Supplementary appendix

Is percutaneous mitral commissurotomy better than surgical commissurotomy for rheumatic mitral stenosis? A systematic review and meta-analysis of randomized controlled trials

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Search strategy

Search Date: 20 February 2018 (updated August 2018)
Database: Embase <1974 to 2018 February 16>, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions(R) <1946 to February 14, 2018>
Search Strategy:

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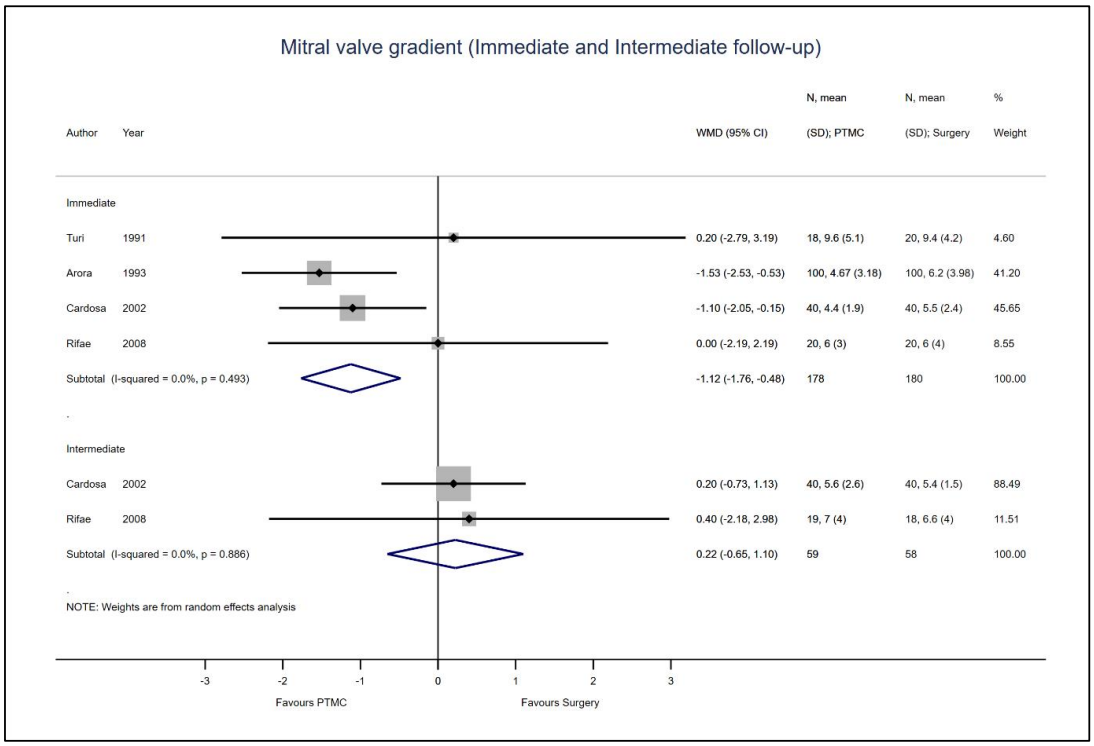
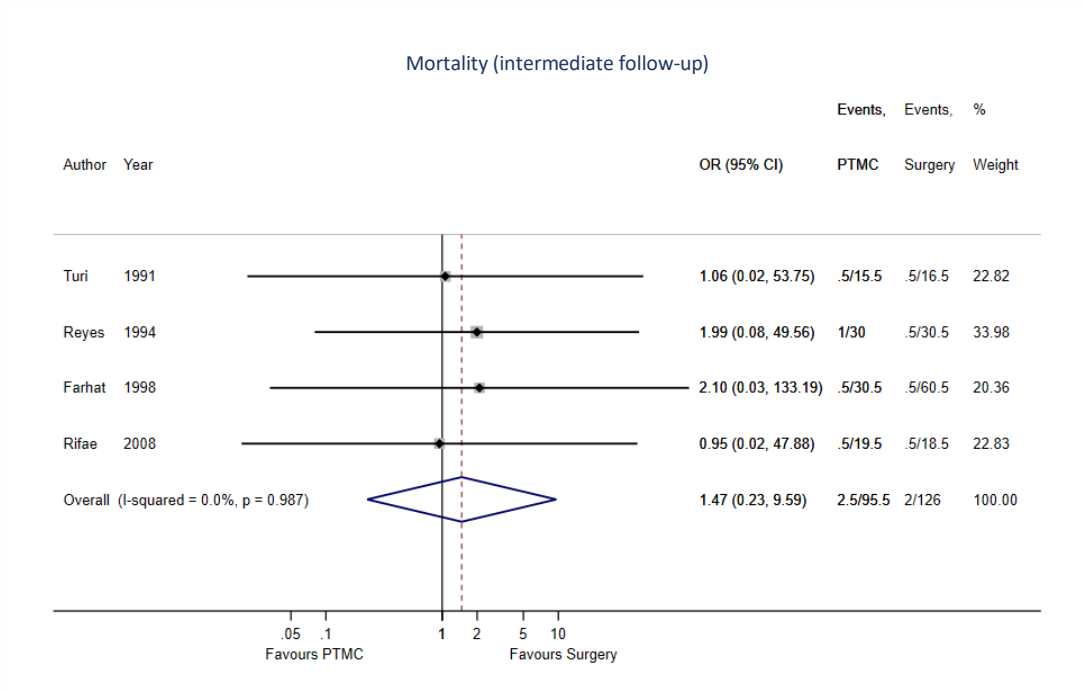
1 randomized*.mp. (1642974)
2 percutaneous mitral valvotomy.mp. (127)
3 balloon mitral valvotomy.mp. (507)
4 balloon mitral valvuloplasty.mp. (1004)
5 percutaneous mitral valvuloplasty.mp. (603)
6 (PTMC or PBMV or BMV).mp. (3365)
7 2 or 3 or 4 or 5 or 6 (4909)
8 randomized*.mp. (213515)
9 1 or 8 (1722809)
10 7 and 9 (154)
11 closed mitral valvotomy.mp. (189)
12 open mitral valvotomy.mp. (53)
13 surgical mitral valvotomy.mp. (15)
14 surgical mitral commissurotomy.mp. (72)
15 11 or 12 or 13 or 14 (325)
16 9 and 15 (12)
17 10 or 16 (160)

