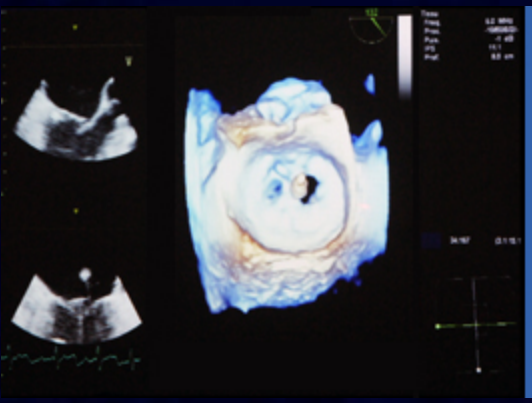

EuroValve
March 27-28 2015
Radisson BLU Hotel, Nice, FRANCE

Pulmonary hypertension (PHT) in valvular heart disease

PHT in primary MR

UNIVERSITÉ de Picardie Jules Verne

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CHU AMIENS PICARDIE

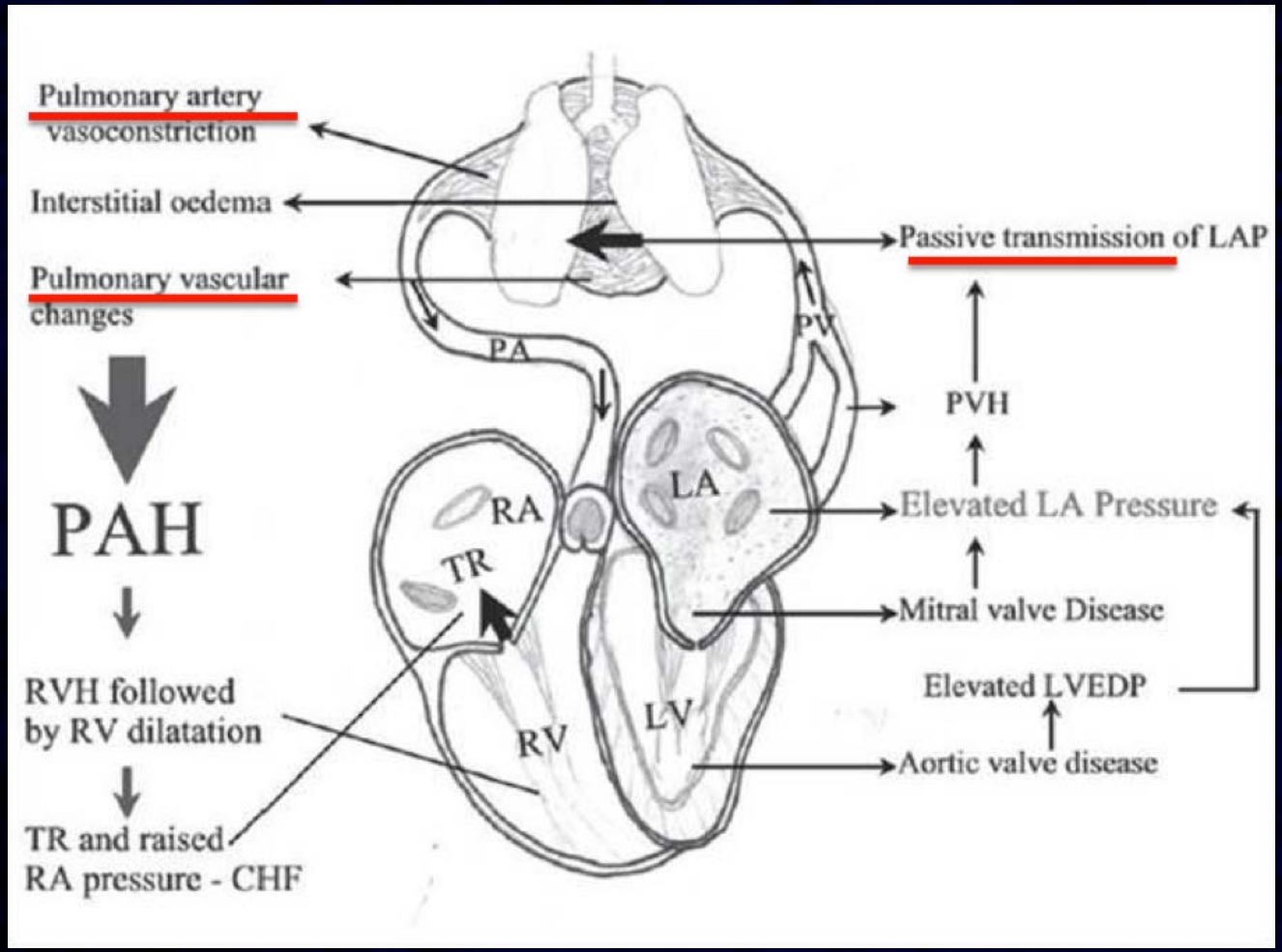
Disclosures related to this presentation

None

PHT in MV disease

- Elevation of PA pressures is commonly observed in symptomatic patients with MV disease
- Elevated PA leads to a cascade of adverse effects on the pulmonary circulation and RV function
- PHT is a risk factor for poor outcome in MVD
- The presence of PHT in MVD is a key element in the decision making algorithm for intervention on the mitral valve

Pathophysiology of PHT in MV disease



Primary MR
Indications for MV treatment

- **ESC guidelines**

	Class	Level
Surgery should be considered in asymptomatic patients with preserved LV function and new onset of atrial fibrillation or pulmonary hypertension (systolic pulmonary pressure at rest > 50 mmHg).	IIa	C
Surgery may be considered in asymptomatic patients with preserved LV function, high likelihood of durable repair, low surgical risk, and: • left atrial dilatation (volume index ≥ 60 ml/m² BSA) and sinus rhythm, or • pulmonary hypertension on exercise (SPAP ≥ 60 mmHg at exercise).	IIb	C

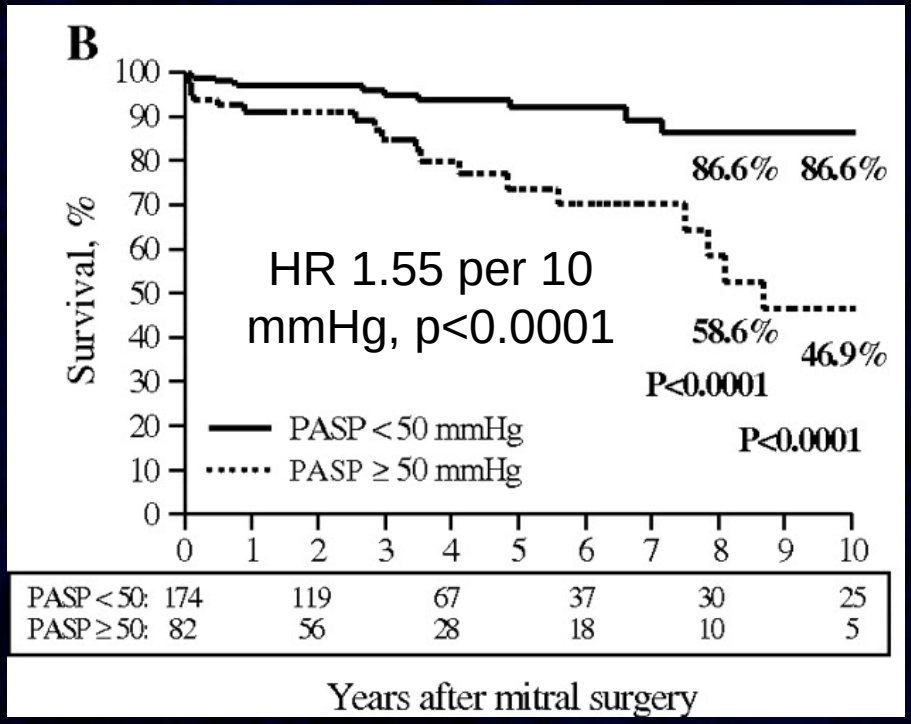
- **ACC/AHA guidelines**

MV repair is reasonable for asymptomatic patients with chronic severe nonrheumatic primary MR (stage C1) and preserved LV function in whom there is a high likelihood of a successful and durable repair with 1) new onset of AF or 2) resting pulmonary hypertension (PA systolic arterial pressure >50 mm Hg)	IIa	B

