Early Percutaneous Mitral Commissurotomy or Conventional Management for Asymptomatic Mitral Stenosis: A Randomized Clinical Trial

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Disclosure

No Disclosure Relevant to This Presentation

Introduction

- Although percutaneous mitral commissurotomy (PMC) has become the standard treatment for symptomatic patients with rheumatic mitral stenosis (MS), the timing and indications for PMC in asymptomatic, severe MS remain controversial
- The decision to perform PMC on asymptomatic patients requires careful weighing of the potential benefits against the risks of early PMC

Introduction

- Current guidelines recommended PMC for asymptomatic patients with significant pulmonary hypertension, high thrombo-embolic risk or very severe MS
- Preemptive PMC can be justified only when there is clear evidence that early PMC improves long-term outcomes compared with conventional treatment
- The major hypothesis of the MITIGATE (Mitral Intervention versus Conventional Management in Asymptomatic Mitral Stenosis) trial was that early PMC would decrease the rate of cardiovascular mortality and systemic thromboembolic events, as compared with conventional treatment

Method: Study Design and Patients

MITIGATE A prospective, multicenter, open-label, randomized trial to compare long-term clinical outcomes of early PMC vs. conventional management in asymptomatic pts with severe MS

Inclusion	Exclusion
▪ Age 20-70 years	▪ Exertional dyspnea
▪ Severe MS (defined as mitral valve area between 1.0 and 1.5 cm^2)	▪ LV ejection fraction <50% ▪ Significant mitral regurgitation ▪ Significant pulmonary hypertension
▪ Candidates for early PMC	▪ Total echocardiographic score > 10
▪ Informed consent	▪ Left atrial thrombi

Clinicaltrials.gov NCT01406353

Method: Study Procedures

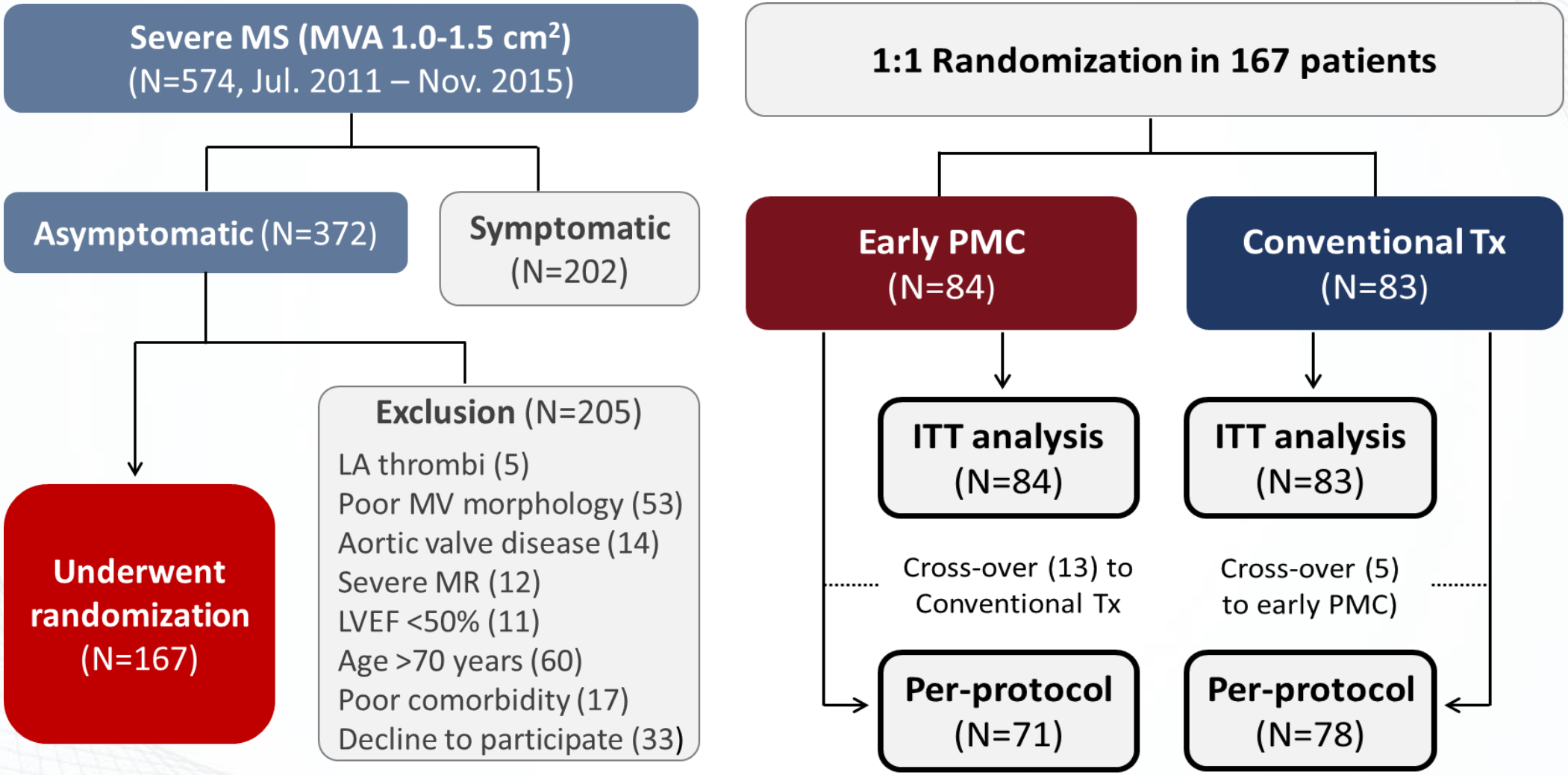
- Patients were randomly assigned on a 1:1 basis to early PMC or conventional treatment using a Web-based interactive response system
- In the early PMC group, PMC should be performed within 3 months of randomization
- Patients in the conventional treatment group were treated according to the current guidelines and referred for PMC if they became symptomatic, or if MV area decreased to smaller than 1.0 cm^2
- Anticoagulation was effectively maintained during the entire follow-up period in patients with atrial fibrillation or prior embolic events.

