Systematic Review

Early and late outcomes of mitral valve surgery in the setting of mitral annular calcification: a systematic review with narrative synthesis

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Background: Mitral annular calcification (MAC) is a degenerative calcific pathology of the mitral valve (MV) associated with MV dysfunction and poor patient outcomes. The pathophysiologic complexity of MAC presents unique challenges for surgical management. In this systematic review, we summarize the heterogenous approaches to MV surgery for MAC and assess early and late outcomes of each approach.

Methods: A systematic literature search was performed in the PubMed, EMBASE, and Web of Science databases. Three reviewers independently selected relevant studies through a sequential three-step review process. Based on included descriptions of intraoperative methods, each study was categorized as either a "MAC Respect" or "MAC Resect" intervention. Quantitative data were collected, aggregated across all studies, and analyzed by surgical approach.

Results: Our initial search yielded 635 unique studies, of which 19 studies met inclusion criteria for quantitative data extraction. Based on the operative approach, two cohorts of "MAC Respect" (N=550) and "MAC Resect" (N=487) were created. Baseline characteristics were similar; the median patient age and proportion of female patients were 71.5 years and 66.4% in the "Respect" group and 70.3 years and 54.9% in the "Resect" group, respectively. A median of 26.9% of patients in the "Resect" group and 12.5% in the "Resect" group were classified as New York Heart Association (NYHA) class III or IV. "Respect" studies had a median cardiopulmonary bypass time of 156 minutes, while "Resect" studies had a median time of 181.5 minutes. The median intensive care unit stay was two days for the "Respect" group and 3.5 days for the "Resect" group. Ranges of complication rates largely overlapped between groups. Thirty-day, one-year, and long-term mortality rates were 0–25%, 0–44%, and 0–27% in the "Respect" group and 0–14%, 0–18%, and 0–50% in the "Resect" group.

Conclusions: Surgical intervention remains the gold-standard for management of MAC-related MV dysfunction; however, there is no standardized consensus for the optimal surgical approach. This systematic review evaluates the advantages, disadvantages, and outcomes of several approaches to MAC surgical intervention. Our findings underscore the heterogeneous presentation of MAC and the associated complications to avoid in order to improve patient outcomes.

Keywords: Mitral surgery; annular calcification; annular reconstruction

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Introduction

Mitral annular calcification (MAC) is a millennia-old degenerative disease process, identified in two ancient Egyptian mummies by Allam *et al.* in 2011 (1). MAC was first reported in the modern literature by Bonninger *et al.* (2), yet in over a century since that first report, MAC remains a prevalent issue in mitral valve (MV) surgery with significant morbidity and mortality. Prevalence of MAC has been estimated at 8% to 42% depending on the study population (3). In a recent analysis of all adults undergoing echocardiography at a single center in one year, MAC was present in 23%, and prevalence of MAC in a subset of the Framingham Heart Study population was reported at 14% (4,5). Age, female gender, and atherosclerotic risk factors such as hypertension, hyperlipidemia, diabetes, and obesity have been associated with MAC (3-8).

The pathophysiology of MAC remains incompletely understood. Initially hypothesized to be an age-related degenerative process, newer studies suggest that other potential mechanisms could include atherosclerosis, increased MV stress due to aortic stenosis or hypertension, or dysregulated calcium-phosphate handling in chronic kidney disease (CKD) (9). MV dysfunction (stenosis, regurgitation, or mixed valvular disease) is present in a minority of patients with MAC; however, MAC alone is linked to poorer cardiovascular outcomes, and MAC-related MV dysfunction is associated with worse prognosis compared to other etiologies of MV disease (10).

Surgical management of MV dysfunction is particularly challenging in the setting of MAC, and there is a lack of consensus regarding the best approach. In this review, we aim to summarize the predominant techniques used today, and we evaluate early and late outcomes of these approaches.

Methods

Literature search strategy

We performed a systematic search in PubMed, EMBASE, and Web of Science databases using a query incorporating both MeSH and free text terms (Table S1). Our initial search yielded an initial cohort of 635 references, including both full-text articles and abstracts, published from December 1964 to April 2025. The study was registered in PROSPERO under CRD420251087629 on July 14, 2025, available at https://www.crd.york.ac.uk/PROSPERO/view/CRD420251087629.