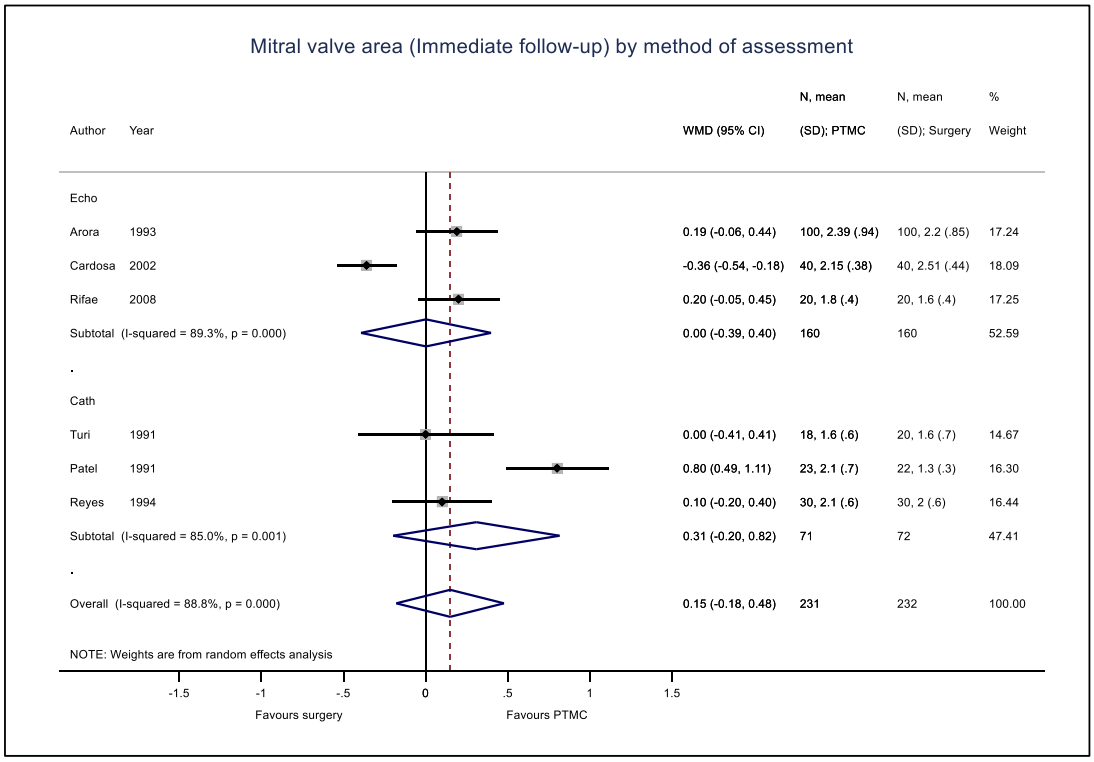
Supplement Figure 1: Mitral valve gradients following the procedures