Vahanian et al., Eur Heart J 2012, Nishimura et al,. Circulation. 2014

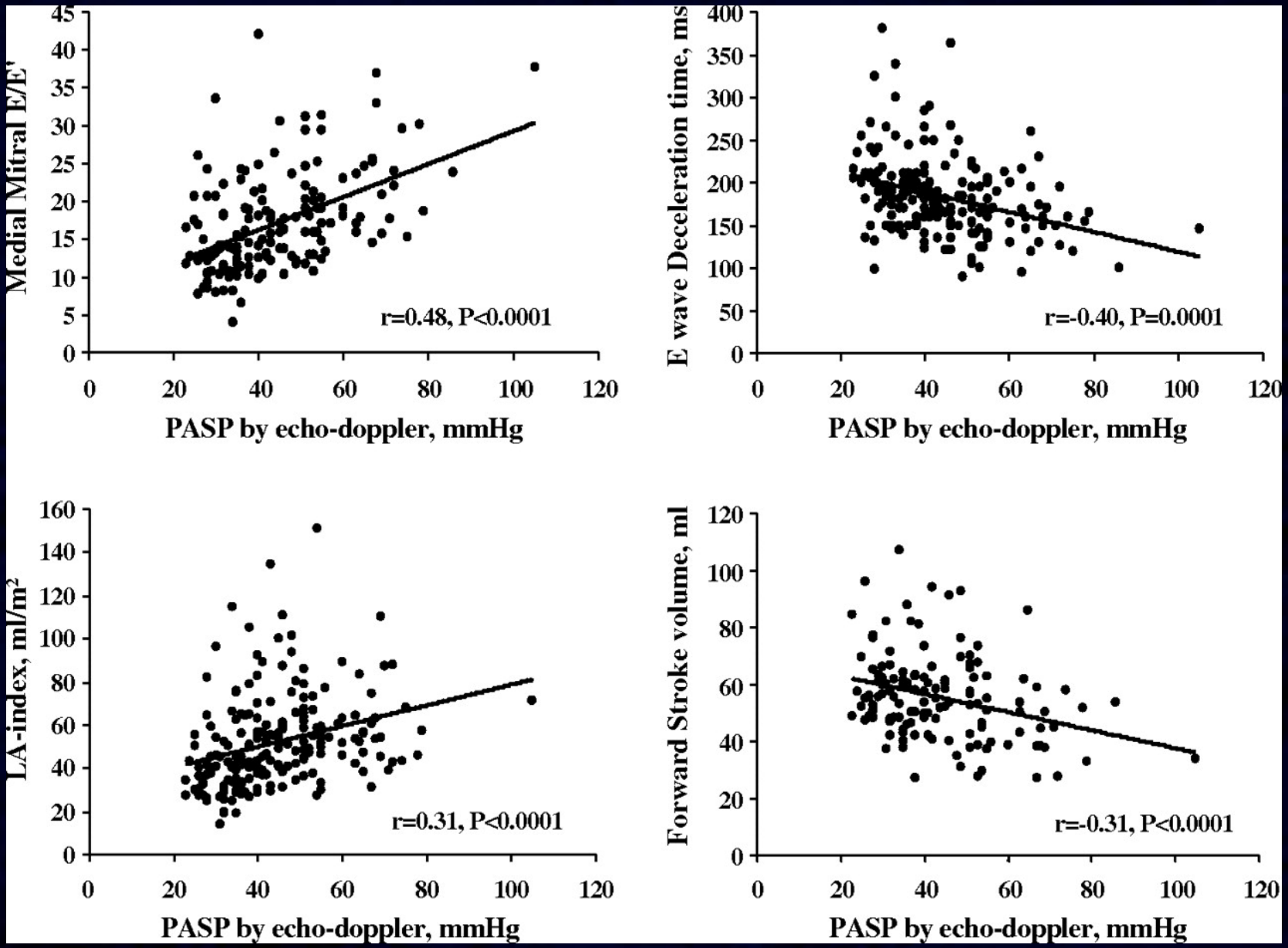
PHT and outcome

- 256 patients with chronic severe organic MR referred for surgery
- 36% of NYHA class III-IV, 32% sPAP > 50 mmHg
- Post-op end points: death + CardioVasc death



Le Tourneau et al., Heart 2010

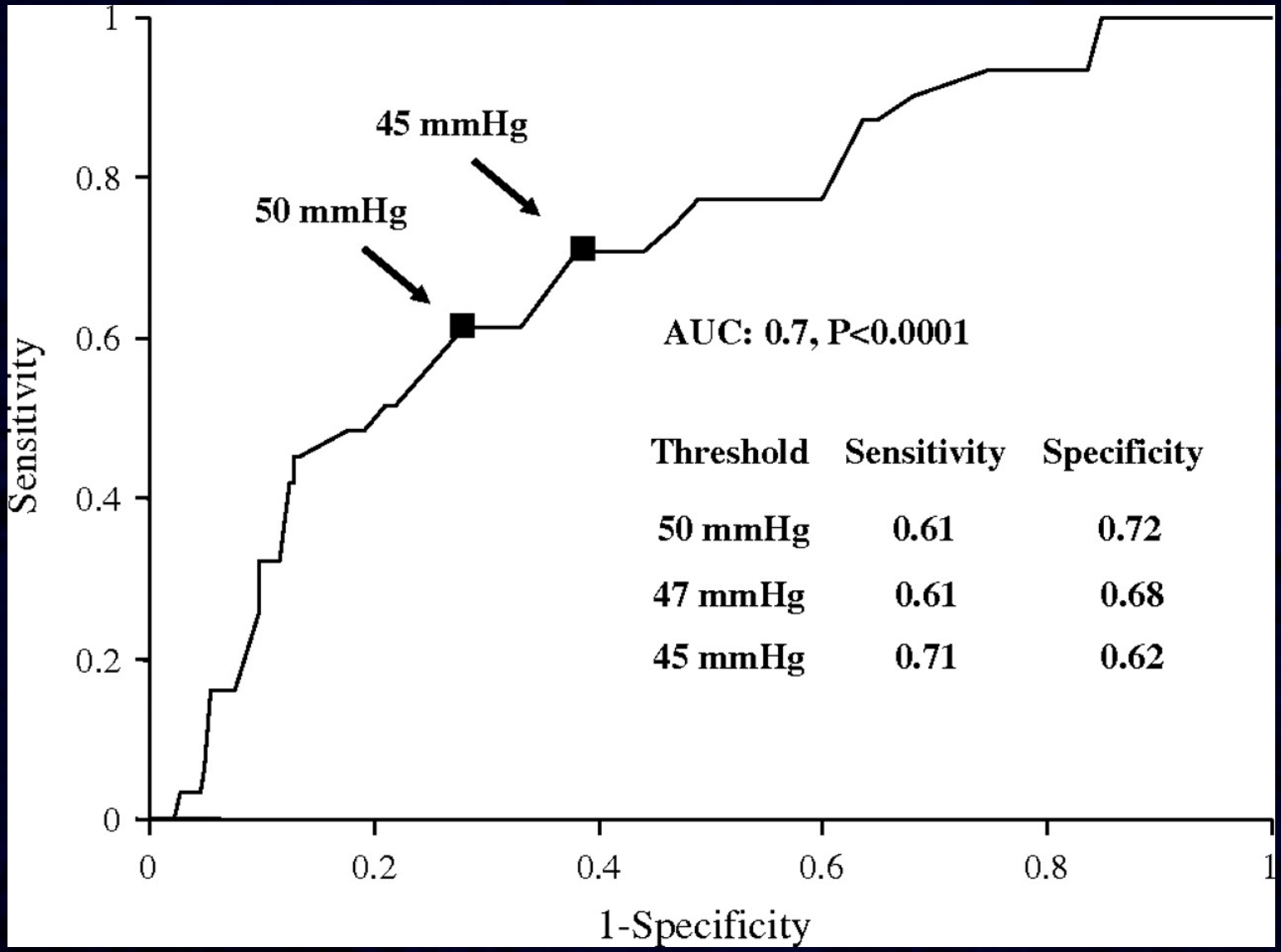
Characteristics	All patients (n=256)	PASP <50 mmHg (n=174)	PASP ≥50 mmHg (n=82)	p Value
Age, years	63±12	61±13	68±11	<0.0001
Male, n (%)	170 (66)	121 (70)	49 (60)	0.16
Atrial fibrillation, n (%)	75 (29)	45 (26)	30 (37)	0.11
NYHA class 3–4, n (%)	92 (36)	50 (29)	42 (51)	<0.0001
Hypertension, n (%)	58 (23)	43 (25)	15 (18)	0.40
Diabetes mellitus, n (%)	10 (3.9)	8 (4.6)	2 (2.4)	0.73
BMI, kg/m^2	25±4	25±4	23±3	<0.0001
Coronary artery disease, n (%)	27 (11)	16 (9)	11 (13)	0.38
MR mechanism				0.22
Degenerative, n (%)	234 (91)	159 (91)	75 (91)	
Rheumatic or endocarditis, n (%)	22 (9)	15 (9)	7 (9)	
LVEDD index, mm/m^2	31±4	31±4	33±4	<0.0001
LVESD index, mm/m^2	20±4	19±4	21±4	<0.0001
LVEF, %	65±10	65±10	63±10	0.13
Mitral E wave, m/s	1.4±0.4	1.3±0.3	1.5±0.3	<0.0001
Mitral E/A	2.1±0.9	1.9±0.8	2.7±1.1	<0.0001
Mitral deceleration time, ms	183±47	193±49	162±36	<0.0001
Mitral medial E/E'	17±7	15±6	21±6	<0.0001
Mitral lateral E/E'	12±6	11±4	13±7	0.015
LAD, mm	48±8	47±7	50±9	0.004
LA index, ml/m^2	52±21	49±22	58±19	0.005
PASP, mmHg	45±14	37±7	61±10	–
Additive Euroscore	4.7±2.2	4.2±2.1	5.6±2.3	<0.0001
Charlson index	2.1±1.4	1.9±1.4	2.6±1.4	<0.0001
Mitral valve repair, n (%)	194 (76)	135 (78)	59 (72)	0.35
CABG, n (%)	9 (3.5)	6 (3.4)	3 (3.7)	0.93
Radiofrequency ablation, n (%)	51 (20)	37 (21)	14 (17)	0.50