Eligibility criteria

We excluded single case reports, systematic reviews or meta-analyses, and non-English studies. We also excluded any studies on non-human or pediatric cohorts, studies including non-surgical MV interventions, studies that did not examine an independent cohort of patients with MAC, and any studies that did not report post-intervention outcomes.

Three reviewers (A.A., C.A.S., J.T.W.) independently reviewed abstracts and full text articles according to these exclusion criteria. Conflicts on study agreement were resolved through a majority vote by all three reviewers. The process of study inclusion and review is documented in *Figure 1*.

Data extraction and critical appraisal

After isolation of the appropriate articles, three reviewers (A.A., C.A.S., J.T.W.) independently extracted data from each study. Extracted quantitative variables included parameters of study design, demographics of study cohorts, operative parameters, and short- or long-term postoperative outcomes. Extracted qualitative variables included study-specific definitions of postoperative outcomes or complications, and descriptions of intraoperative methods.

For studies that compared two separate patient cohorts in relation to MAC surgical interventions, the Newcastle-Ottawa score was used to evaluate the validity and quality of each study's methodology (11). The Newcastle-Ottawa score evaluates three domains of cohort selection (external validity), inter-cohort comparability (internal validity), and assessment or reporting of outcomes. When evaluating outcomes, reviewers graded studies based on both postoperative and long-term mortality endpoints, to maintain parity with the data extracted for this systematic review. Individual case series were not eligible for Newcastle-Ottawa evaluation and were excluded from quality assessment analysis.

Study coding

Incidence of postoperative complications was aggregated into categories of pulmonary, infectious, cardiovascular, hematological, cerebrovascular, and genitourinary/renal complications based on qualitative assessment of the definitions documented in each study (Table S2). All three reviewers also categorized the intraoperative methods documented in each study against a general framework of

