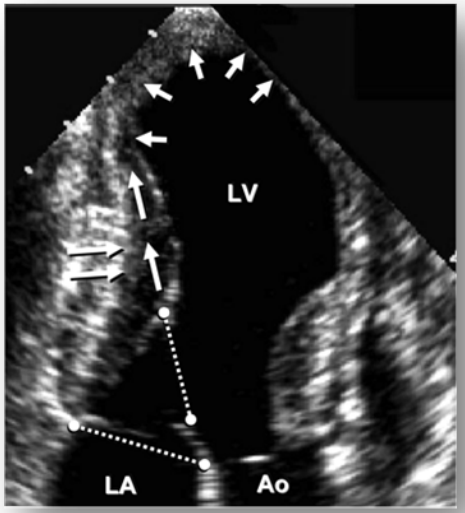
Courtesy of Dr Yutaka Otsuji

Levine, R. A. N Engl J Med 2004;351:1681-1684

Mechanism- Apical MI







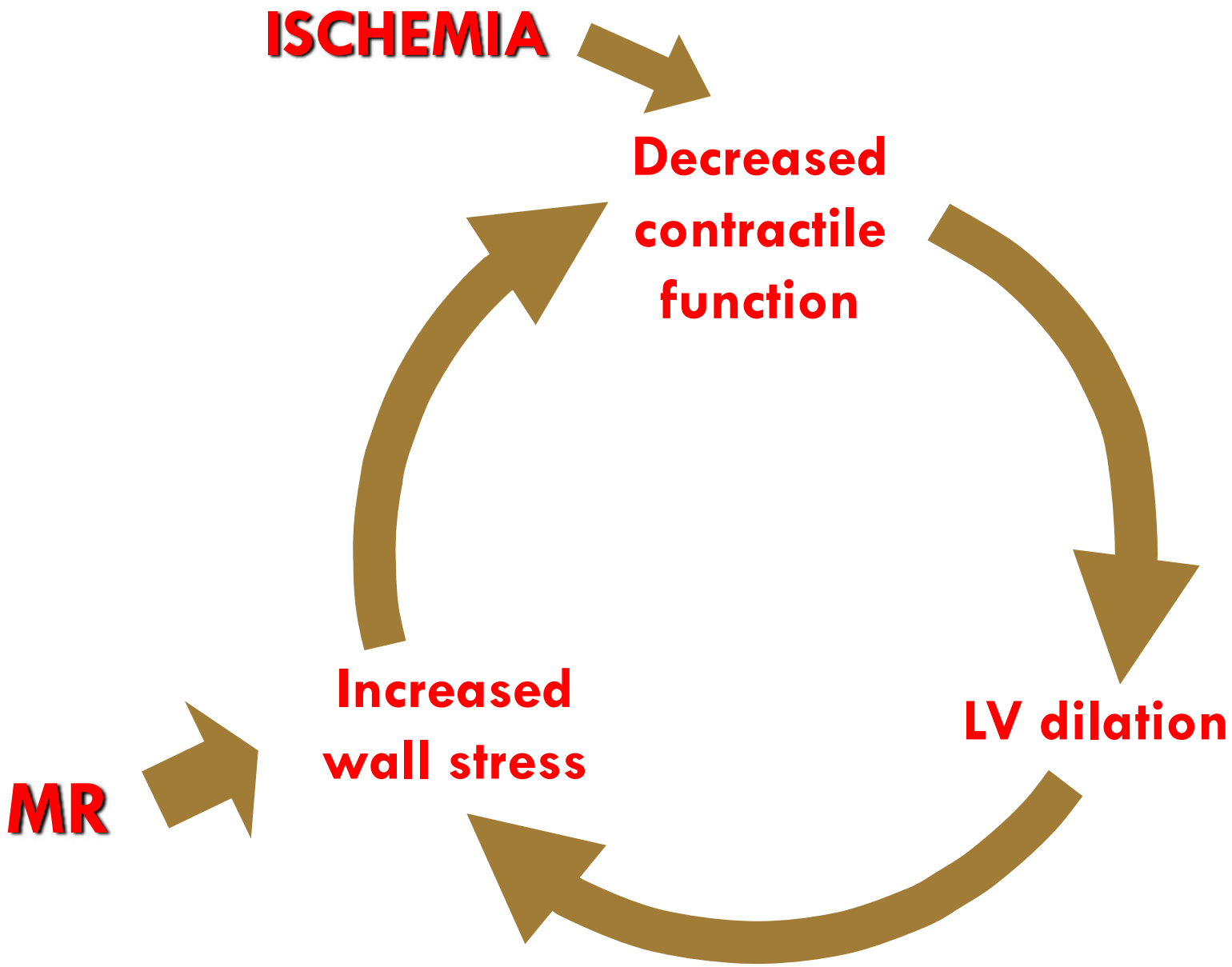
Yosefy C, et al. Circulation. 2011; 123: 1529-1536