Le Tourneau et al., Heart 2010

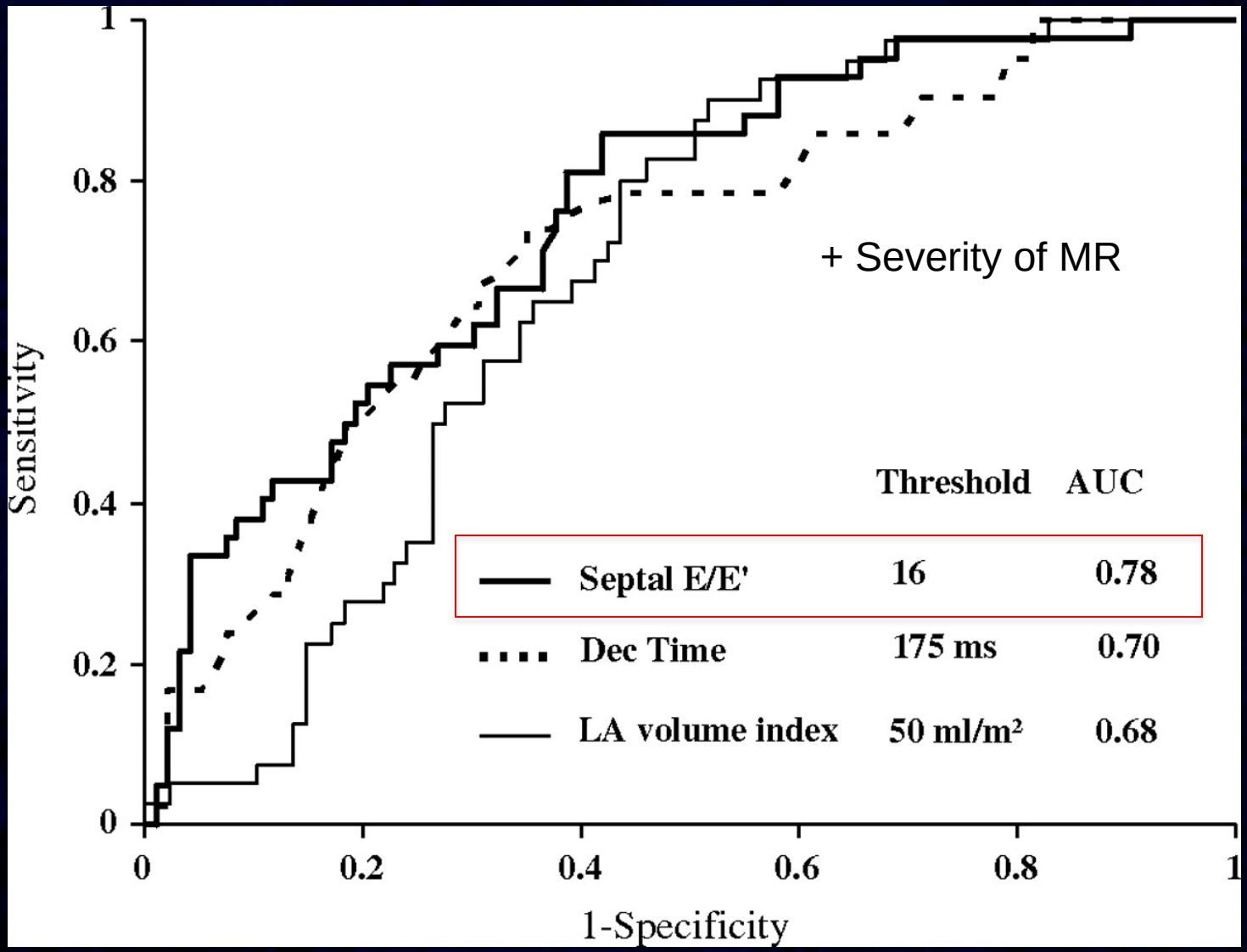
Determinants of PHT: E/E' ratio, mitral DT, LA index

	Medial E/E'	Mitral DT	LA index	R	p Value
Overall	β=0.43	β=−0.30	β=0.21	0.64	<0.0001
	p<0.0001	p<0.0001	p=0.003		
SR	β=0.39	β=−0.27	β=0.28	0.67	<0.0001
	p<0.0001	p<0.0001	p=0.001		
AF	β=0.42	β=−0.36	—	0.52	0.003
	p=0.006	p=0.02			
EF ≤60%	β=0.24	β=−0.38	β=0.30	0.61	<0.0001
	p=0.05	p=0.003	p=0.02		
EF >60%	β=0.52	β=−0.24	β=0.18	0.67	<0.0001
	p<0.0001	p=0.003	p=0.02		