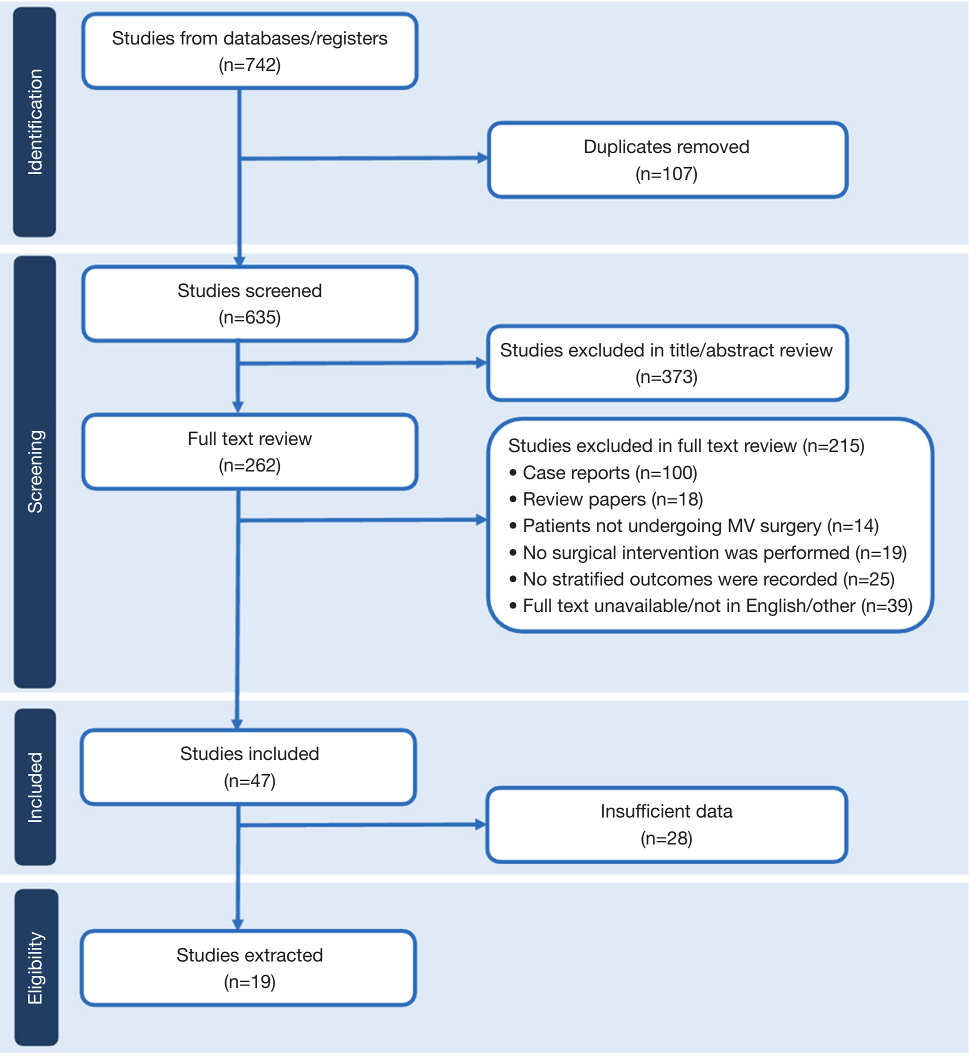

Figure 1 PRISMA flow diagram. MV, mitral valve; PRISMA diagram demonstrating the number of references reviewed and excluded based on the criteria explained in the Methods section.

"MAC Respect" or "MAC Resect".

"MAC Respect" studies included operative approaches where the MAC bar did not undergo systematic resection, and the intraoperative approach maximally preserved the integrity of the annulus. Under "MAC Respect", we defined three methodological subcategories: calcium-avoidant suturing techniques, minimal/partial decalcification techniques, and hybrid transcatheter MV replacement.

Under "MAC Resect", we defined five methodological subcategories: *en-bloc* decalcification/resection of the whole calcium bar, partial decalcification/resection, and method of atrioventricular groove reconstruction using either primary repair, a pericardial patch (autologous or bovine) or a polytetrafluoroethylene (Teflon) strip.

For secondary analyses, reviewers classified studies based on intervention type between "MV Replacement" and "MV Repair". Reviewers also identified and analyzed a subset of studies that utilized ultrasonic decalcification (CUSA), and a subset of studies that did not reconstruct the annulus after decalcification/debridement. A graphical representation of the categorization scheme used by the reviewers is provided in *Figure 2*. Conflicts in classification of operative methodologies were resolved through a majority vote between all three reviewers.