Introduction- Remodeling and MR

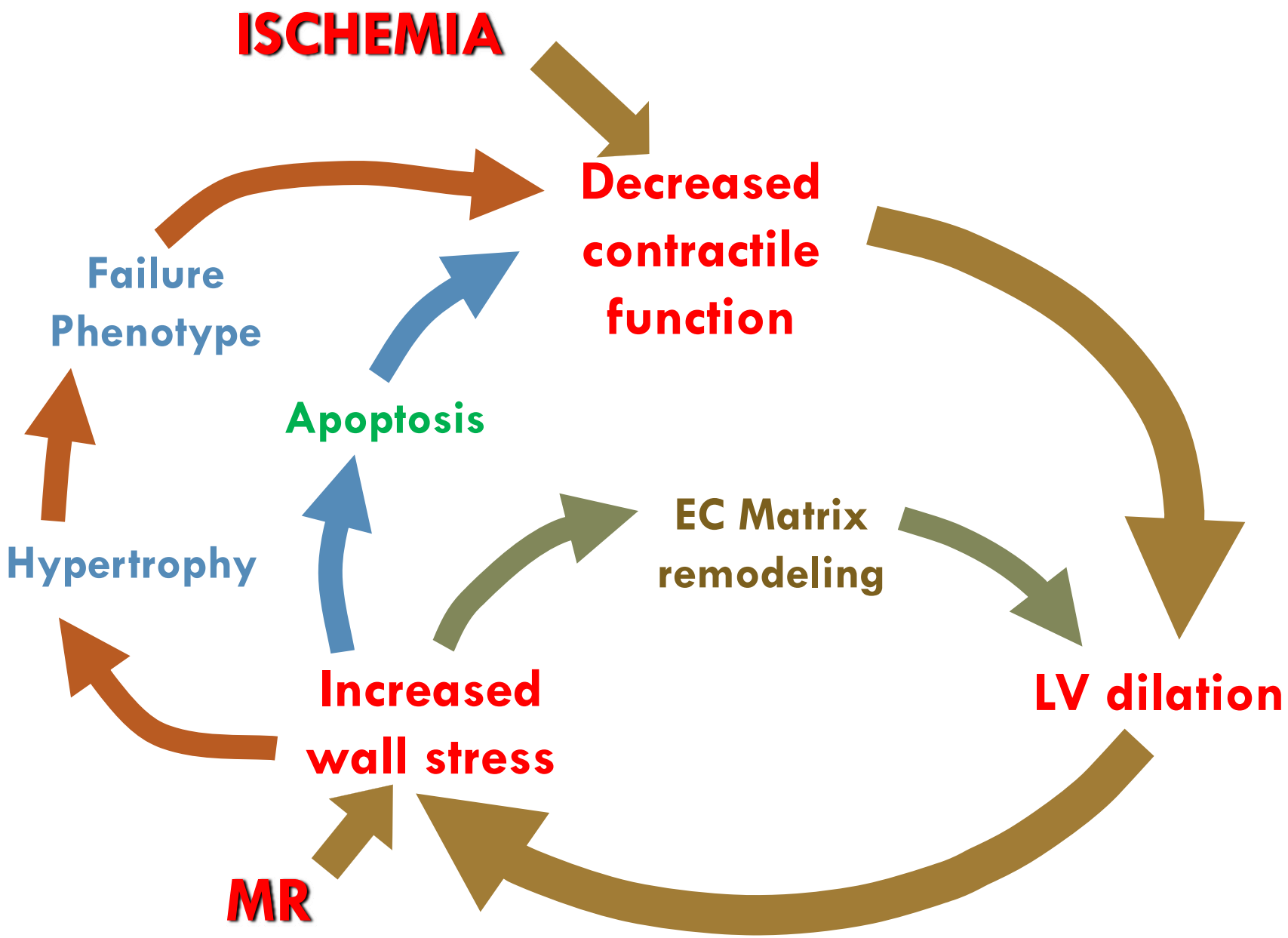
- Expansion of infarcted tissue after myocardial infarction begins acutely
- A more gradual remodeling process, however, also involves the non-infarcted areas
- Initially compensatory, this process subsequently becomes maladaptive, generating a larger, more spherical ventricle with decreased contractile function.
- Mitral regurgitation doubles mortality following myocardial infarction.
- Its additive effect on LV remodeling has not been addressed in a controlled fashion.

Cohn JN, Ferrari R, Sharpe N. *J Am Coll Cardiol* 2000; 35:569-82.
Gianuzzi P, et al , for the GISSI-3 echo substudy investigators. Am Heart J 2001;141:131-8.
Lehmann KG, et al for the TIMI study group. Ann Intern Med 1992; 117:10-7.