Le Tourneau et al., Heart 2010

Prediction of PHT



Le Tourneau et al., Heart 2010

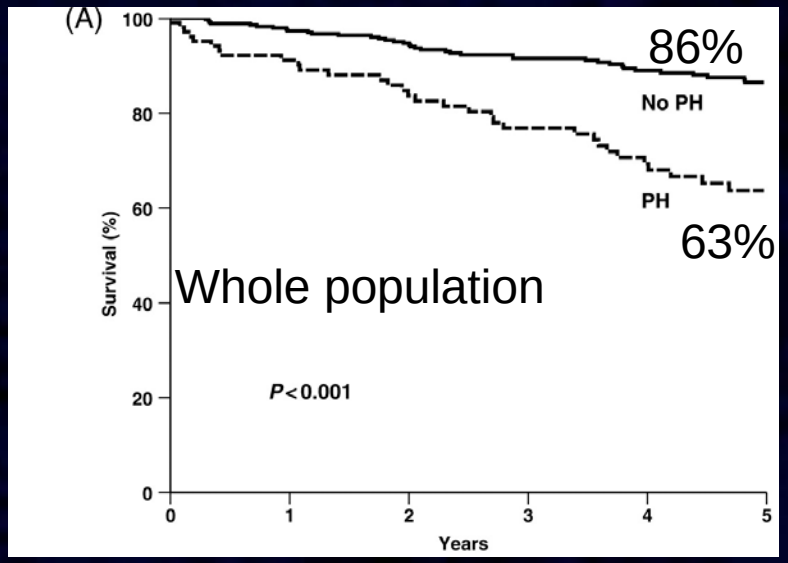
PHT and outcome

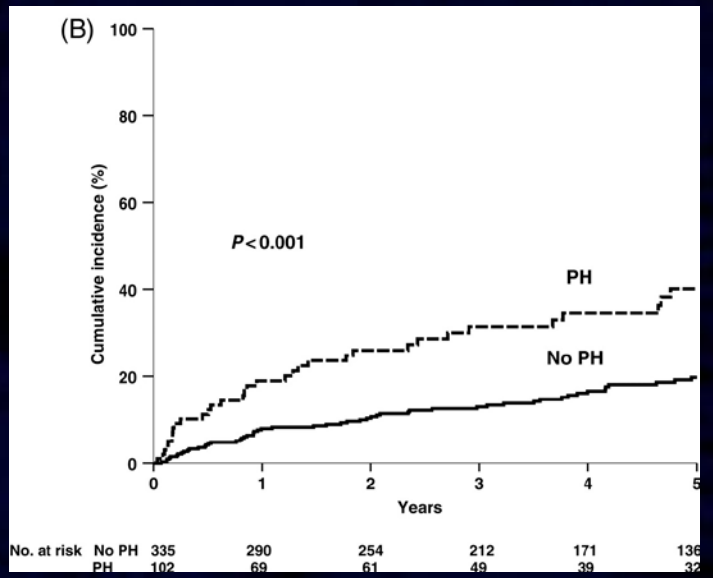
- 437 patients flail organic MR
- 35% of NYHA class III-IV (MIDA)
- 23% sPAP > 50 mmHg
- Event: Death + heart failure

	Overall, *n* = 437	PH present, *n* = 102	PH absent, *n* = 335	*P*-value
Age (years)	67.5 ± 11.4	71.8 ± 10.3	66.1 ± 11.4	<0.0001
BSA (m^2)	1.8 ± 0.21	1.79 ± 0.23	1.81 ± 0.20	0.418
Male gender, *n* (%)	290 (66)	60 (59)	230 (69)	0.066
NYHA Classes III–IV, *n* (%)	153 (35.0)	65 (63.7)	88 (26.3)	<0.0001
Atrial fibrillation, *n* (%)	104 (23.8)	37 (36.3)	67 (20.0)	0.001
History of coronary artery disease, *n* (%)	36 (8.2)	11 (10.8)	25 (7.5)	0.285
Left atrial dimension (mm)	51.1 ± 9.5	55.1 ± 10.6	49.9 ± 8.7	<0.0001
Left ventricular end-diastolic dimension (mm)	59.4 ± 8.5	60.3 ± 8.1	59.1 ± 8.6	0.239
Left ventricular end-systolic dimension (mm)	36.5 ± 7.7	36.9 ± 7.7	36.4 ± 7.7	0.612
Left ventricular ejection fraction (%)	64.1 ± 10.1	63.7 ± 10.1	64.2 ± 10.0	0.712
Grade 3–4 MR by Doppler echocardiography, *n* (%)	409 (94.5)	97 (96.0)	312 (94.0)	0.427
ACE-inhibitors/ARB, *n* (%)	219 (50.7)	59 (60.2)	160 (47.9)	0.032
Beta-blockers, *n* (%)	79 (18.2)	18 (18.2)	61 (18.3)	0.985
Digoxin, *n* (%)	144 (33.3)	48 (48.5)	96 (28.7)	0.0002
Diuretics, *n* (%)	203 (47.0)	62 (62.62)	141 (42.3)	0.0003