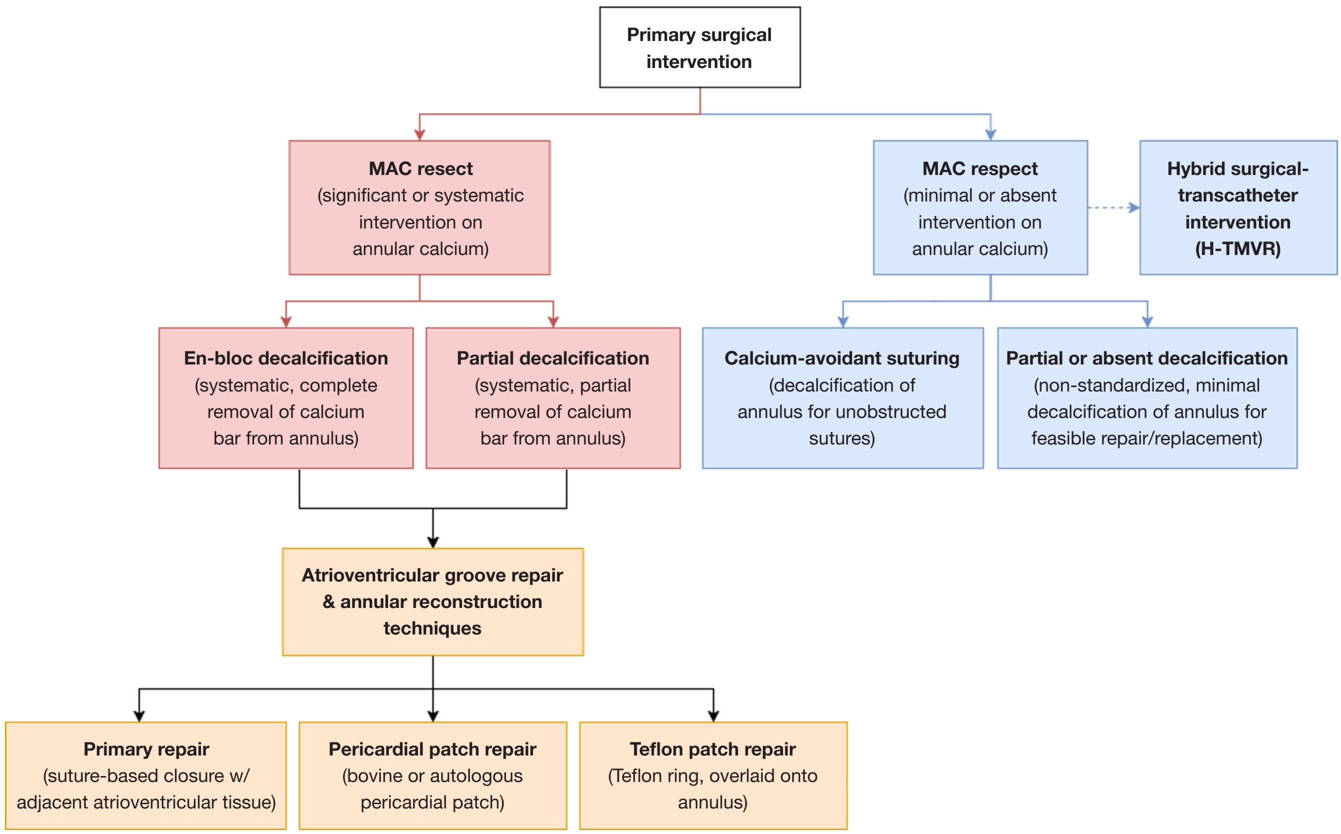

Figure 2 Flowchart representation of the categorization scheme used by the reviewers to evaluate methods of intraoperative MAC management. MAC, mitral annular calcification.

Statistical analysis

Quantitative variables from each study were initially analyzed as individual patient counts, with manual extraction of statistics from case series when necessary. Quantitative variables were subsequently presented as median and range, stratified by category of operative method. Due to heterogeneous methods and modalities of data reporting, statistical significance for inter-cohort differences could not be directly addressed; we qualitatively evaluated the clinical significance of differences in each endpoint through aggregated median and range. Long-term postoperative outcomes of mortality or reoperation due to recurrent MV pathology were manually extracted from each study, and recorded into time intervals of 30 days, 1 year, and 5 years.

Results

Eligible studies & study characteristics

The initial database search yielded 742 studies: 107 duplicates were removed, and 373 studies were excluded during title and abstract review; 262 studies underwent full text review, after which 215 articles were excluded for the following reasons: case reports (n=100), patients were not undergoing MV surgery (n=14), no surgical intervention was performed (n=19), no stratified outcomes were recorded (n=25), review papers (n=18), full text unavailable/not in English/other (n=39). Forty-seven studies remained, and 19 studies (12-30) had sufficient data to extract for this analysis (*Figure 1*).

Table 1 summarizes the characteristics of all the studies that were included in our review. Study publication date ranged from 1986 to 2023. There were 16 observational prospective studies (12-25,27,30) and three observational retrospective studies (26,28,29). Study populations ranged from six patients (12) to 500 patients (15). Demographic variables for total population of all studies: age, female gender, and comorbidities (hypertension, diabetes, cardiovascular disease, myocardial infarction) were also recorded.

During the review process, it was not possible to

Table 1 Characteristics of included studies and preoperative patient characteristics

