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A review of comparative studies of MitraClip versus surgical repair for mitral regurgitation

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ABSTRACT

Objectives: We summarized comparative studies of MitraClip versus surgical repair for mitral regurgitation (MR) with a systematic literature search and meta-analytic estimates.
Methods: MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through June 2016. Eligible studies were randomized controlled or observational comparative studies of MitraClip versus surgical repair enrolling patients with MR and reporting early (30-day or in-hospital) or late (≥6-month including early) all-cause mortality. For each study, data regarding all-cause mortality and incidence of recurrent >2+ MR in both groups were used to generate odds ratios (ORs). Alternatively, ORs or hazard ratios (HRs) for mortality and recurrent MR themselves were directly abstracted from each study.
Results: Eight reports of 7 studies comparing MitraClip with surgical repair enrolling a total of 1015 patients with MR were identified and included. Pooled analyses demonstrated significantly higher age and logistic European System of Cardiac Operative Risk Evaluation and significantly lower ejection fraction in the MitraClip than surgical repair group, no significant difference in rate of women and patients with New York Heart Association functional class of >II, no statistically significant difference in early- (OR, 0.54; $p = 0.08$) and late-mortality (HR/OR, 1.17; $p = 0.46$), and significantly higher incidence of recurrent MR in the MitraClip than surgical repair group (HR/OR, 4.80; $p < 0.00001$).
Conclusions: In patients with MR, the MitraClip procedure achieves similar survival to surgical MV repair despite higher risk profiles. Recurrent MR, however, occurs more frequently (4.8-fold) after the MitraClip than surgical repair.

1. Introduction

An approximately half number of patients with severe mitral regurgitation (MR) are not treated because of high age, reduced left ventricular function, co-morbidities, or other contraindications to open mitral valve (MV) surgery [1], and accordingly less invasive percutaneous transcatheter MV repair procedures have been developed [2]. The MitraClip-System (Abbott Vascular-Structural Heart, Menlo Park, CA) is an approved system for transcatheter repair, with which both MV leaflets are attached with one or more clips, resulting in a so-called "double-orifice MV" [2]. In high-risk, elderly patients mainly affected by functional MR, the MitraClip procedure is effective with low rates of hospital mortality and adverse events [3]. MitraClip represents an efficacious strategy for patients with heart failure and severe MR and offers a significant improvement in functional class and in cardiac remodeling in patients with severely dilated hearts as well [4]. A number of studies have compared the outcomes of MitraClip with those of surgical repair. We summarized comparative studies of MitraClip versus surgical repair for MR with a systematic literature search and meta-analytic estimates in the present article.

Abbreviations: CI, confidence interval; EF, ejection fraction; EuroSCORE, European System of Cardiac Operative Risk Evaluation; EVEREST, Endovascular Valve Edge-to-Edge Repair Study; HR, hazard ratio; MD, mean difference; MR, mitral regurgitation; MV, mitral valve; OR, odds ratio; NYHA, New York Heart Association; RCT, randomized controlled trial; RD, risk (rate) difference.

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2. Methods

2.1. Search strategy

All studies, including randomized controlled trials (RCTs) and observational comparative studies, of MitraClip versus surgical MV repair enrolling patients with MR were identified using 2-level strategy. First, databases including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials were searched through June 2016 using Web-based search engines (PubMed and OVID). Second, relevant studies were identified through a manual

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search of secondary sources including references of initially identified articles and a search of reviews and commentaries. Search terms included *mitral*; *regurgitation* or *insufficiency*; *MitraClip*, *clip*, *clipping*, *catheter*, *transcatheter*, *percutaneous*, or *edge-to-edge*; *repair* or *reconstruction*; *replacement*, *surgery*, *surgical*, *open*, *operation*, or *operative*; and *comparison*, *compared*, *comparative*, *propensity*, *randomized*, *randomized*, or *randomization*.

2.2. Study selection and data abstraction

Studies considered for inclusion met the following criteria: the design was a RCT or observational comparative study: the study population was patients with MR; patients were assigned to MitraClip versus surgical repair; and main outcomes included early (30-day or in-hospital) or late (≥6-month including early) all-cause mortality. Data regarding detailed inclusion criteria, baseline patient profiles, duration of follow-up, all-cause mortality, and incidence of recurrent MR of >2+ (≥3+) were abstracted (as available) from each individual study.