Method: Endpoints

End point	Sample size
▪ **Primary end point*** - PMC-related complications - Cardiovascular death - Cerebral infarction - Thromboembolic events ▪ **Secondary end point*** - All-cause death - Mitral valve replacement-	▪ **Assumptions** - Event rate of 2% in the early PMC group vs. 13% in the conventional treatment group during minimum follow-up of 3 years *(Kang DH et al. EHJ 2012)* - 80% Power at 2-sided significance level of 0.05 ▪ **Estimated sample N=166**

*occurred during 4-year follow-up period after enrollment of the last patient

Results: Study Flow



Results: Baseline Characteristics

Patient characteristics		
	Conventional (n=83)	Early PMC (n=84)
Age (years)	56±9	54±9
Female	70 (84%)	69 (82%)
Diabetes	6 (7%)	4 (5%)
Hypertension	41 (49%)	33 (39%)
Coronary disease	1 (1%)	0 (0%)
Previous stroke	7 (8%)	9 (11%)
Atrial fibrillation	40 (48%)	45 (54%)
Anticoagulation	45 (54%)	48 (57%)
Creatinine (mg/dl)	0.8±0.1	0.8±0.2

Echocardiographic Findings		
	Conventional (n=83)	Early PMC (n=84)
Mitral valve area (cm^2)		
Planimetry	1.24±0.15	1.23±0.13
Pressure half-time	1.26±0.09	1.28±0.19
Mitral gradient (mmHg)	8.1±4.0	8.2±3.6
Total echo score	8.2±1.1	8.0±1.0
Peak velocity of TR (m/s)	2.6±0.3	2.7±0.3
Moderate or severe TR	6 (7%)	7 (8%)
LA dimension (mm)	50±7	51±6
LV ejection fraction (%)	62±7	62±6