Barbieri et al., Eur Heart J 2011

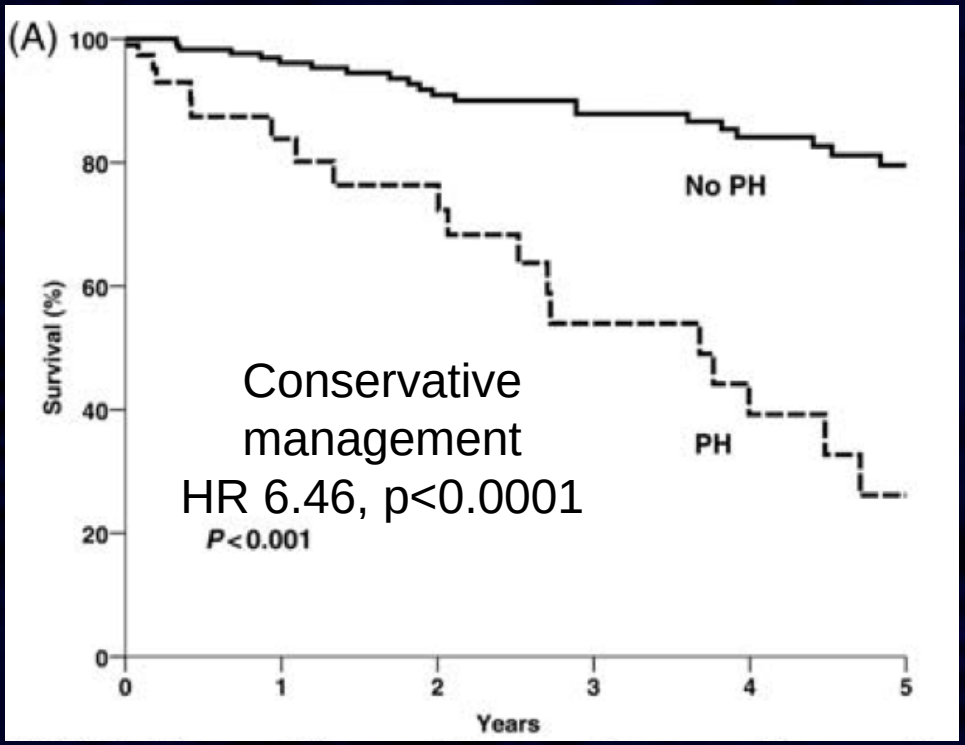
PHT and outcome

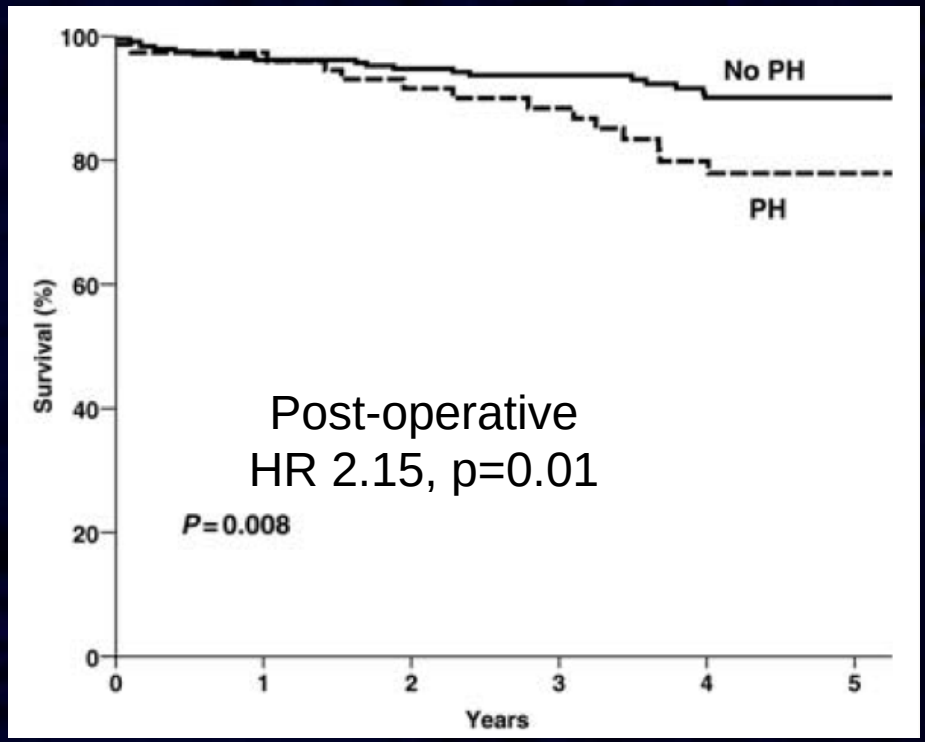




	PASP > 50 mmHg (categorical variable)			PASP per 10 mmHg increase (continuous variable)		
	HR (95% CI)	*P*-value	ROC	HR (95% CI)	*P*-value	ROC
Overall death						
Adjusted for age, gender, symptoms, LVEF, AFib, and MV surgery	2.03 (1.30–3.18)	0.002	0.665	1.16 (1.03–1.31)	0.013	0.665
Death from cardiovascular causes						
Adjusted for age, gender, NYHA Class, LVEF, AFib, and MV surgery	2.21 (1.30–3.76)	0.0003	0.711	1.15 (1.00–1.32)	0.0042	0.709
Heart failure						
Adjusted for age, gender, symptoms, LVEF, AFib, and MV surgery	1.70 (1.10–2.62)	0.018	0.515	1.19 (1.06–1.35)	0.004	0.516

PHT and outcome

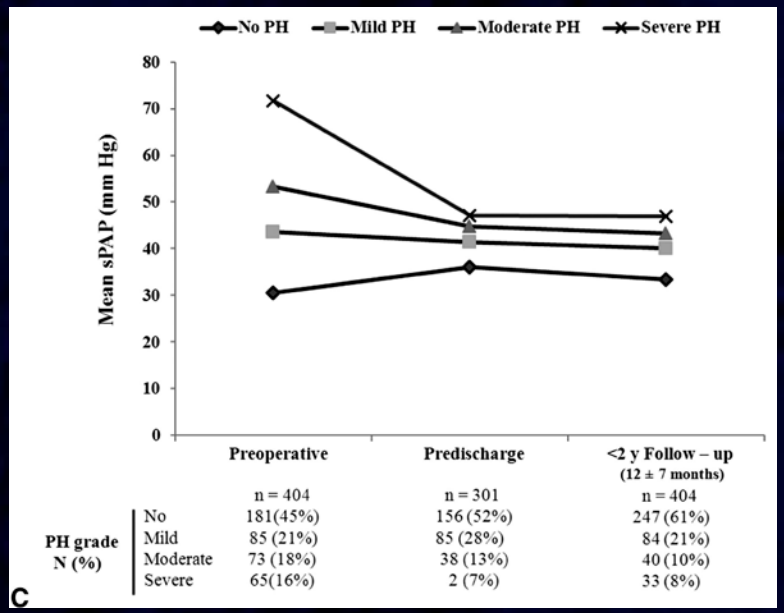


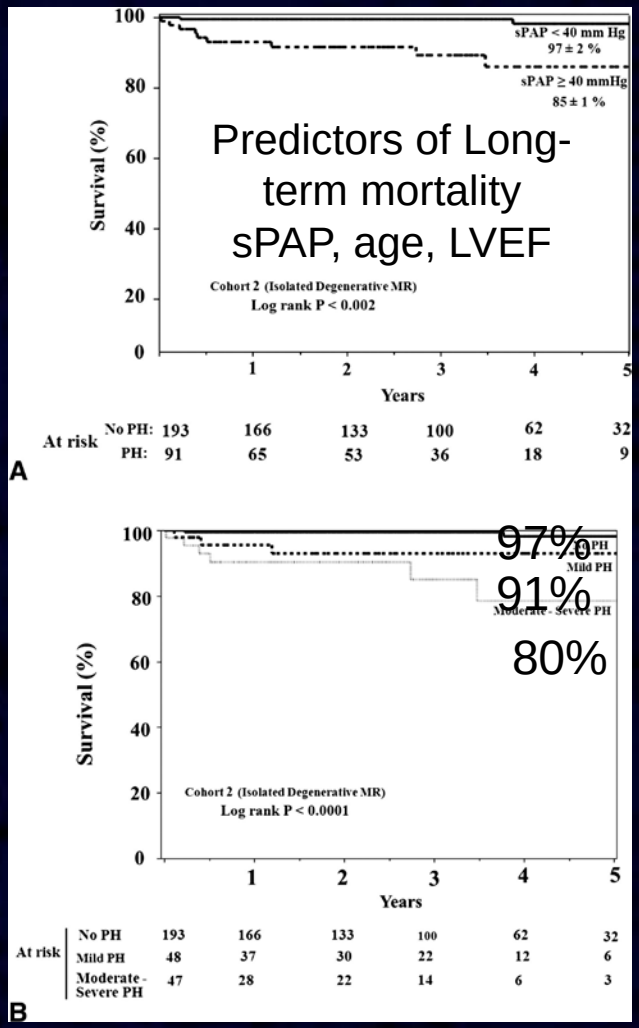


Barbieri et al., Eur Heart J 2011

Any Grade of PHT affects the outcome after MVS

- 284 patients with chronic severe degenerative MR referred for surgery
- 39% of NYHA class III-IV (retrospective)
- 17% sPAP 40-50 mmHg and 15% sPAS > 50 mmHg
- Operative mortality was 0.8%

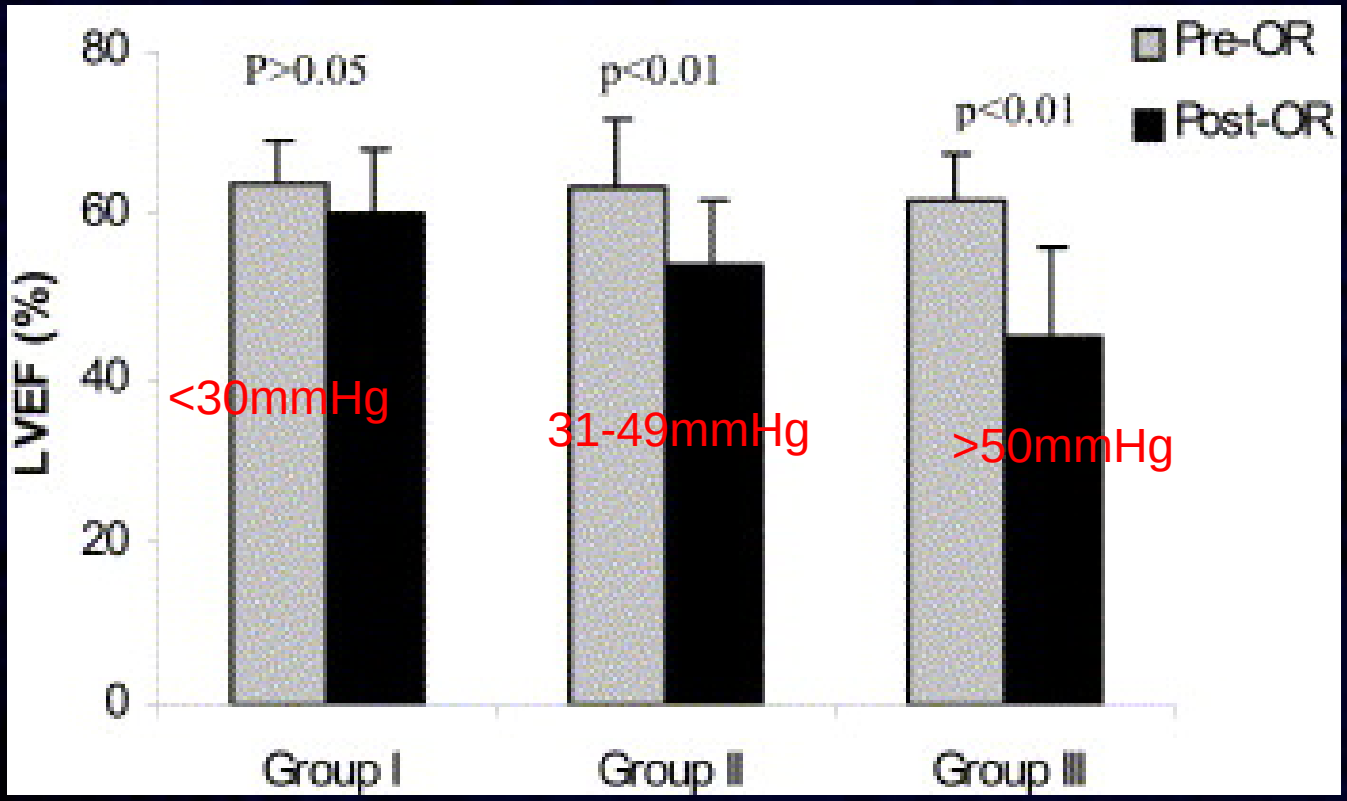




Goreishi et al., J Thorac Cardiovasc Surg 2011

Pulmonary Hypertension and Post-Operative LV dysfunction

- 79 patients with chronic severe organic MR referred for surgery
- 36 % sPAP > 50 mmHg