REMODELING: A VICIOUS CYCLE



REMODELING: FAILED COMPENSATION



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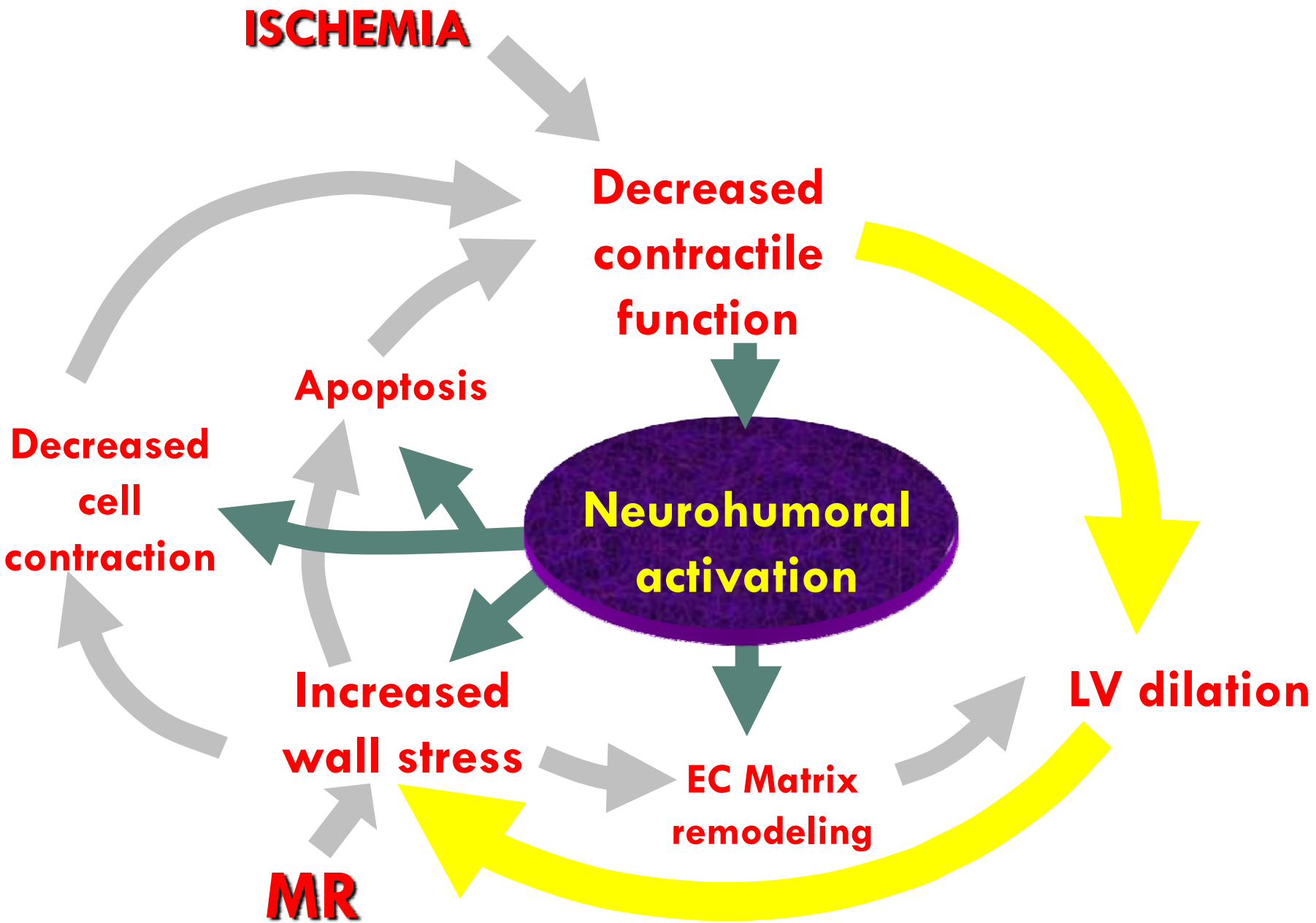
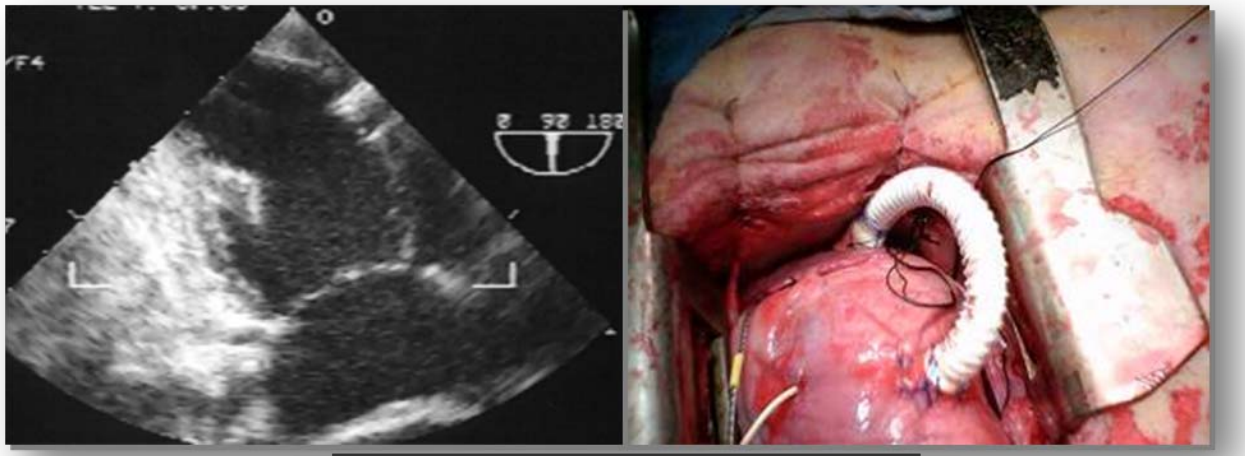
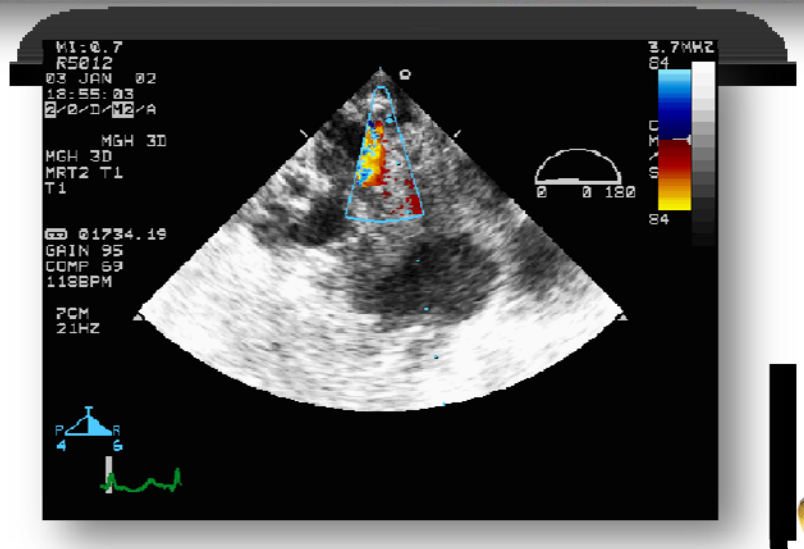