Intervention category	Reference	Intervention description	Age[†], years	Male sex[‡]	BMI[§], kg/m^2	Hypertension[‡]	Dyslipidemia[‡]	Diabetes[‡]	Arrhythmia[‡]	Endocarditis[‡]	NYHA class I–II[‡]	NYHA class III–IV[‡]	CKD[‡]	Mortality risk[§]
MAC respect, replacement	(12)	Hybrid TAVI, SAPIEN 3	76 [9]	0 [0]	29 [4.5]						0 [0]	6 [100]	5 [83.3]	5.7 [1.9], EuroScore II
MAC resect, replacement	(13)	Partial decalcification w/ CUSA, pericardial patch repair	73 [8]	2 [13.3]		13 [86.7]	8 [53.3]	3 [20]	5 [33.3]	2 [13.3]			4 [26.7]	
MAC resect, repair	(14)	*En bloc*, primary closure	[11–78]	12 [100]					2 [16.7]		6 [50]	6 [50]		
MAC resect, repair	(15)	*En bloc*, pericardial patch repair 3 [0], primary closure [11] *vs.* non-MAC repair	Women 65 (IQR, 57–72), men 61 (IQR, 52–68)	318 [63.6]	BMI >30: 82 [16.4]			29 [5.8]	139 [27.8]					
MAC resect, replacement	(16)	Partial decalcification, pericardial patch repair	69 [12]	44 [37]		85 [72]	76 [60]	35 [30]	16 [14]		44 [37]	74 [63]	38 [32]	
Non-MAC replacement	(16)	Non-MAC replacement	70 [11]	53 [45]		81 [69]	71 [60]	39 [33]	13 [11]		54 [46]	64 [53]	32 [27]	
MAC resect, repair	(17)	*En bloc*, primary leaflet repair	[61–81]	13 [93]					6 [43]		2 [14]	12 [86]		
MAC respect, replacement	(18)	Partial decalcification	73 [6]	1 [7]				4 [27]	6 [40]					
MAC respect, replacement	(18)	Partial decalcification with CUSA	67 [13]	50 [30]				64 [39]	46 [28]					
MAC respect, repair	(19)	*En bloc*, pericardial patch repair	69.7 [11.8]	9 [64]					7 [50]					
MAC respect, repair	(19)	Partial decalcification, no annular reconstruction	78.5 [6.7]	11 [85]					5 [38]					
MAC respect, repair	(20)	Repair no annular decalcification	49.2 [33–69]	14 [23]					47 [78.3]		33 [36.7]	38 [63.3]		
MAC respect, replacement	(20)	Replace no annular decalcification	51.6 [30–68]	31 [41.3]					61 [81.3]		11 [14.7]	64 [85.3]		
MAC resect, replacement	(21)	Resect partial decalcification, no annular reconstruction	70.9 [10.7]	19 [34]							17 [30.4]	39 [69.6]		4.1, STS score
MAC respect, replacement	(21)	Respect hybrid TAVI, SAPIEN 3	73.9 [11.3]	3 [19]							4 [25]	12 [75]		4.7, STS score
MAC resect, repair	(22)	Partial decalcification, no annular reconstruction	62.3 [13–83]											
MAC resect, replacement	(23)	Partial decalcification, Teflon repair	75 [18]	5 [25]		15 [75]		5 [25]					7 [35]	
MAC Resect, replacement	(24)	*En bloc* w/ CUSA, pericardial patch repair	72.2 [13.6]	4 [66.7]		1 [16.7]			1 [16.7]	1 [16.7]			2 [33.3]	
MAC resect, replacement	(25)	Resect *en bloc*, Teflon repair	71.5 [11]	3 [50]							0 [0]	6 [100]		
MAC respect, replacement	(25)	Respect Drill suture, suture through, Teflon coil	66.4 [10.6]	2 [18]							0 [0]	11 [100]		
MAC resect, repair	(31)	*En bloc*, autologous pericardial patch repair	[36–79]	16 [43]					26 [70.3]		0 [0]	37 [100]		
MAC respect, replacement	(26)	Doublelayer calcium avoidant sutures	68.5 [7.3]	4 [40]		5 [50]	0 [0]	2 [20]			1 [10]	9 [90]	0 [0]	5.1 [2.9]
MAC respect, replacement	(26)	Singlelayer calcium avoidant sutures	67.1 [5.9]	7 [35]		9 [45]	4 [20]	5 [25]			15 [75]	5 [25]	2 [10]	4.1 [2.3]
MAC resect, replacement	(27)	Replace *en bloc* w/ CUSA	69.4 [10.1]	17 [30]				13 [22.8]	21 [37]	3 [5.3]	37 [64.9]	20 [35]	14 [25.6]	6.6 [6.7]
MAC resect, repair	(27)	Repair *en bloc* w/ CUSA, pericardial patch repair	78 [11.2]	1 [25]				0 [0]	0 [0]	0 [0]	4 [100]	0 [0]	0 [0]	8.4 [7.9]
Non-MAC replacement	(28)	Non-MAC replacement	62.8 [14.3]	180 [47]	28.1 [6]	224 [58.8]	260 [68.2]	588 [15.2]					12 [3.2]	
MAC respect, replacement	(28)	Calcium-avoidant sutures	69.9 [11.8]	37 [32]	28.1 [7.4]	75 [65.2]	84 [73]	31 [27]					17 [14.8]	
MAC respect, replacement	(29)	Calcium-avoidant sutures	75.2 [9.2]	16 [36]	26.9 [5.1]	17 [37.8]	23 [51.1]	8 [17.8]	27 [60]		21 [47]	24 [53]		8.8 [7.2]