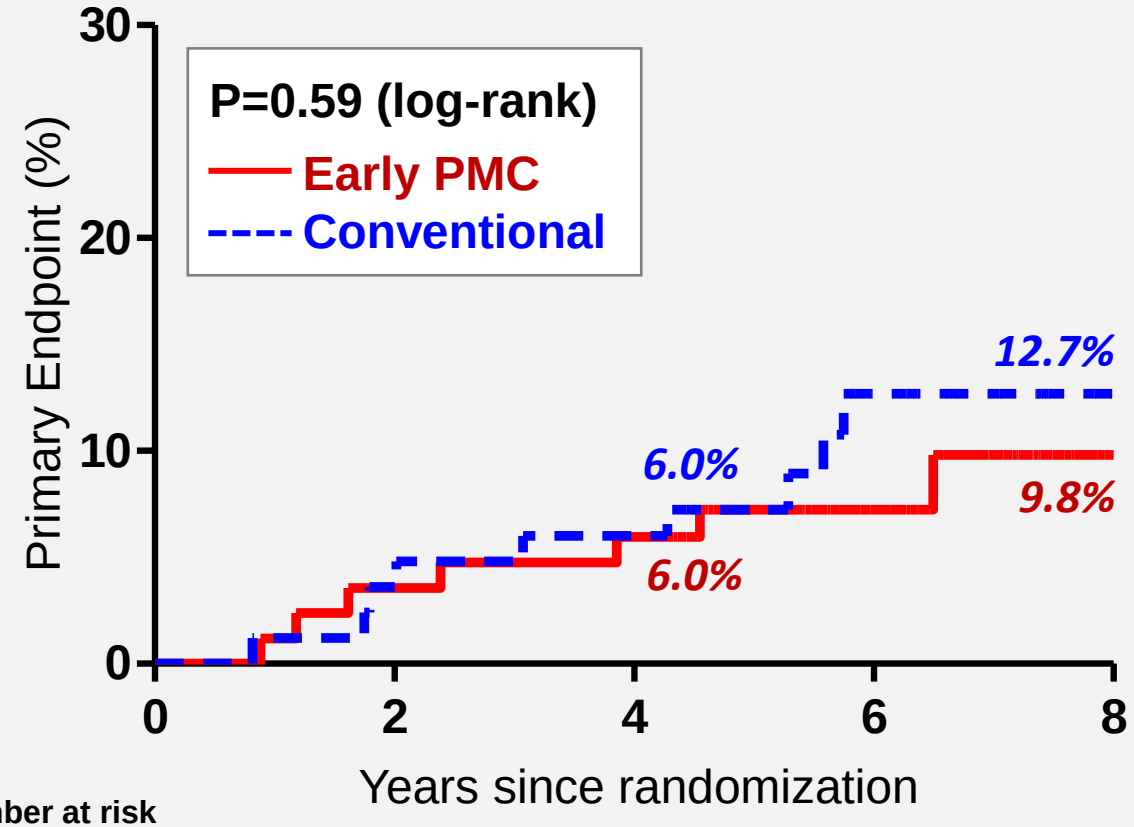
Results: End Points

	Conventional	Early PMC	Hazard ratio	P value
Primary end point	**9 (10.8%)**	**7 (8.3%)**	**0.77** (0.29-2.07)	**0.61**
PMC complications	1 (1.2%)	0 (0%)		
CV mortality	0 (0%)	3 (3.6%)		
Nonfatal stroke	6 (7.2%)	3 (3.6%)		
Thromboembolic events	2 (2.4%)	1 (1.2%)		
Death from any cause	3 (3.6%)	4 (4.8%)	1.30 (0.29-5.77)	0.73
MV replacement	17 (20.5%)	10 (11.9%)	0.59 (0.27-1.29)	0.19

Kang DH, et al. Heart 2021;1980-6.