Remodeling and Ischemic MR- Model



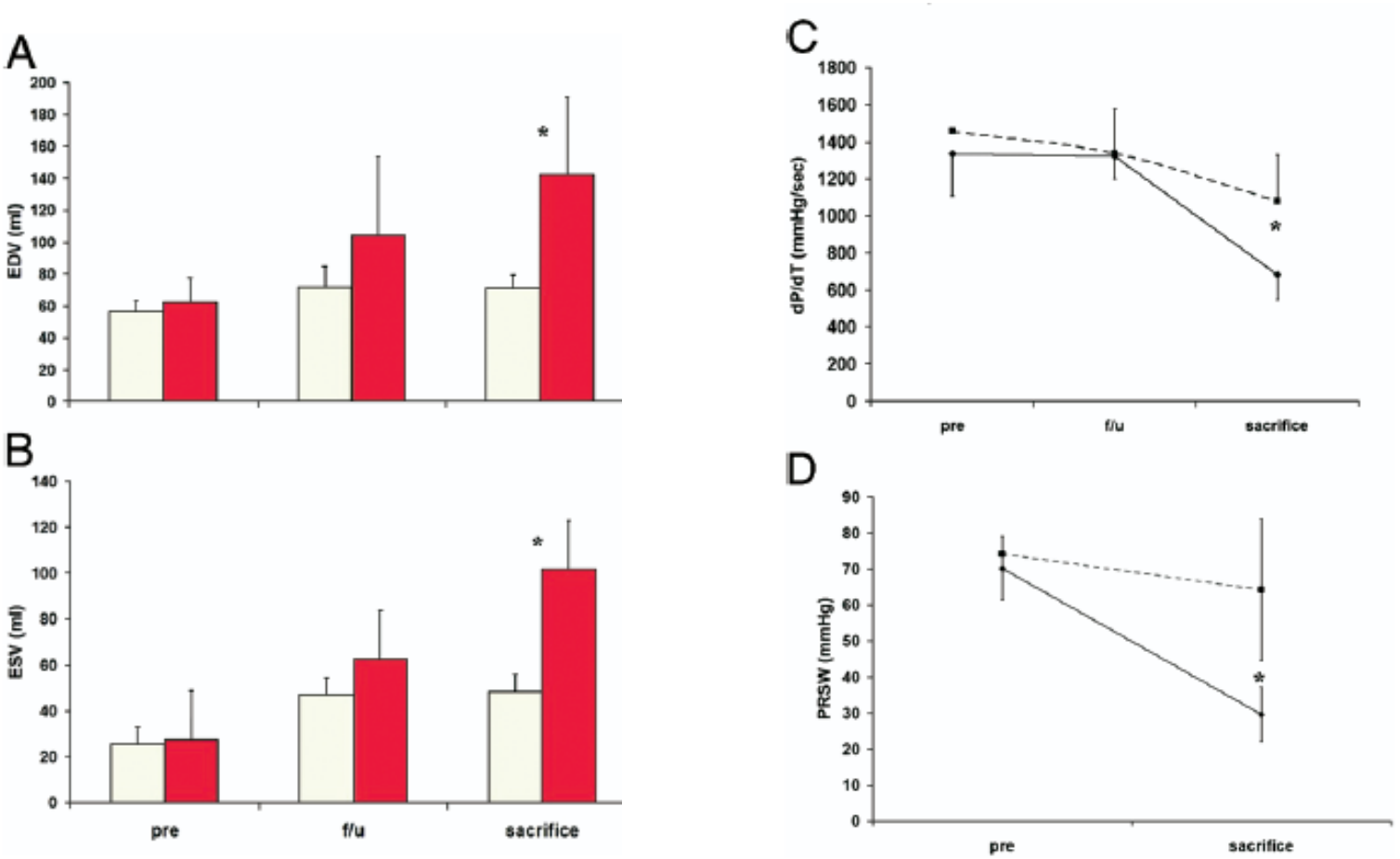


Beeri R. et al. J Am Coll Cardiol 2008;51:476–86

Remodeling and Ischemic MR- Methods

- Standardized septo-apical MI In 18 sheep.
- Shunt implanted between the LV and LA. 6 animals with sham (closed shunt) implantation. Regurgitant fractions were ~30%.
- Compared at baseline, 1 and 3 months using 3D echo, Millar hemodynamics and biopsies.
- In 6 sheep, the shunt was closed at 1 month, **simulating MV repair**.

Remodeling and Ischemic MR Volumes and Function



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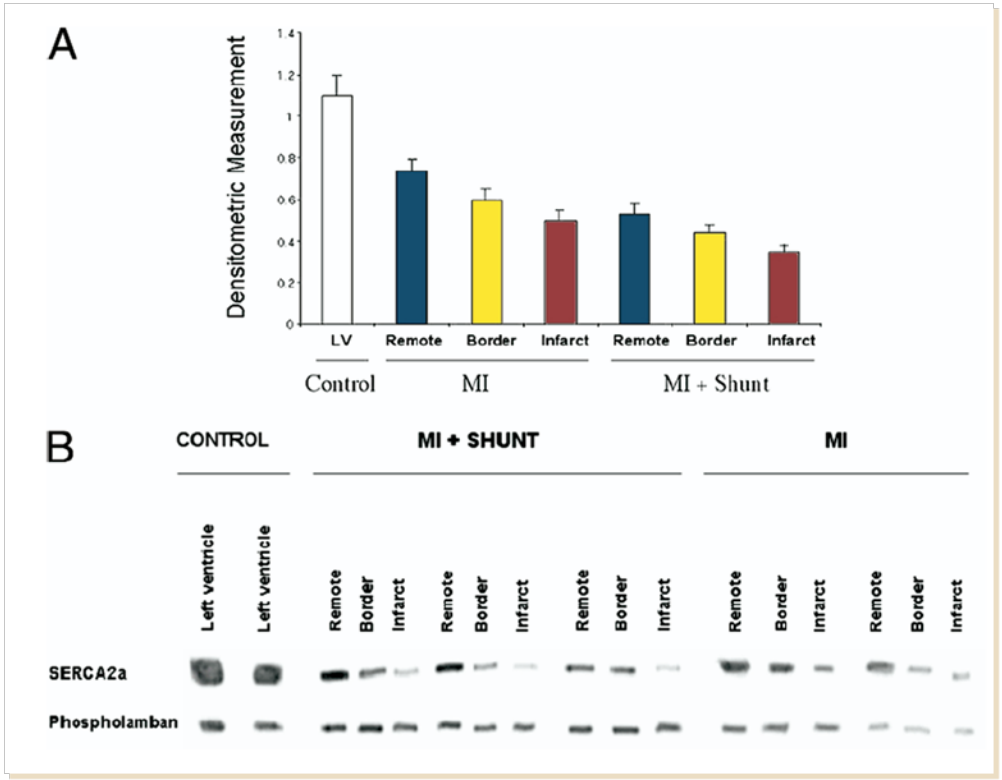
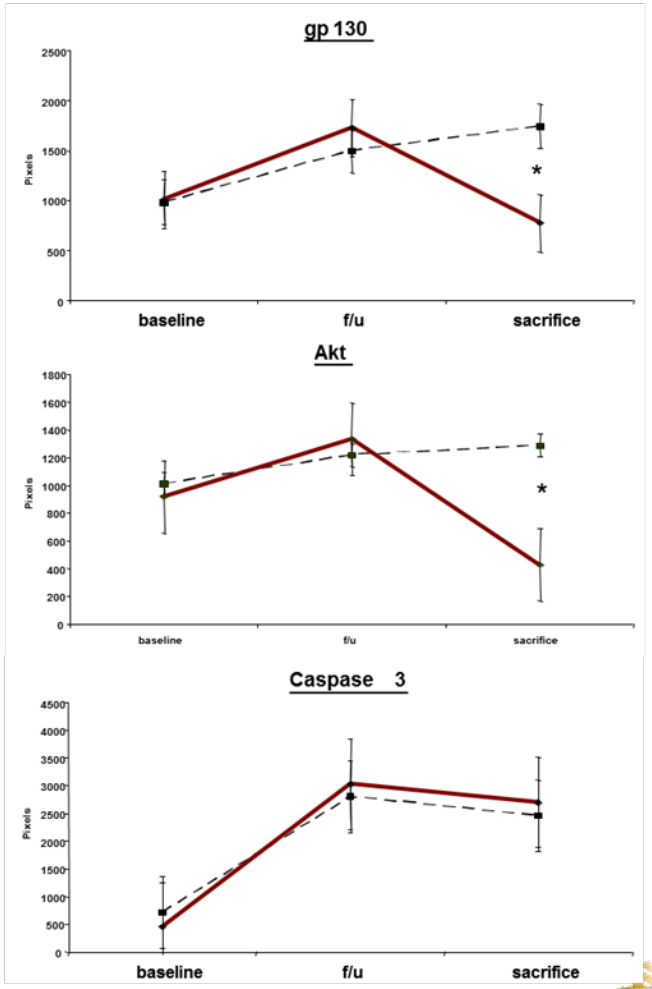
Remodeling and Ischemic MR Molecular Changes