[†], mean [SD]/[range]; [‡], n (%); [§], mean [SD]. BMI, body mass index; CKD, chronic kidney disease; CUSA, cavitron ultrasonic surgical aspirator; IQR, interquartile range; NYHA, New York Heart Association; SD, standard deviation; TAVI, transcatheter aortic valve implantation.

differentiate between MAC in the setting of myxomatous MV degeneration *vs.* MAC in non-myxomatous setting, and therefore the studies included are comprised of patients with MAC and MV dysfunction, without specifying the nature of MV disease.

A total of 10 studies were eligible for quality assessment by the Newcastle-Ottawa Cohort Study criterion, as they were structured as single-cohort observational studies. Our specific approach to the Newcastle-Ottawa evaluation criterion assessed outcome quality in both postoperative complications and long-term mortality, leading to a maximum score of 12 points. Results of our evaluation are documented in *Table 2*. With the exception of one observational prospective study (Mills *et al.*), all studies scored six points or above, suggesting that the quality of evidence examined in this study is relatively robust.

MAC respect *vs.* MAC resect

Table 3 describes the aggregate characteristics, comorbidities, complications and outcomes of the studies grouped into "MAC Respect" (12,18-21,25,26,28,29) or "MAC Resect" (13-17,19,21-25,27,30) categories. The "MAC Respect" studies had a total of 550 participants and the "MAC Resect" studies had a total of 487 study participants. The median age was 71.5 years (range, 66.4–78.5 years) in the "Respect" group and 70.3 years (range, 62.3–78 years) in the "Resect" group. The proportion of women was 66.4% in the "Respect" group and 54.9% in the "Resect" group. Both groups included studies where there were no women as noted by the minimum proportion being 0% (14,20), while one study in the "Respect" group had only women (100%) (12). The "Resect" group had a median of 26.9% New York Heart Association (NYHA) class III or IV patients, and the "Respect" group had 12.5%. Two studies in the "Respect" group (12,25) and two studies in the "Resect" group (25,30) reported that 100% of their patients were classified as NYHA class III or IV. In the "Respect" group, 5 of 9 studies (18-20,25,29) had no subjects with CKD, but the study with the highest proportion of subjects with CKD had 83.33% (12). This can be compared to the seven of 13 studies (14,15,17,19,22,25,30) that had no subjects with CKD in the "Resect" group, and the study with the highest proportion of CKD subjects being 35% (23). The preoperative mortality risk as calculated by the EuroScore or STS score was 7.3% "Resect" group and 5.1% in the "Respect" group.

Patients in the "Respect" group had a median time on cardiopulmonary bypass (CPB) of 156 minutes, and a median intensive care unit (ICU) course of two days. Median CPB time in the "Resect" group was 181.5 minutes, and median ICU course was 3.5 days. The studies with the highest proportion of pulmonary complications (31.9%) (29) and cardiovascular complications (50%) (12) were both in the "Respect" group.

The prevalence range of renal complications and arrhythmias in the "Respect" group were 5.00% (26) to 22.29% (29) and 6.96% (28) to 20% (29), respectively. In the "Resect" group, renal complication prevalence ranges were 1.69% (16) to 16.22% (30) and arrhythmia ranges 7.14% (19) to 16.67% (30). The range of reported cardiovascular complications in the "Respect" group studies was 0 (12,21,28) to 2.22% (29). In the "Resect" group, all studies had 0% rates of cardiovascular complications. Rates of infectious complications ranged from 0% to 20% in the "Respect" group and 0% to 21.43% in the "Resect" group.

