A Surgically Created Model of Ischemic Mitral Regurgitation in Swine

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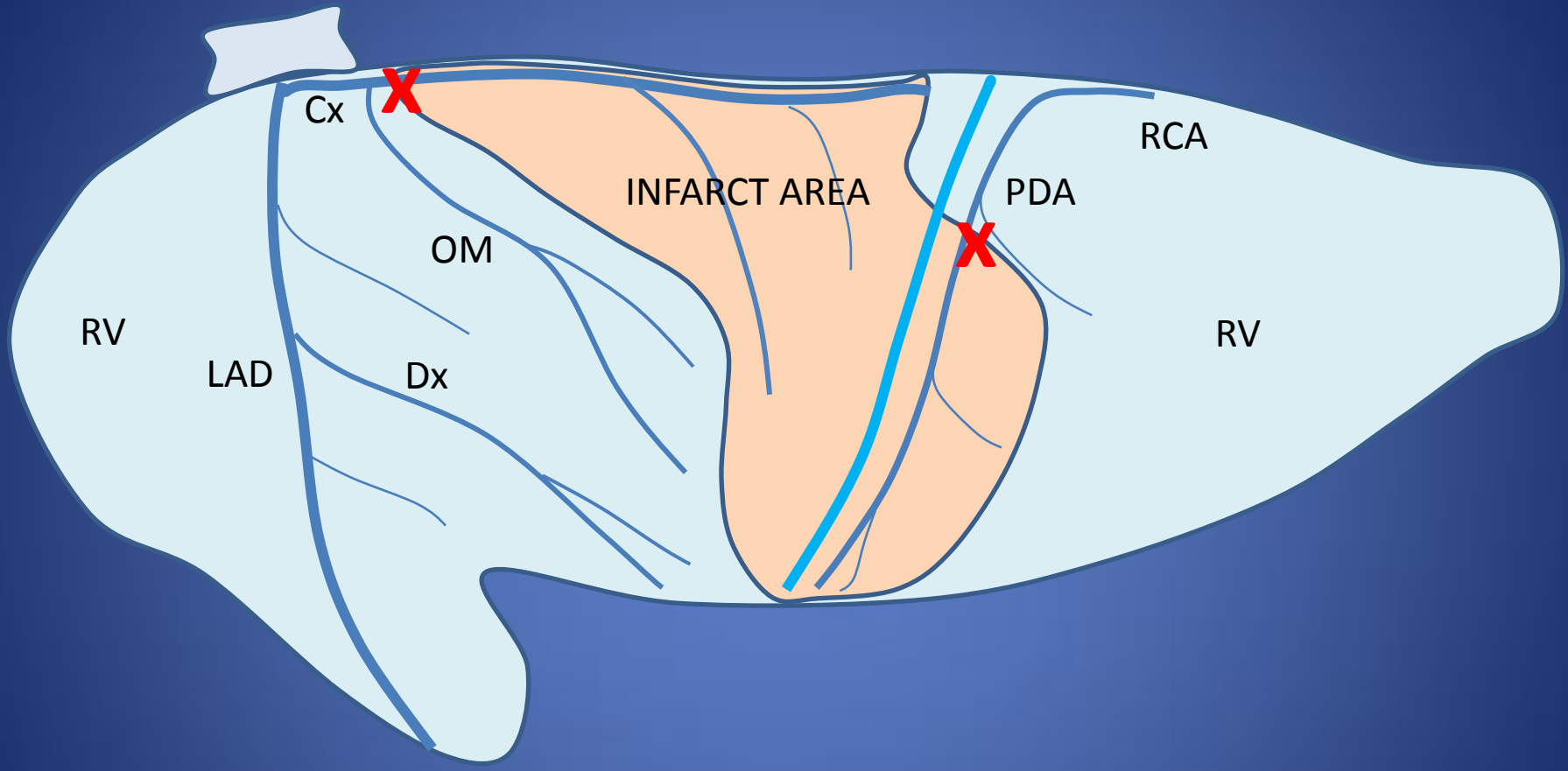
OBJECTIVES

- Ischemic mitral regurgitation (IMR) occurs as a result of annular dilatation, and leaflet tethering, secondary to ventricular remodeling. It remains a significant clinical problem. A surgical model of IMR is well established in sheep, where the coronary anatomy is left dominant. Swine have a right dominant coronary system which is more akin to most humans. Therefore a porcine model may be more consistent with the human disease process. The aim of this study was to create a surgical model of IMR in swine and to describe the changes to mitral valve geometry which were found.