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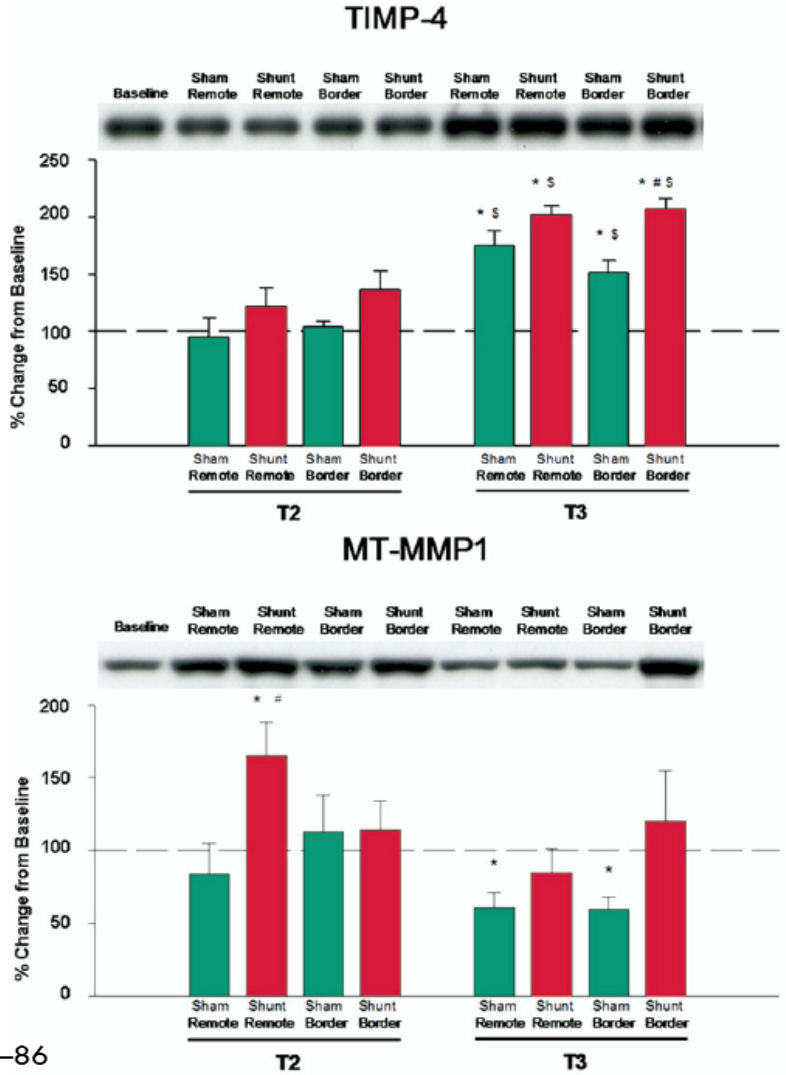
Remodeling and Ischemic MR Extra-Cellular Matrix



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Remodeling and Ischemic MR Conclusions

- In this controlled model, moderate MR worsens post-MI remodeling, with larger LVs and reduced contractility.
- While at first pro-hypertrophic pathways are up-regulated, they subsequently fall, and transformation to a failure phenotype occurs.
- Therefore, MR can precipitate an earlier onset of dilated heart failure.