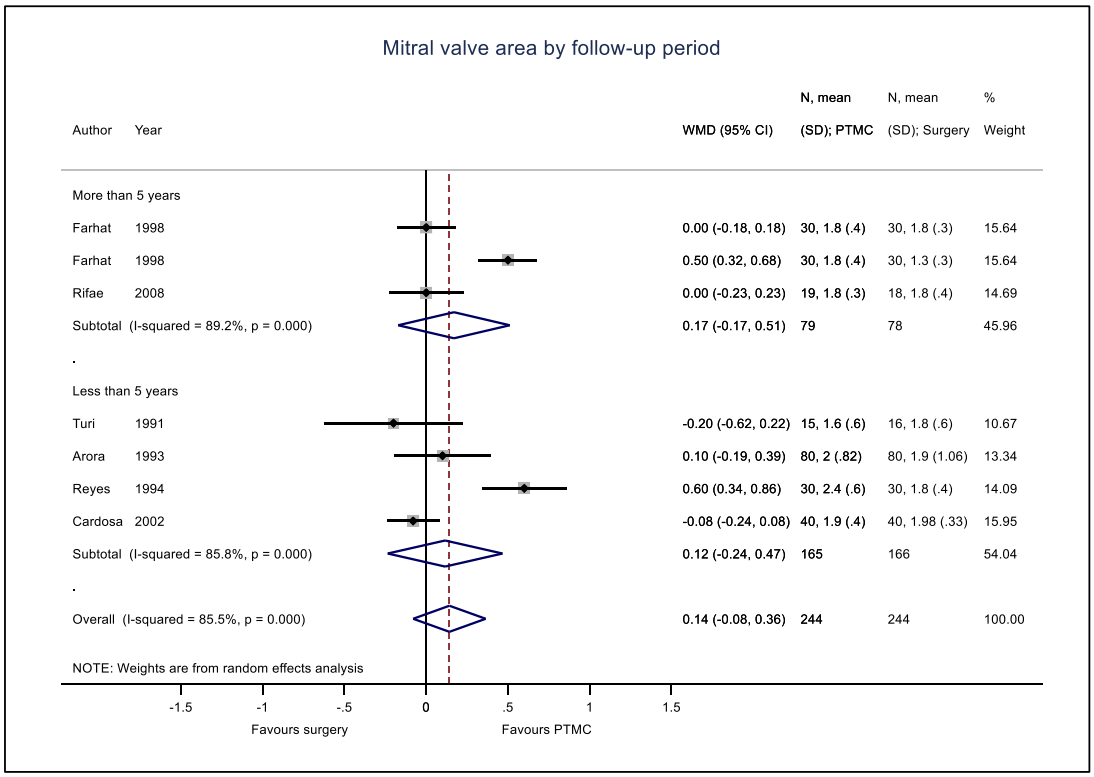
Supplement Figure 2: Mortality following the procedures



Supplement Figure 3: Mitral valve area by method of assessment



Supplement Figure 4: Mitral valve area by the duration of follow-up



Supplement table 1: Risk of bias assessment

Author, Publication year	Outcome	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome*	Selection of the reported result	Overall Bias
Rifaie,2008	MVA/ MVG / MR	Some concerns	Low	Low	Some concerns	Low	Some concerns
	Mortality/ Reintervention	Some concerns	Low	Low	Low	Low	Some concerns
Turi, 1991	MVA/MVG/ MR	Low	Some concerns	Low	Low	Low	Some concerns
	Mortality/ Reintervention	Low	Some concerns	Low	Low	Low	Low
Farhat1998	MVA/MVG/ MR	Low	Low	Low	Low	Low	Low
	Mortality/ Reintervention	Low	Low	Low	Low	Low	Low
Cardoso2002	MVA/ MVG/MR	Some concerns	Low	Some concerns†	Some concerns	Low	Some concerns†
	Mortality/ Reintervention	Some concerns	Low	Some concerns	Low	Low	Some concerns
Patel 1991	MVA/MVG/ MR	Some concerns	Low	Low	Low	Low	Some concerns
	Mortality	Some concerns	Low	Low	Low	Low	Low
Arora 1993	MVA/MVG/MR	Some concerns	Low	Low	Some concerns	Low	Some concerns
	Mortality/ Reintervention	Some concerns	Low	Some concerns‡	Low	Low	Some concerns
Reyes 1994	MVA/MVG/MR	Some concerns	Low	Low	Low	Low	Some concerns
	Mortality/ Reintervention	Some concerns	Low	Low	Low	Low	Some concerns

Abbreviations: MR- Mitral Regurgitation, MVA- Mitral valve area in cm^2, MVG- Mitral Valve gradient in mmHg.