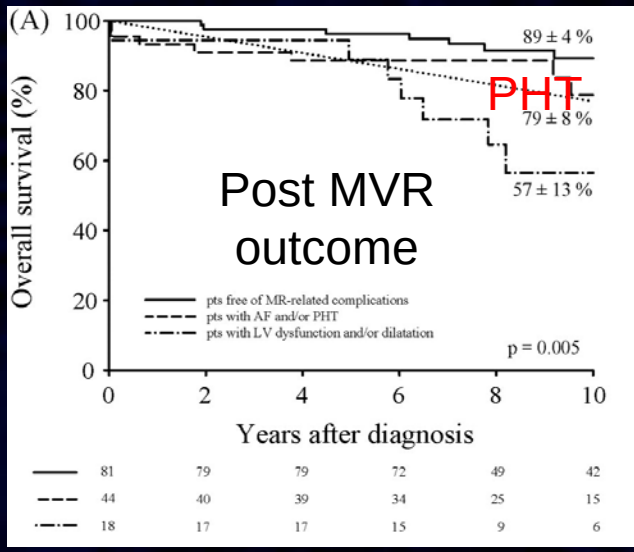


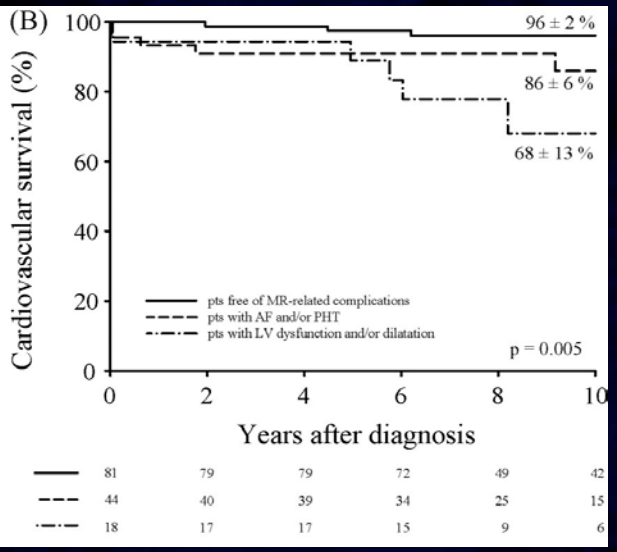
- By a stepwise multivariate regression analysis, preoperative sPAP and LVD independently correlated with postoperative LVEF

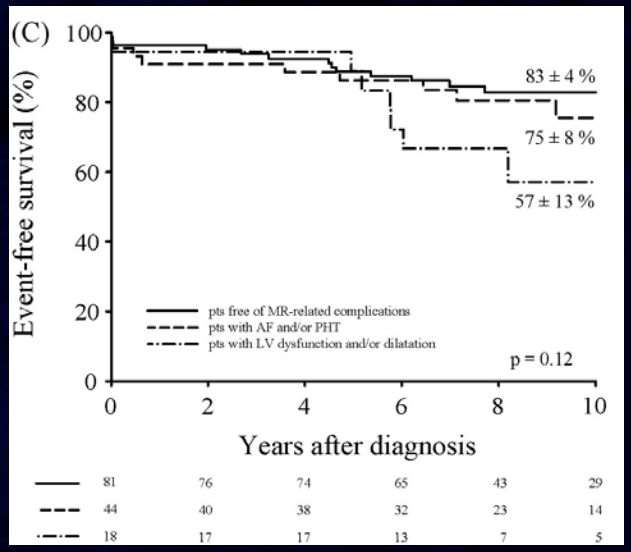
Yang et al., JASE 2006

Primary MR (asymptomatic patients)
PHT and Post-Op survival after MVRepair

- 143 patients (prospective)
- 12% (18 with LV dysfunction)
- 8 years
- Overall outcome after MVR







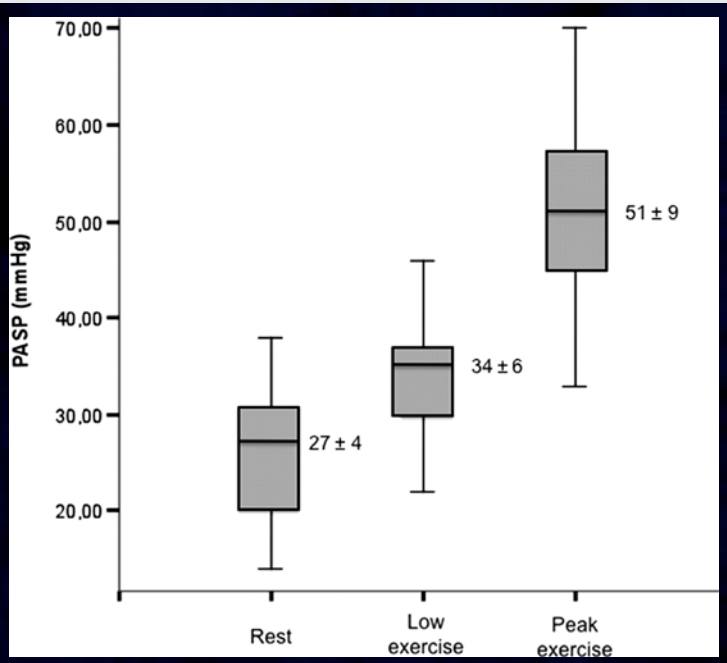
Chenot et al., Eur J CVS 2009

Pulmonary Hypertension at Exercise in normal adults

- 70 healthy volunteers; PHT at rest and exercise

	All ($n = 70$)	Age 20–30 ($n = 13$)	Age 30–40 ($n = 10$)	Age 40–50 ($n = 14$)	Age 50–60 ($n = 12$)	Age 60–70 ($n = 11$)	Age 70–80 ($n = 10$)
PASP at rest (mmHg)	27 ± 4	27 ± 4	29 ± 3	28 ± 3	26 ± 4	27 ± 4	28 ± 6
PASP at first workload step (mmHg)	34 ± 6	31 ± 4	33 ± 5	34 ± 4	31 ± 6	37 ± 9	37 ± 5
PASP at peak exercise (mmHg)	51 ± 9	45 ± 7	51 ± 6	52 ± 9	53 ± 4	54 ± 12*	58 ± 7*
Increase in PASP (mmHg)	27 ± 8	22 ± 8	24 ± 7	27 ± 10	29 ± 5	29 ± 9	30 ± 8

36% 50%



Mahjoub et al., Eur J Echocardiogr 2009

Table 5 Correlation between pulmonary artery systolic pressure at peak exercise and clinical and echocardiographic variables

Variable	*r*	*P*-value
Age (years)	0.42	0.0001
Body mass index	0.26	0.035
Systolic blood pressure at rest (mmHg)	0.37	0.002
Diastolic blood pressure at rest (mmHg)	0.18	0.13
Heart rate at peak exercise (bpm)	−0.085	0.48
Systolic blood pressure at peak exercise (mmHg)	0.31	0.01
Diastolic blood pressure at peak exercise (mmHg)	0.33	0.005
Increase in systolic blood pressure (mmHg)	0.084	0.49
Cardiac output at peak exercise	−0.21	0.08
Maximum workload (W)	0.12	0.33
PASP at rest	0.40	0.001
Left ventricular end-diastolic diameter (mm)	0.18	0.14
Left ventricular mass	0.35	0.003
Left ventricular ejection fraction (%)	−0.054	0.68
Right ventricular fractional area change (%)	−0.33	0.0009
E (cm/s)	−0.15	0.21
A (cm/s)	0.13	0.27
E-wave deceleration time (ms)	0.25	0.04
E/*A*	−0.15	0.22
E′	−0.36	0.007
E/*E*′	0.30	0.025
Left atrial surface (cm^2)	0.27	0.049