METHODS

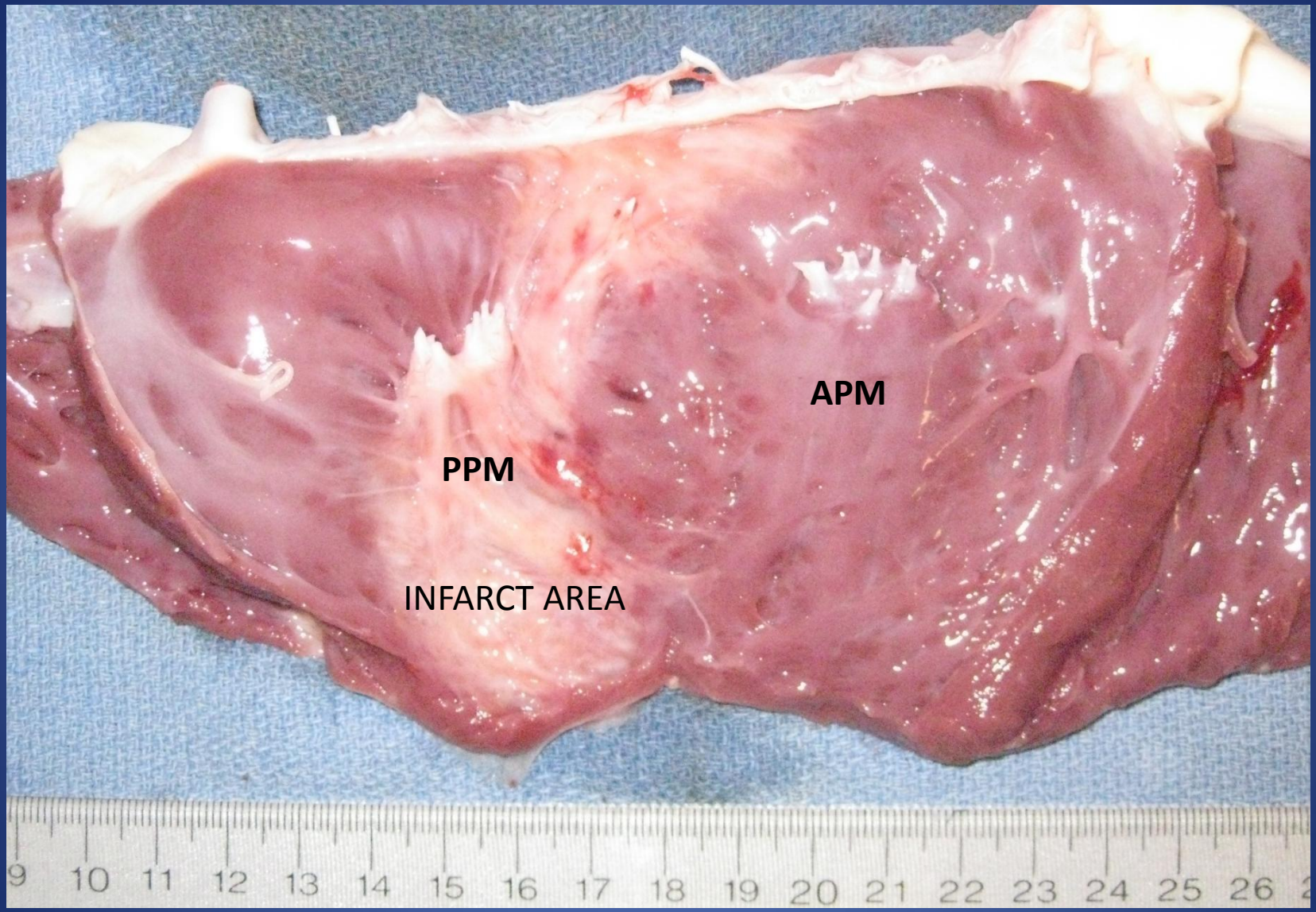
- 21 swine weighing 30.6±5.1kg underwent left thoracotomy and ligation of the main circumflex and distal right posterior descending coronary arteries to create a postero-lateral myocardial infarction.
- Real-time three-dimensional echocardiography was performed at baseline, 30minutes and 8 weeks after MI to assess geometrical changes in the mitral valve.

Epicardial view of the infarct area and ligation sites



Ligation sites are indicated by " X ". Cx, circumflex artery; LAD; left anterior descending artery; RCA, right coronary artery; OM, obtuse marginal branch, PDA; right posterior descending artery; Dx; diagonal branch.