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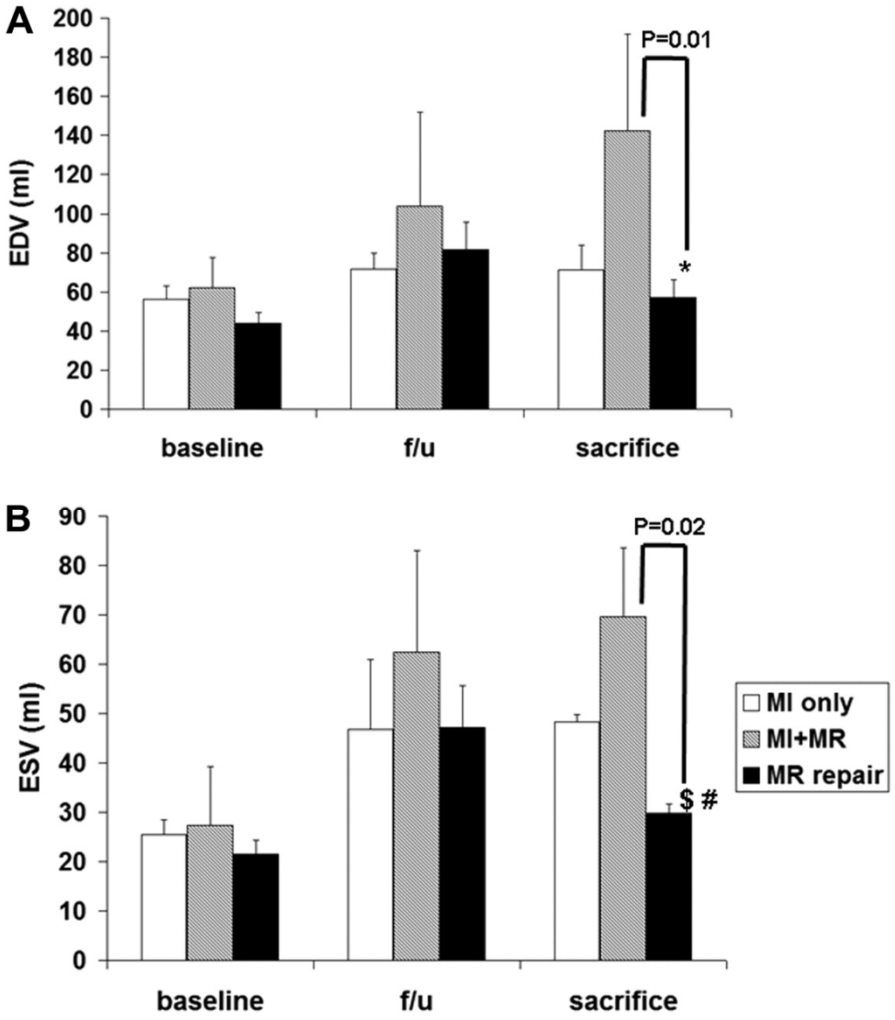
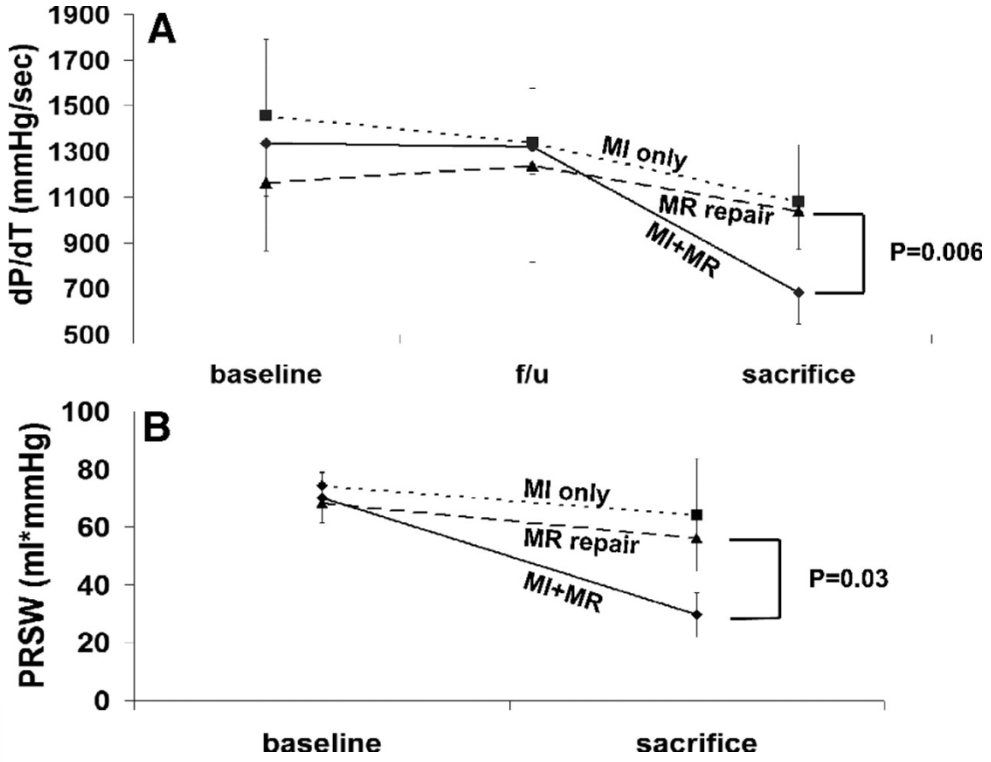
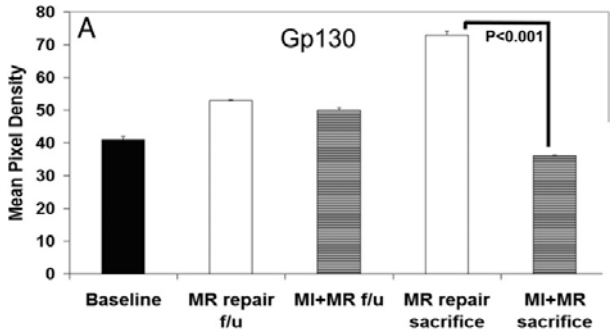
Early Repair of Ischemic MR Volumes and Function