	Unstandardized coefficients	
	B	SE
Predictors of exercise capacity		
Left ventricular mass	0.47	0.09
E/*A*	34.19	0.35
Predictors of PASP at peak exercise		
Age	0.23	0.09
Left ventricular mass	0.12	0.03
PASP at rest	1.29	0.37
Predictors of increase in PASP with exercise		
Age	0.11	0.06
Left ventricular mass	0.13	0.03

Mahjoub et al., Eur J Echocardiogr 2009

Exercise Pulmonary Hypertension

- **Exercise PHT may develop in patients with degenerative MR, even when resting sPAP is normal**
- **PHT (≥60mmHg) is a criterion for surgical decision-making in patients with severe asymptomatic degenerative MR (Class IIbC, ESC)**

Pulmonary Hypertension at Exercise in Asymptomatic Patients

- 78 asymptomatic patients with moderate to severe degenerative MR
- Symptom-Free survival

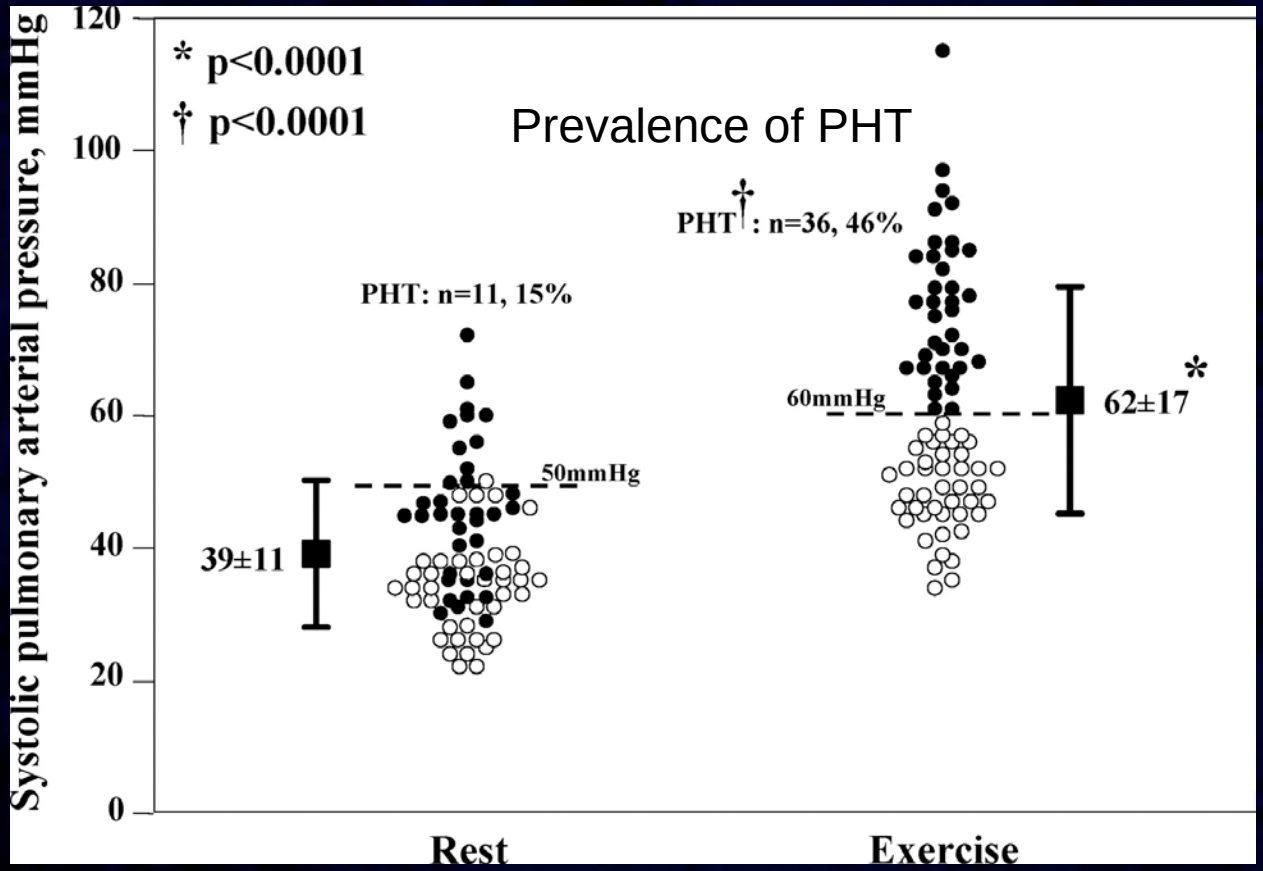
Prevalence of PHT

Magne et al., Circulation 2010

Demographic and Clinical Data

Variables	All Patients (n=78)	No Exercise PHT (n=42, 54%)	Exercise PHT (n=36, 46%)	P
Demographic and clinical data				
Age, y	61±13	57±14	65±11	0.006
Male gender, n (%)	44 (56)	19 (45)	25 (69)	0.03
Body mass index, kg/m^2	26±4	27±4	26±4	0.27
Heart rate, bpm	73±11	73±11	72±11	0.69
Systolic arterial pressure, mm Hg	138±18	133±15	143±19	0.02
Diastolic arterial pressure, mm Hg	78±12	76±11	79±13	0.27
Risk factors, n (%)				
Hypertension	43 (55)	18 (43)	25 (69)	0.05
Hypercholesterolemia	16 (20)	7 (17)	9 (25)	0.53
Diabetes mellitus	8 (10)	3 (7)	5 (14)	0.72
Smoker	27 (35)	13 (30)	14 (39)	0.62
Medication, n (%)				
ACE inhibitor	34 (44)	17 (40)	17 (47)	0.71
β-blockers	34 (44)	17 (40)	17 (47)	0.71
Diuretic	2 (3)	1 (2)	1 (3)	1
Mitral valve prolapse, n (%)				
Anterior	5 (7)	2 (5)	5 (14)	0.24
Posterior	37 (47)	17 (40)	20 (56)	0.27
Both	36 (46)	23 (55)	13 (36)	0.16
Mitral flail	8 (10)	3 (7)	5 (14)	0.46