Results: Primary Analysis

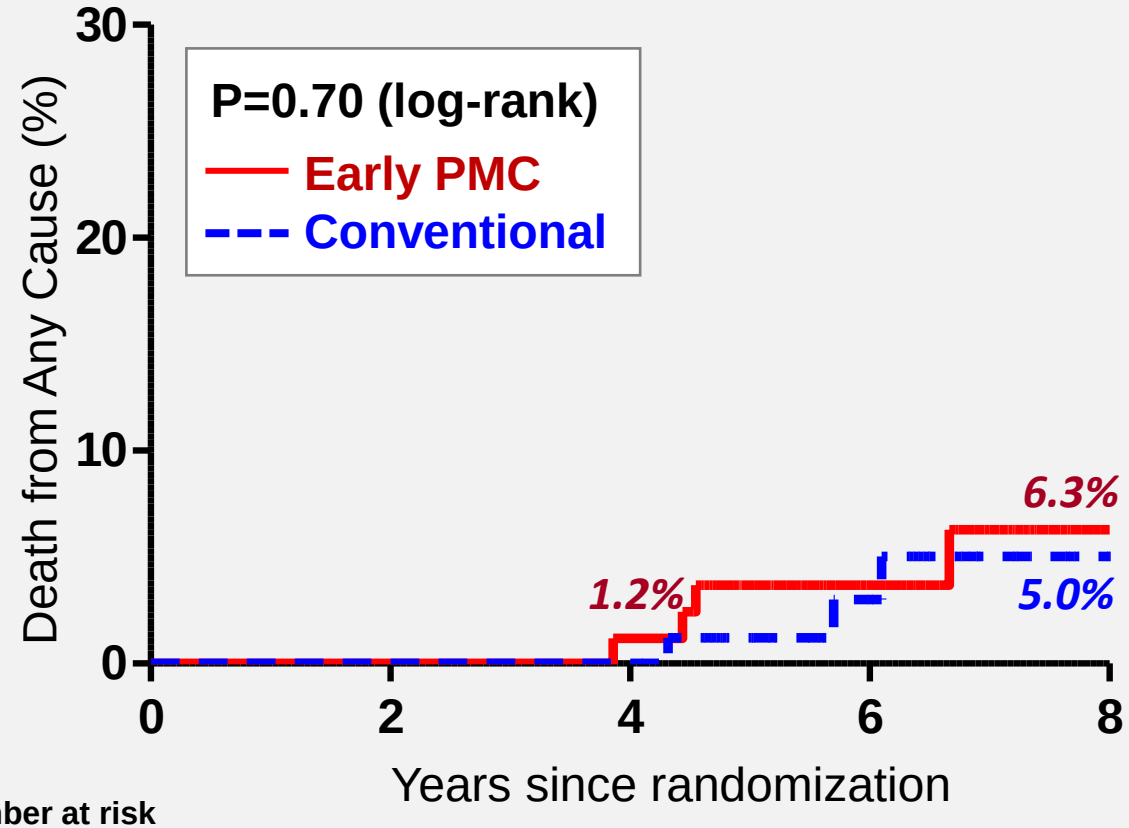
Primary Endpoints



Number at risk

Early PMC	84	81	79	44	7
Conventional	83	80	78	42	8

Death from Any Causes

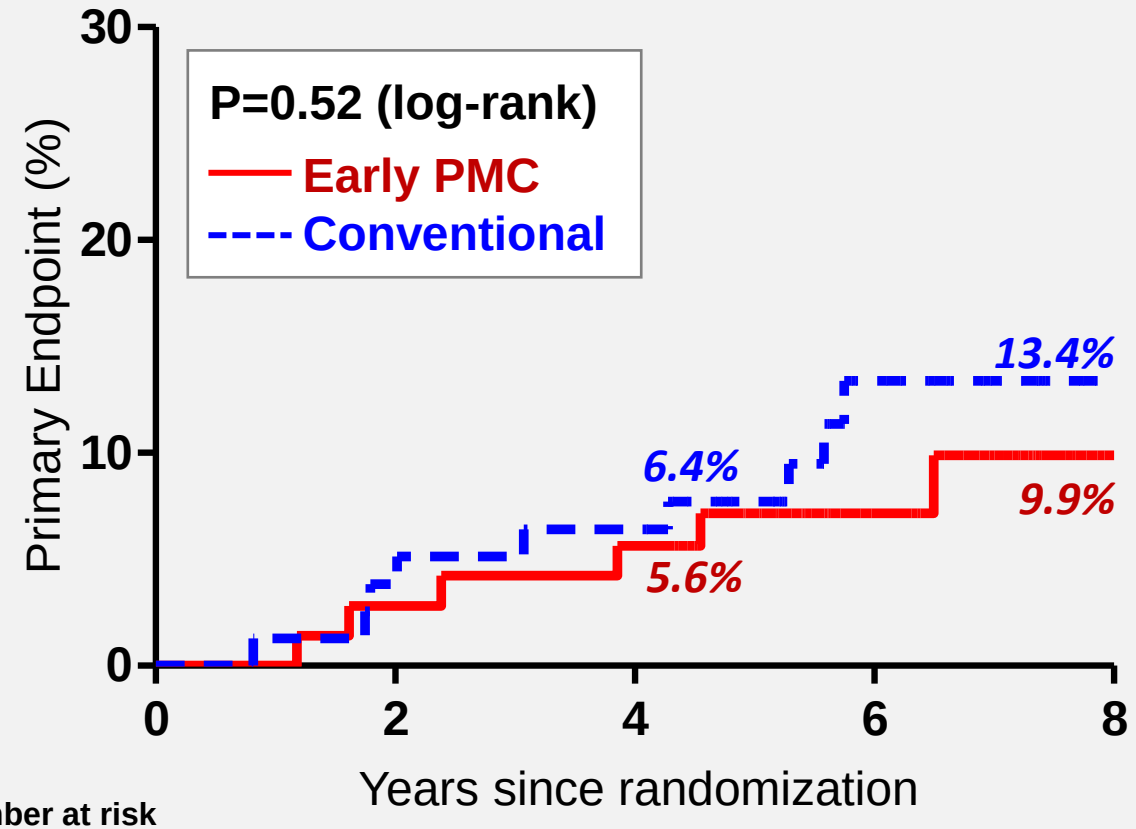


Number at risk

Early Surgery	84	84	83	46	7
Conventional	83	83	83	49	8

Results: Secondary Per-Protocol Analysis

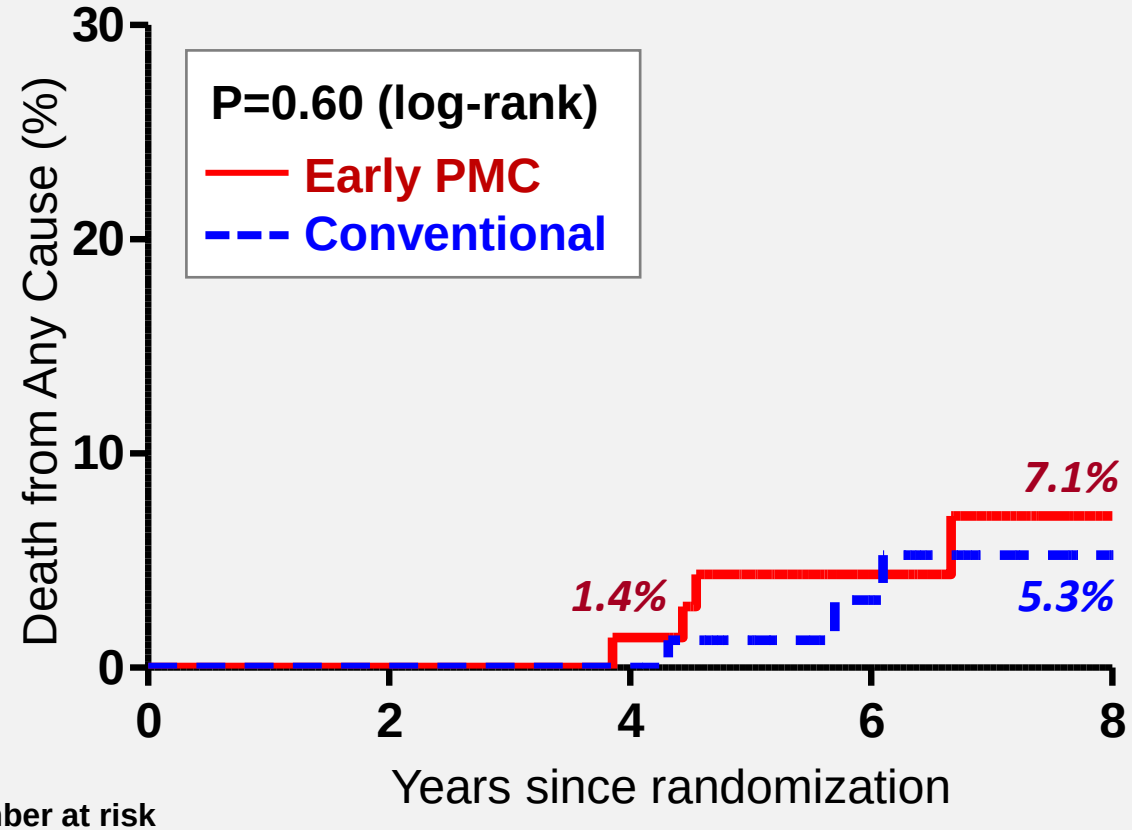
Primary Endpoints



Number at risk

Early PMC	71	69	67	38	7
Conventional	78	75	73	42	8

Death from Any Causes



Number at risk

Early Surgery	71	71	70	40	7
Conventional	78	78	78	47	8

Limitations

- Patients with very severe MS (MVA < 1.0 cm^2), pulmonary hypertension, age >70 years, poor medical condition, or unfavorable MV morphology for PMC were not included
- Cross-over in 11%: Similar results in per-protocol analysis
- Open-label trial

Conclusions

- **Early PMC (vs. conventional management) did not reduce the incidence of the composite of cardiovascular events among asymptomatic patients with severe MS**
- **The MITIGATE trial supports current guidelines emphasizing careful clinical and echocardiographic surveillance in such patients**

Kang DH, et al. Heart 2021;1980-6