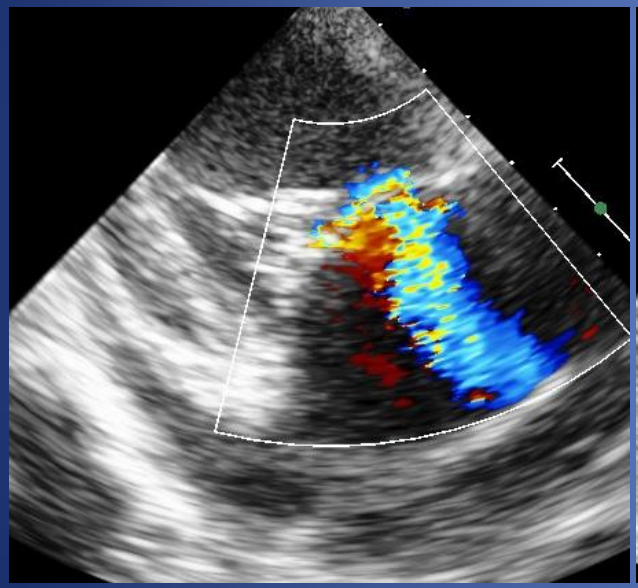
Endocardial view of the infarct area in 8 weeks after the infarct.



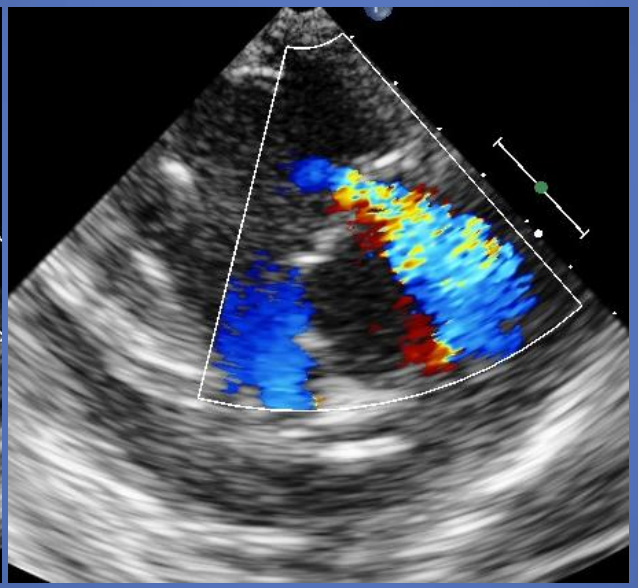
APM, anterior papillary muscle; PPM, posterior papillary muscle.

MR in 8 weeks
- Baseline and under Dobutamine stress -

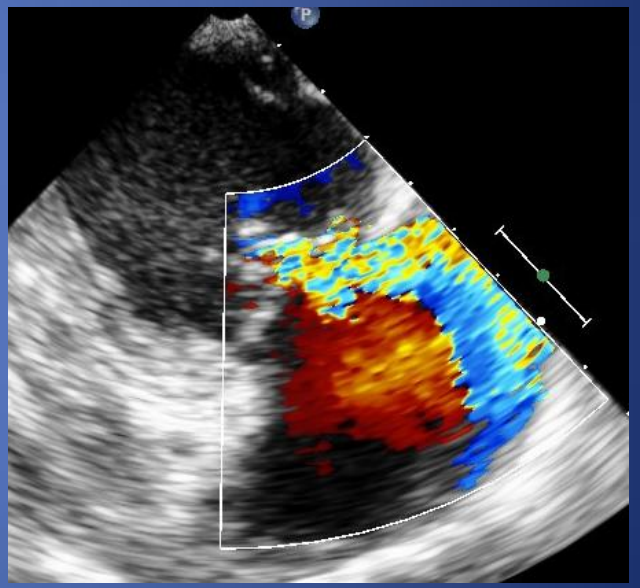
Baseline



Dobutamine 5µg/Kg/min



Dobutamine 10µg/Kg/min



Hemodynamic data

Hemodynamic parameters	baseline	30 min after infarction	8 weeks after infarction: Dobutamine 0μg/Kg/min	8 weeks after infarction: Dobutamine 5μg/Kg/min	8 weeks after infarction: Dobutamine 10μg/Kg/min
Systolic ABP (mmHg)	89.0±9.6	81.1±9.3[a]	88.1±9.9[b]	97.8±12.9[c]	99.6±14.9[c]
Systolic PAP (mmHg)	29.2±4.6	31.2±7.8	35.1±2.3[a]	35.8±3.0	37.2±2.0[c]
Maximum dP/dt (mmHg/sec)	909±244	988±464	840±158	1529±377[c]	2284±436[c, d]
Minimum dP/dt (mmHg/sec)	-1151±257	-986±473	-963±159[a]	-1251±221[c]	-1646±495[c, d]
PCWP (mmHg)	13.7±3.3	17.1±6.7[a]	20.3±3.8[a]	20.3±3.5	18.3±3.7[d]
CVP (mmHg)	11.4±4.4	11.6±3.9	17.3±3.5[a]	16.7±2.6	14.0±3.2[c, d]
Cardiac output (L/min)	3.5±1.0	3.1±0.6[a]	4.5±1.6[a, b]	7.1±2.4[c]	6.7±1.9[c]