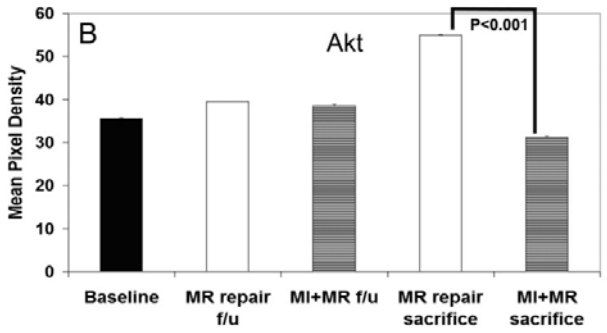


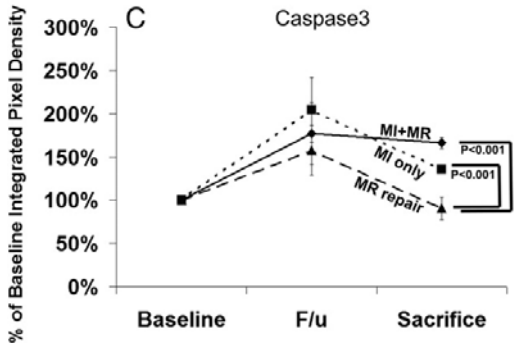


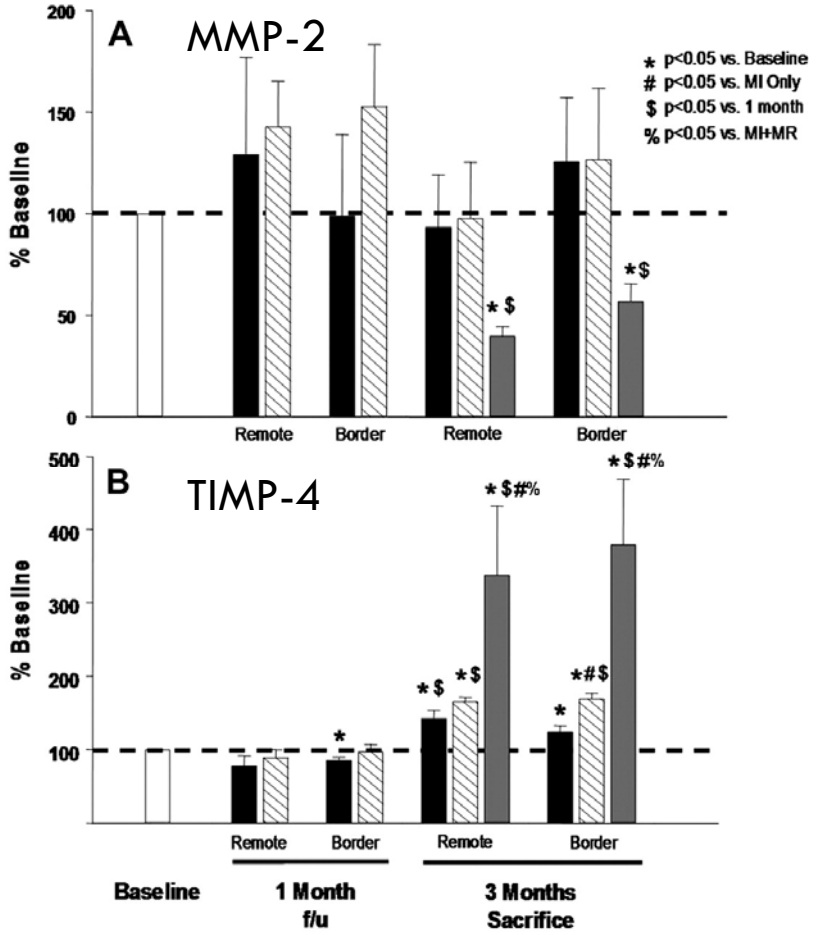
Beeri, R. et al. Circulation 2007;116:I-288-I-293

Early Repair of Ischemic MR Molecular and Extra-Cellular Matrix









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Early Repair of Ischemic MR Conclusions

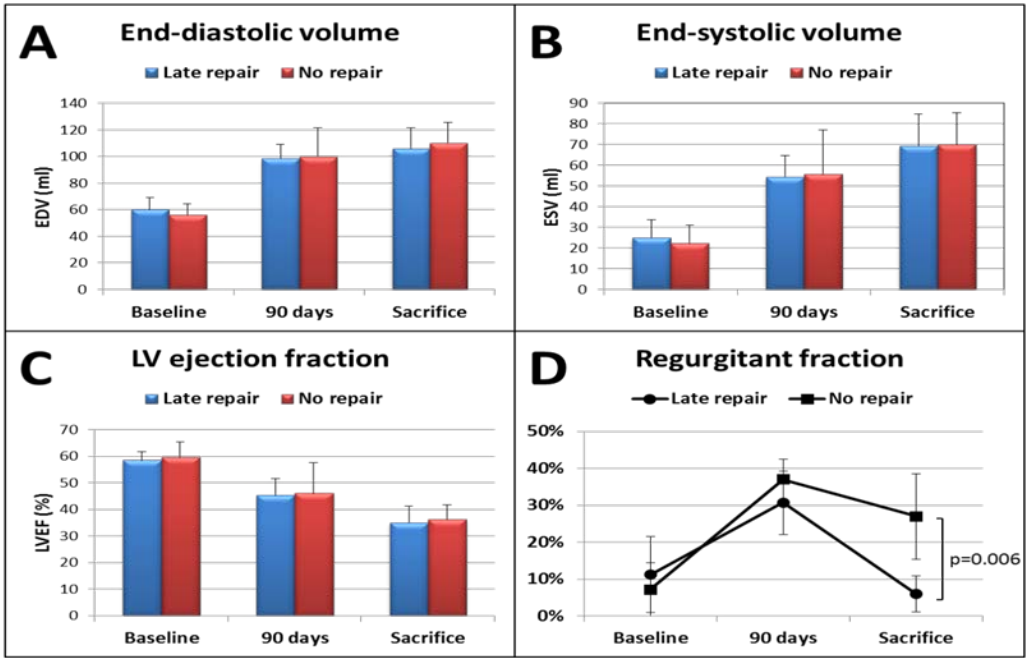
- Repairing moderate ischemic MR after 1 month reverses ventricular remodeling at 3 months compared with persistent MR.
- Adverse molecular events that typify remodeling myocardium are suppressed after MR repair to levels similar to those seen in MI alone.
- Compensatory mechanisms, including matrix stabilization, remain activated.
- Therefore, repairing moderate MR <u>early</u> after MI reverses the remodeling process exacerbated by mitral regurgitation.