2.3. Statistical analysis

We conducted a meta-analysis of summary statistics from the individual studies. For each study, we generated (1) mean differences (MDs) and 95% confidence intervals (CIs) using means (with standard deviations) of age, ejection fraction (EF), and logistic European System of Cardiac Operative Risk Evaluation (EuroSCORE) in both the MitraClip and surgical repair groups and (2) risk (rate) differences (RDs) using rates of women and patients with New York Heart Association (NYHA) functional class of >II (≥III) in both groups. Data regarding all-cause mortality and incidence of recurrent >2+ (≥3+) MR in both groups were used to generate odds ratios (ORs). Alternatively, ORs or hazard ratios (HRs) for mortality and recurrent MR themselves were directly abstracted from each study. For a study without an available HR, a HR was calculated from Kaplan–Meier curve or summary data using the methods by Parmar et al. [5] and Williamson et al. [6]. Study-specific estimates (preferentially adjusted estimates) were combined using the random-effects model. All analyses were conducted using Review Manager version 5.3 (available from http://tech.cochrane.org/revman).

3. Results

3.1. Search results

Of 212 potentially relevant articles screened initially, 8 reports [7–14] of 7 studies comparing MitraClip with surgical MV repair enrolling a total of 1015 patients with MR were identified and included. Only one study was a RCT, the Endovascular Valve Edge-to-Edge Repair Study (EVEREST) II [10,11], whereas the others [7–9,12–14] were observational comparative studies (Table 1). One study [7] exclusively included > 80-year patients. One study [7] exclusively enrolled patients with degenerative MR and 3 studies [8,9,14] exclusively included those with functional MR, whereas 3 studies [10,11,12,13] enrolled both those with functional MR and those with degenerative MR. The late follow-up duration was from 180 days [8] to 5 years [11,14].

3.2. Patient profiles

3.2.1. Age

In all but one study (EVEREST II [10,11]), mean age was significantly higher in the MitraClip than surgical repair group (Table 1). A pooled analysis demonstrated significantly higher age in the MitraClip than surgical repair group (pooled MD, 5.6 years; 95% CI, 2.8 to 8.4 years; $p < 0.0001$; Supplemental Fig. S1).

3.2.2. Women

In 2 studies [8,13], rate of women was significantly lower in the MitraClip than surgical repair group (Table 2). A pooled analysis indicated no significant difference in rate of women between the MitraClip and surgical repair groups (pooled RD, −1.5%; 95% CI, −13.4% to 10.4%; $p = 0.81$; Supplemental Fig. S2).

3.2.3. NYHA functional class

In 3 studies [7,8,14], rate of patients with NYHA functional class of >II (≥III) was significantly higher in the MitraClip than surgical repair group (Table 2). A pooled analysis demonstrated no significant difference in rate of patients with >II class between the MitraClip and surgical repair groups (pooled RD, 5.3%; 95% CI, −2.2% to 12.9%; $p = 0.17$; Supplemental Fig. S3).

Table 1
Study design.

Study	Inclusion criterion	Surgical procedure	Patient number			MR Etiology	MC	SR	p	Follow-up		Age (year)		
			MC	SR	Total					Early	Late	MC	SR	p
Buzzatti 2015 [7]	>80 years; isolated degenerative MR	Repair or replacement	25	35	60	Degenerative				30 days	3 years	84.5 ± 3.2	81.9 ± 2.0	<0.01
Conradi 2013 [8]	Pure secondary MR	Repair	95	76	171	Secondary (functional)				30 days	180 days	72.4 ± 8.1	64.5 ± 11.4	<0.001
De Bonis 2016 [9]	Severe or moderately severe secondary MR	Repair with the edge-to-edge technique combined with annuloplasty	55	65	120	Secondary (functional)				Hospital	4 years	68.3 ± 9.17	63.2 ± 10.05	0.005
EVEREST II (Feldman 2011 [10], Feldman 2015 [11])	Chronic MR ≥3+	Repair or replacement	184	95	279	Functional	26.6	27.4	0.81	30 days	5 years	67.3 ± 12.8	65.7 ± 12.9	0.32
						Degenerative	66.7	72.6						
Paranskaya 2013 [12]	EuroSCORE <20%; EF ≥45%; MR ≥3+	Repair	24	26	50	Functional	33.3	26.9	0.62	30 days	1 year	80 ± 5	63 ± 12	<0.001
						Degenerative/mixed	66.7	73.1						
Swaans 2014 [13]	Symptomatic MR ≥3+	Repair or replacement	139	53	192	Functional	77.0	58.5	N/A	N/A	3 years	74.6 ± 9.4	70.2 ± 9.5	N/A
						Degenerative	18.0	32.1						
						Mixed	5.0	9.4						
Taramasso 2012 [14]	Symptomatic MR ≥3+	Undersized annuloplasty with a complete ring, rigid or semirigid	52	91	143	Functional				Hospital	5 years	68.4 ± 9.2	64.9 ± 9.8	0.04
Total							574	441	1015			MD, 5.6 [2.8, 8.4]*		<0.0001

EVEREST = Endovascular Valve Edge-to-Edge Repair Study; EF = ejection fraction; MC = MitraClip; MD = Mean difference; MR = mitral regurgitation; N/A = not available; SR = surgical repair.
* Point estimate [95% confidence interval].