Foot notes: * Unblinded studies using echocardiography for outcome assessment were considered to have some concerns regarding underlying bias. Mortality and the need for reinterventions would not be influenced by subjectivity of the outcomes assessors and were considered not to be associated with any concerns regarding assessment. †- No mention of loss to follow-up. Though the results indicate no loss to follow-up patients.

‡- Significant loss to follow-up patients (20% in each arm) led to some concerns of bias.

Supplement table 2: GRADE Evidence profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Percutaneous Mitral commissurotomy**	**Surgical commissurotomy**	**Relative (95% CI)**	**Absolute Risk Difference (95% CI)**		
Symptoms and heart failure due to mitral stenosis as inferred from immediate post-procedure mitral valve area (MVA immediate), by echocardiography or cardiac catheterization												
6	randomised trials	not serious	serious	serious	serious	none	231	232	-	The mean immediate Mitral Valve Area (cm^2) in the intervention group was 0.15 higher (0.18 lower to 0.48 higher)	⊕◯◯◯ VERY LOW[a]	CRITICAL
Symptoms and heart failure due to mitral stenosis as inferred from mitral valve area (MVA intermediate term) at 30 months, by echocardiography or cardiac catheterization												
6	randomised trials	not serious	serious	serious	serious	none	214	244	-	The mean intermediate term- Mitral Valve Area (cm^2) was 0.13 higher with PTMC (0.09 lower to 0.35 higher)	⊕◯◯◯ VERY LOW[a]	CRITICAL
Severe Mitral Regurgitation Immediately after the procedure (Severe MR-immediate), by echocardiography or cardiac catheterization												
5	randomised trials	not serious	not serious	not serious	serious	none	5/121 (4.1%)	2/152 (1.3%)	**RR 2.12** (0.50 to 8.92)	**3 per 100 more with PTMC** (Fewer than 1 per 100 to 10 more per 100)	⊕⊕⊕◯ MODERATE[b]	CRITICAL
Residual symptoms as inferred from the presence of non-severe mitral regurgitation immediately after the procedure (MR- Immediate), by echocardiography or cardiac catheterization												
6	randomised trials	not serious	not serious	serious	Serious	None	35/221 (15.8%)	36/252 (14.3%)	**RR 1.16** (0.75 to 1.81)	**2 per 100 more with PTMC** (Fewer than 4 per 100 to 12 more per 100)	⊕⊕◯◯ LOW[c]	IMPORTANT
Residual symptoms as inferred from the presence of non-severe mitral regurgitation at 30 months follow-up (MR: intermediate term), by echocardiography or cardiac catheterization												
3	randomised trials	not serious	not serious	serious	serious	none	5/79 (6.3%)	10/108 (9.3%)	**RR 0.83** (0.29 to 2.34)	**3 per 100 fewer with PTMC** (Fewer than per 100 to 12 more per 100)	⊕⊕◯◯ LOW[c]	IMPORTANT
Symptoms and heart failure due to mitral stenosis as inferred from mitral restenosis (Restenosis), by echocardiography or cardiac catheterization												

3	randomised trials	not serious	not serious	serious	serious	none	10/79 (12.7%)	22/108 (20.4%)	**RR 0.66** (0.32 to 1.37)	**8 per 100 fewer with PTMC** (Fewer than 14 per 100 to 8 more per 100)	⊕⊕◯◯ LOW[c]	IMPORTANT
Mitral Re-intervention (**Re-intervention)**												
2	randomised trials	not serious	not serious	not serious	serious	none	5/60 (8.3%)	21/90 (23.3%)	**RR 0.42** (0.13 to 1.34)	**15 per 100 fewer with PTMC** (Fewer than 20 per 100 to 8 more per 100)	⊕⊕⊕◯ MODERATE[d]	CRITICAL

a. Rated down for serious imprecision considering the wide confidence interval which overlaps no effect and fails to rule out important benefit or harm; for serious inconsistency due to the high statistical heterogeneity (I^2 >50%), and for indirectness as MVA is a surrogate marker for improvement in symptoms and heart failure.
b. Rated down for serious imprecision considering the wide confidence interval which overlaps no effect..
c. Rated down for serious imprecision as the wide confidence interval fails to rule out important benefits or harm, and for indirectness as MR is a surrogate for lack of improvement or worsening of symptoms and heart failure
d. Rated down for serious imprecision as the wide confidence interval fails to rule out important benefits or harm