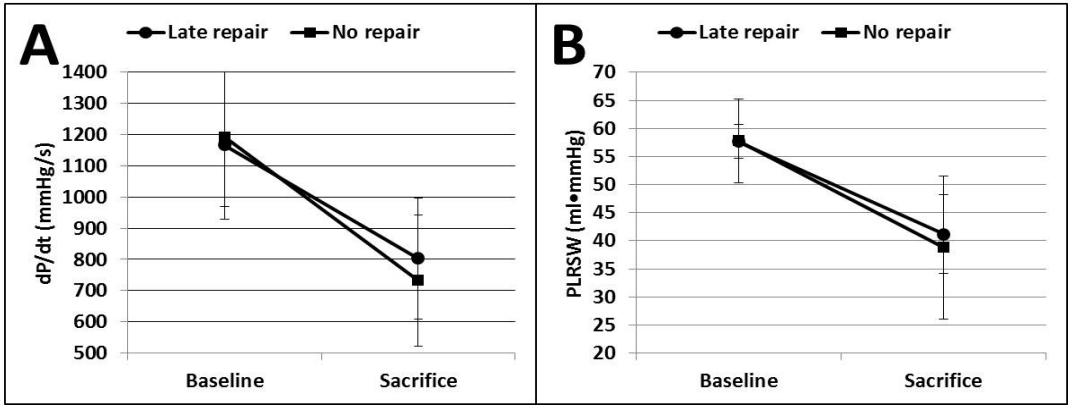
Late Repair of Ischemic MR

- Immediate and especially long term benefit from repairing ischemic MR are conflicting*
- Possible reasons:
  - Wrong technique
  - Too late
  - Not addressing the ventricle
- 12 sheep followed for 5 months. 6 sheep- MR repaired at 3 months

* Geidel S., Schneider C., Lass M., et al. J Thorac Cardiovasc Surg 2007; 55:1-6.
Calafiore A.M., Gallina S., DiMauro M., et al Ann Thorac Surg 2001; 71:1146-1152.
Tahta S.A., Oury J.H., Maxwell J.M., et al. J Heart Valve Dis 2002; 11:11-14.
McGee E.C., Gillinov A.M., Blackstone E.H., et al. J Thorac Cardiovasc Surg 2004; 128:916-924.
Mihaljevic T., Lam B.K., Rajeswaran J., et al. J Am Coll Cardiol 2007; 49:2191.201
Dahlberg P.S., Orszulak T.A., Mullany C.J., et al. Ann Thorac Surg 2003; 76:1539-1547.
Hung J, et al Circulation. 2004;110:II-85 – II-90

Late Repair of Ischemic MR Volumes and Function





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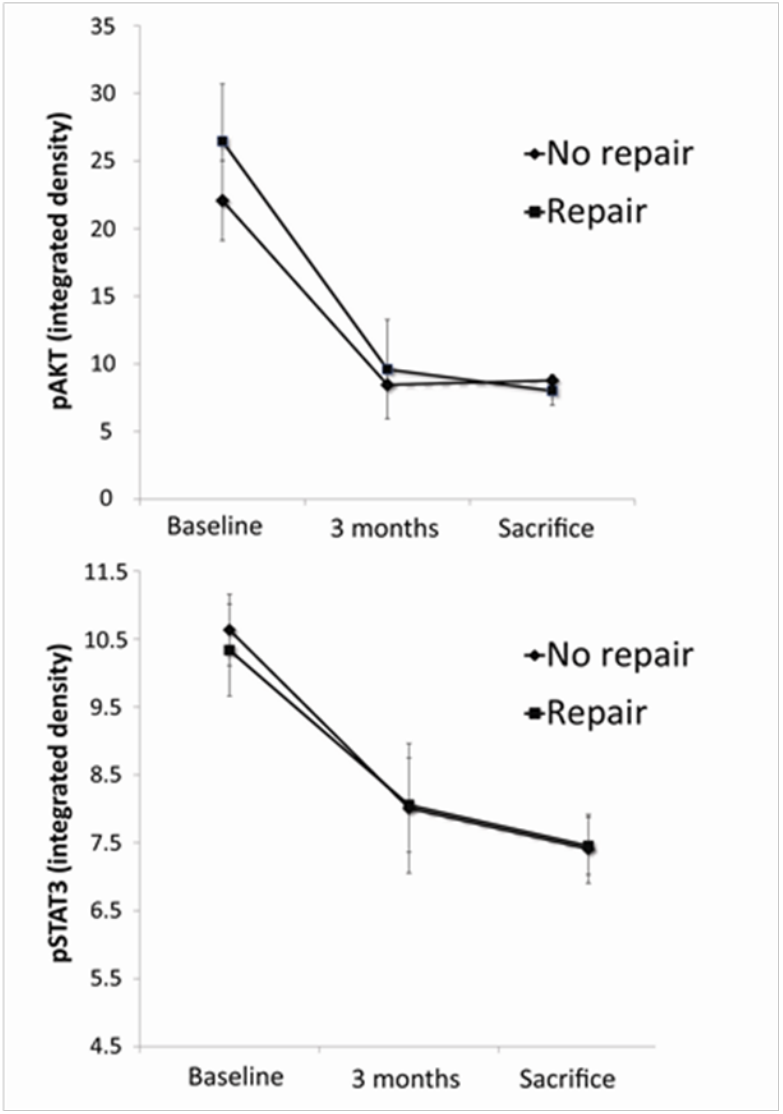
In press

Late Repair of Ischemic MR Molecular Pathways



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In press

Summary

- The presence of MR after a myocardial infarction worsens prognosis
- Mere moderate MR increases remodeling and worsens its impact after a myocardial infarction
- Early repair, before failure phenotype has set in, permits reverse remodeling
- Late repair is not associated with reverse remodeling in a controlled model
- A robust ventricular solution for this ventricular problem is yet to be found

Acknowledgements

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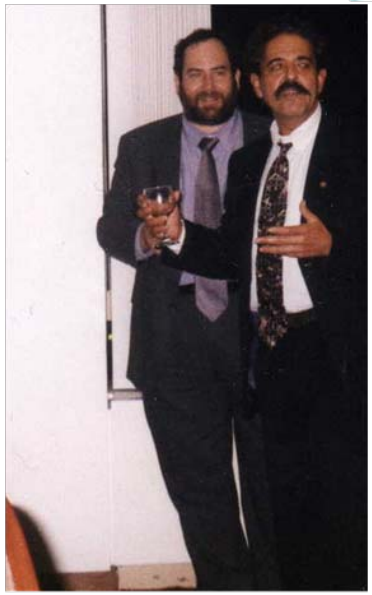
AHA Grant-in-Aid 0350422N, NIH/NHLBI grant R01HL38176, R01HL72265, and K24HL67434, and USA-Israel Binational Science Foundation grants (no. 2001037 and 2005250).

Thanks!!!

The Hadassah HCVRC team



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