Values are expressed as mean ± standard deviation. ABP, arterial blood pressure; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; CVP, central venous pressure. [a] $P<0.05$ vs. baseline; [b] $P<0.05$ vs. 30 min after infarction; [c] $P<0.05$ vs. Dobutamine 0μg/Kg/min; [d] $P<0.05$ vs. Dobutamine 5μg/Kg/min

Echo cardiographic data

Hemodynamic parameters	baseline	30 min after infarction	8 weeks after infarction		
			Dobutamine 0μg/Kg/min	Dobutamine 5μg/Kg/min	Dobutamine 10μg/Kg/min
MR grade	0.7±0.5	0.9±0.7	2.0±1.2[a,b]	2.6±1.2	2.6±1.3
LVEF (%)	40.3±6.6	31.4±5.8[a]	25.8±7.7[a]	29.8±7.5	32.6±10.7[c]
LVEDV (ml)	51.9±8.7	57.9±8.5[a]	102.0±24.1[a,b]	84.4±24.0[c]	70.6±19.1[c]
LVESV (ml)	31.2±6.8	39.8±7.3[a]	75.8±20.3[a,b]	59.6±20.8[c]	47.7±16.1[c]
Sphericity index	0.59±0.10	0.61±0.09	0.42±0.06[b]	0.39±0.07	0.45±0.10

Values are expressed as mean ± standard deviation. MR, mitral regurgitation; LVEF, left ventricular ejection fraction; LVEDP, left ventricular end-diastolic pressure; LVESV, left ventricular end-systolic pressure.

[a] $P<0.05$ vs. baseline; [b] $P<0.05$ vs. 30 min after infarction; [c] $P<0.05$ vs. Dobutamine 0μg/Kg/min

Mid-systolic dimensions calculated by three-dimensional mitral echo cardiograph

Dimension	baseline	30 min after infarction	8 weeks after Infarction
Mitral annular area (mm^3)	596 ± 85	621 ± 138	931 ± 181[a, b]
Anterior leaflet area (mm^3)	318 ± 83	345 ± 95	635 ±132 [a, b]
Posterior leaflet area (mm^3)	328 ± 36	329 ± 88	348 ± 92
Tenting volume (mm^3)	1577 ± 645	1878 ± 913	2040 ± 755 [a]
Tenting index	2.6 ± 0.8	2.9 ± 1.0	2.4 ± 0.9
Annular height (mm)	4.6 ± 0.5	4.7 ± 1.5	4.7 ± 0.5
Intercommissural width (mm)	30.1 ± 3.2	29.4 ± 3.1	35.1 ± 2.9 [a, b]
Annular height to commissural width ratio	15.7 ± 2.6	16.7 ± 4.4	13.7 ± 1.9 [a]
Septolateral diameter (mm)	25.0 ± 2.0	25.4 ± 3.5	33.8 ± 5.9 [a, b]
PMPM to PMC (mm)	20.9 ± 2.7	20.2 ± 1.2	24.1 ± 2.8 [a, b]
ALPM to PMPM (mm)	23.9 ± 2.5	25.0 ± 3.4	30.9 ± 5.2 [a, b]

Values are expressed as mean ± standard deviation. ALPM, antero-lateral papillary muscle; PMPM, postero-medial papillary muscle; PMC, postero-medial commissure.

[a] $P<0.05$ vs. baseline; [b] $P<0.05$ vs. 30 min after infarction.

RESULTS

- MR grade and LVEDP increased significantly at 8 weeks, with a significant decrease in LVEF (see Table). Compared to baseline values and to those at 30minutes post-MI, there were significant increases at 8 weeks in commissural width and septolateral diameter, with a resultant increase in mitral annular area and a decrease in the annular height to commissural width ratio. The mitral valve tenting volume increased significantly. The distance between the papillary muscle tips at baseline and at 8 weeks increased significantly (23.9±2.5mm vs. 30.9±5.2, $p<0.01$) as did the distance between the posterior papillary muscle tip and the posterior commissure (20.9±2.7 vs. 24.1±2.8mm, $p<0.01$).

CONCLUSION

- The surgical model described here reliably replicates the changes seen in humans with IMR. It may thus be used for further study of the pathophysiology of IMR and also for the study of novel interventions in this challenging clinical area.