Among the 550 patients treated using the "MAC Respect" technique, 477 (87.63%) underwent MV replacement, while 73 (13.27%) received MV repair. Thirty-day mortality—including in-hospital deaths up to 30 days post-surgery—was reported in seven of the nine studies, with rates ranging from 0% (18,25) to 25% (21). One-year mortality was reported in four studies, ranging from 0% (12,29) to 43.75% (21). Long-term mortality beyond two years was also documented in four studies, with a range of 0% (12) to 26.96% (28).

Among the 487 patients treated using the "MAC Resect" technique, 278 (57.08%) underwent MV replacement, while 209 (42.92%) received MV repair. Thirty-day mortality—including in-hospital deaths up to 30 days post-surgery—was reported in twelve studies, with rates ranging from 0% (13,14,17,24,25,27,30) to 14.29% (19). One-year mortality was reported in eight studies, ranging from 0% (14,30) to 17.86% (21). Long-term mortality beyond two years was also documented in seven studies, ranging from 0% (30) to 50% (23).

MAC respect techniques

Table 4 summarizes aggregate patient characteristics, operative data, and short-term outcomes of three subgroups of the "MAC Respect" category: (I) hybrid transcatheter with a SAPIEN 3 valve; (II) MV replacement with calcium-avoidant sutures; and (III) MV replacement or MV repair with minimal decalcification. The hybrid transcatheter studies (12,21) included 22 patients from two studies

Table 2 Evaluation of quality for comparative studies using the Newcastle-Ottawa Cohort criterion, edited to grade outcomes of both postoperative complications and long-term mortality, in accordance with our data collection methods. Studies 1,4,5,11,20,21,22,25,35 underwent data collection but did not meet criteria for analysis by Newcastle-Ottawa criteria

Reference	Cohort definition	Selection				Comparability	Outcome (extended mortality)			Outcome (postoperative complications)			Total score
		Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
(15)	MAC *vs.* non-MAC	1	1	1	1	1	0	0	0	1	1	1	8
(16)	MAC *vs.* non-MAC	1	1	1	1	2	1	1	1	1	1	1	12
(18)	CUSA *vs.* non-CUSA	1	1	1	1	0	1	1	1	1	1	1	10
(19)	Decalcification *vs.* no decalcification/annuloplasty	1	1	1	1	0	1	1	0	0	0	0	6
(20)	Conservative repair *vs.* replacement	1	1	1	1	0	1	1	1	0	0	0	7
(21)	Conventional *vs.* hybrid	1	1	1	1	2	1	0	1	1	1	1	11
(25)	Respect (avoidant sutures, Teflon) *vs.* resect (drill, decalcification)	0	1	1	1	0	0	0	1	0	0	0	4
(26)	Double *vs.* single-layer sutures	1	1	1	1	2	1	0	1	1	1	1	11
(27)	Repair *vs.* replace	1	1	1	1	0	1	0	1	1	1	1	9
(28)	MAC *vs.* non-MAC	1	1	1	1	0	1	1	1	1	1	1	10

CUSA, cavitron ultrasonic surgical aspirator; MAC, mitral annular calcification.

Table 3 Characteristics, comorbidities, complications and outcomes of studies grouped into "MAC Respect" *vs.* "MAC Resect" techniques