sPAP at rest and during exercise



Magne et al., Circulation 2010

Echocardiographic Data

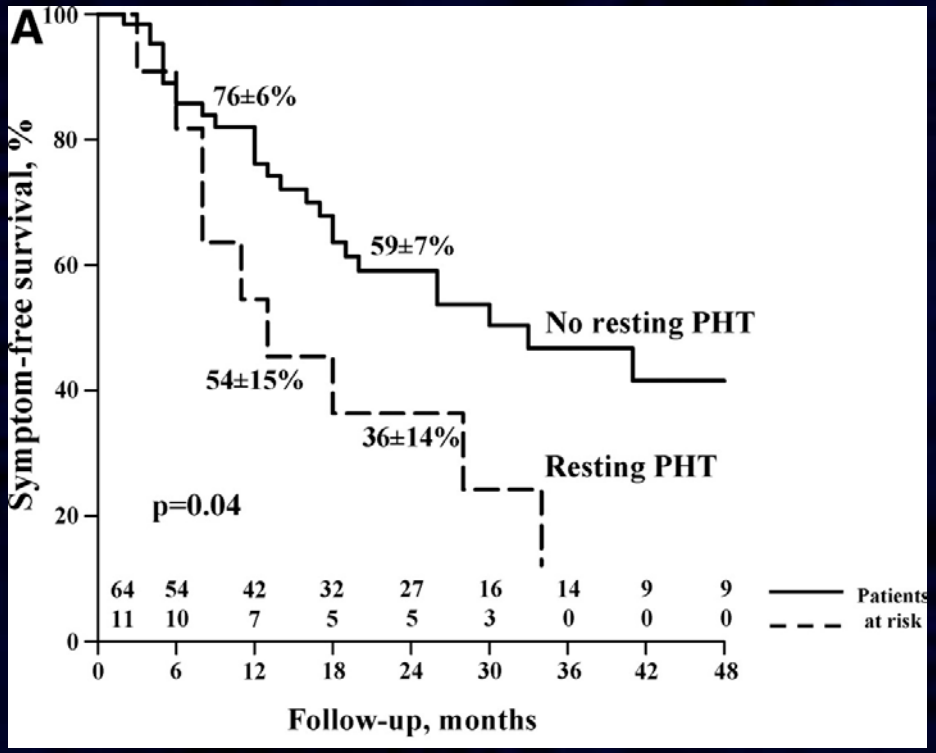
Variables	All Patients (n=78)	No Exercise PHT (n=42, 54%)	Exercise PHT (n=36, 46%)	P
Resting LV function				
LVES volume, mL	36±11	35±12	38±12	0.27
LVED volume, mL	114±35	109±34	123±37	0.015
LV ejection fraction, %	69±6	68±5	69±6	0.42
E-wave velocity, $cm.s^{-1}$	100±33	95±28	107±37	0.11
A-wave velocity, $cm.s^{-1}$	75±25	74±20	77±29	0.59
E/A ratio	1.5±0.7	1.4±0.6	1.6±0.8	0.21
Ea-wave velocity, cm/s	7.4±1.9	7.6±2	7.3±1.7	0.48
E/Ea ratio	14±5	13±4	16±5	0.01
Exercise LV function				
LVES volume, mL	31±16	33±20	31±11	0.59
LVED volume, mL	106±39	103±39	111±39	0.37
LV ejection fraction, %	72±9	70±9	71±10	0.64
E-wave velocity, cm/s	138±42	132±43	146±44	0.046
A-wave velocity, cm/s	94±43	92±56	90±31	0.85
E/A ratio	1.5±0.4	1.5±0.3	1.6±0.4	0.21
Ea-wave velocity, cm/s	9.9±2.3	9.6±2.4	9.4±2.2	0.70
E/Ea ratio	14.5±5	14±5	15±5	0.38
Resting LA volume, mL	71±24	74±27	73±21	0.86
Exercise LA volume, mL	81±29	83±35	87±26	0.56
MR				
Severe MR, n (%)	47 (60)	26 (62)	21 (58)	0.93
Resting ERO, mm^2	43±20	43±23	42±16	0.83
Exercise ERO, mm^2	48±26	42±27	55±23	0.03
Resting RV, mL	71±27	73±35	69±20	0.55
Exercise RV, mL	73±36	65±39	83±28	0.03
Resting SPAP, mm Hg	39±11	33±6	46±10	<0.0001
Exercise SPAP, mm Hg	62±17	46±10	77±12	<0.0001

Variables	Correlation With Resting SPAP	
	r	*P*
Age	0.25	0.04
Resting heart rate*	0.04	0.74
Resting systolic arterial pressure*	0.12	0.56
Resting diastolic arterial pressure*	0.04	0.77
Resting LV function		
LVES volume	0.29	0.04
LVED volume	0.21	0.13
LV ejection fraction*	0.11	0.44
E/A ratio	0.28	0.06
Ea-wave velocity	0.11	0.42
E/Ea ratio	0.32	0.02
Resting LA volume*	0.21	0.15
MR		
Resting ERO	0.19	0.14
Resting RV	0.09	0.42

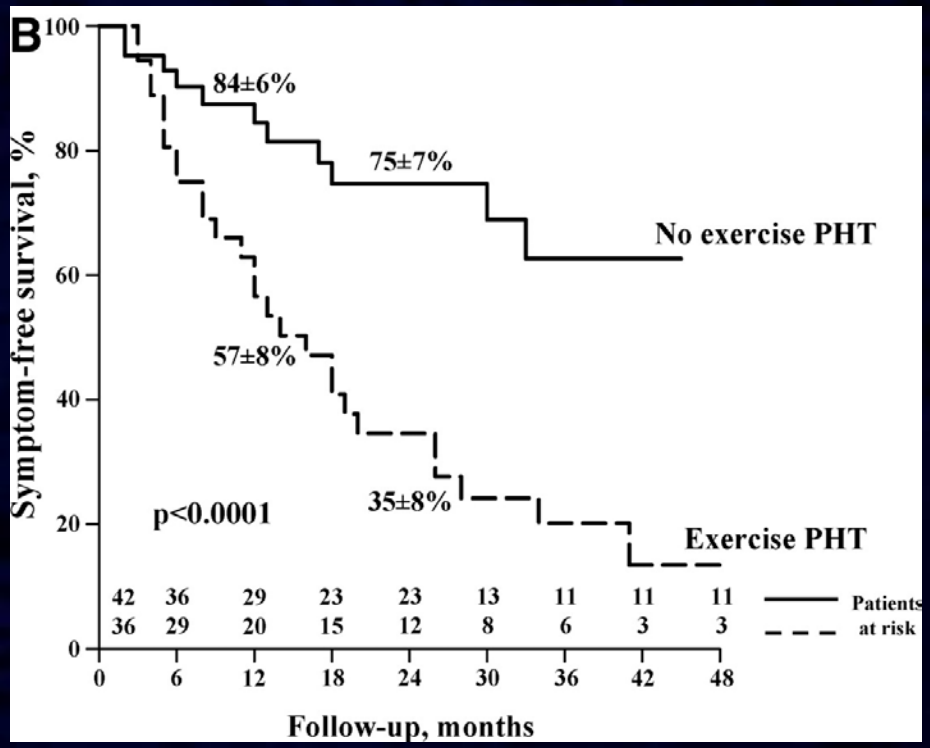
Variables	Correlation With Exercise SPAP	
	r	*P*
Age	0.25	0.03
Resting heart rate*	0.01	0.99
Exercise heart rate*	0.08	0.58
Resting systolic arterial pressure*	0.14	0.39
Exercise systolic arterial pressure*	0.05	0.70
Resting diastolic arterial pressure*	−0.03	0.84
Exercise diastolic arterial pressure*	0.11	0.43
Resting LV function		
LVES volume	0.22	0.10
LVED volume	0.31	0.02
LV ejection fraction*	0.04	0.75
E/A ratio	0.31	0.03
Ea-wave velocity	0.06	0.64
E/Ea ratio	0.29	0.03
Exercise LV function		
LVES volume	0.10	0.24
LVED volume	0.26	0.09
LV ejection fraction*	0.12	0.39
E/A ratio	0.10	0.37
Ea-wave velocity	0.12	0.33
E/Ea ratio	0.04	0.27
Resting LA volume*	0.01	0.96
Exercise LA volume*	0.15	0.32
MR		
Resting ERO	0.16	0.16
Exercise ERO	0.46	<0.0001
Changes in ERO	0.62	<0.0001
Resting RV	0.06	0.56
Exercise RV	0.42	0.0001
Changes in RV	0.62	<0.0001
Resting SPAP	0.69	<0.0001

Pulmonary Hypertension at Exercise and symptom-free survival

Resting PHT (sPAP>50mmHg)



Exercise PHT (sPAP>60 mmHg)



Adjusted HR 2.1, p=NS

Adjusted HR 2.8, p=0.01

Magne et al., Circulation 2010

- **PHT (sPAP≥60 mmHg) is frequent in patients with asymptomatic degenerative MR**
- **Exercise-induced changes in sPAP are unrelated to resting sPAP**
- **Changes in MR severity during exercise are the main determinants of exercise-induced changes in systolic PAP and in exercise PHT**
- **Exercise PHT is associated with reduced symptom-free survival**

Conclusion

- PHT is an indicator of poor outcome in MR
- PHT (sPAP ≥ 50 mmHg) is a criterion for surgical decision-making in patients with severe asymptomatic organic MR
- Exercise PHT may develop in patients with MVP even when resting sPAP is normal. It is associated with occurrence of symptoms
- However, exercise sPAP > 60mmHg may be observed at peak exercise in normal patients


THANK YOU