Variable	MAC respect (patient n=550, study n=9) (ID: 1,7-10,14,16,18,19)	MAC resect (patient n=487, study n=13) (ID: 2-6,8,10-15,17)
Age (years)	71.5 [66.4–78.5]	70.3 [62.3–78]
Female sex (%)	66.4 [0–100]	54.9 [0–86.7]
NYHA class III or IV (%)	12.5 [0–100]	26.9 [0–100]
Preoperative CKD (%)	16.8 [10–83.3]	29.4 [23.2–35]
Preoperative mortality risk (EuroScore or STS calculator, %)	5.1 [4.1–8.8]	7.3 [4.1–8.4]
CPB time (minutes)	156 [82–180]	181.5 [139–240.5]
Total hospital LOS (days)	10 [6.3–13]	11.3 [4–28]
Total ICU LOS (days)	2 [0.9–9]	3.5 [2–5]
Pulmonary complication (%)	0 [0–31.1]	0 [0–13.3]
Infectious complication (%)	0 [0–20]	0 [0–21.4]
Cardiovascular complication (%)	0 [0–2.22]	0 [0–0]
Hematologic complication (%)	0 [0–40]	0 [0–20]
Cerebrovascular complication (%)	0 [0–50]	0 [0–10]
Renal complication (%)	8.9 [5.0–22.2]	5.4 [1.7–16.2]
Arrhythmia complication (%)	15 [7.0–20]	10 [7.1–16.7]
30-day reoperation (%)	0 [0–0]	0 [0–0]
30-day mortality (%)	10 [0–25]	0 [0–14.3]
1-year mortality (%)	6.1 [0–43.75]	10.24 [0–17.9]
Long-term (>2-year) mortality (%)	10.3 [0–27]	14.29 [0–50]

Data are presented as median [range]. Study IDs matched to the author and publication year of each reference are shown in Table S3. CKD, chronic kidney disease; CPB, cardiopulmonary bypass; ICU, intensive care unit; LOS, length of stay; MAC, mitral annular calcification; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons.

(median 90.6% female) with median age 75 (range, 73.9–76) years; the MV replacement with calcium-avoidant suture studies (26,28,29) included 190 patients from three studies (median 64.7% female) with median age 69.2 (range, 67.1–75.3) years; and the minimal decalcification studies (18-20) included 327 patients from three studies (median 15.4% female) with median age 73 (range, 67–78.5) years. Among the hybrid transcatheter studies, a median of 87.5% [range, 75% (21) to 100% (12)] of patients had NYHA Class III or IV heart failure, and a median of 51.4% [range, 18.8% (21) to 83.3% (12)] of patients had CKD. Median preoperative mortality risk was 5.2% in the hybrid transcatheter group and 5.1% in the calcium-avoidant suture group.

Median CPB time was 137 minutes in the hybrid transcatheter group, 156 minutes in the calcium-avoidant suture group, and 180 minutes in the minimal decalcification group. Notably, the calcium-avoidant suture group had the lowest minimum value for CPB time: 82 minutes (28). The calcium-avoidant suture group also had the shortest total length of stay (LOS) (median 7 days) and shortest ICU LOS (median 0.9 days), while the hybrid transcatheter group had median LOS of 10.5 days and median ICU LOS of 6 days, and the minimal decalcification group had median LOS of 11.5 days. Of the three groups, the minimal decalcification studies had the fewest complications, with no pulmonary, infectious, cardiovascular, hematologic, or renal complications. The hybrid transcatheter studies had median incidences of infectious, hematologic, cerebrovascular, and renal complications of 6.3%, 19.8%, 25%, and 6.3%, respectively. The calcium-avoidant suture

Table 4 Patient characteristics, operative data, and short-term outcomes of "MAC Respect" techniques

Variable	Hybrid TAVI (patient n=22, study n=2) (ID: 1,18)	Calcium-avoidant sutures (patient n=190, study n=3) (ID: 28,34,35)	No/minimal decalcification (patient n=327, study n=3) (ID: 12,14,16)
Age (years)	75 [73.9–76]	69.2 [67.1–75.3]	73 [67–78.5]
Female sex (%)	90.63 [81.25–100]	64.72 [60–67.8]	15.4 [0–93.3]
NYHA class III or IV (%)	87.5 [75–100]	39.17 [0–90]	0 [0–0]
Preoperative CKD (%)	51.4 [18.8–83.3]	5 [0–14.8]	0 [0–0]
Preoperative mortality risk (EuroScore or STS calculator, %)	5.2 [4.7–5.7]	5.1 [4.1–8.8]	–
CPB time (minutes)	137 [137–137]	156 [82–169.7]	180 [180–180]
Total hospital LOS (days)	10.5 [10.5–10.5]	7 [6.3–10]	11.5 [10–13]
Total ICU LOS (days)	6 [3–9]	0.9 [0.9–0.9]	–
Pulmonary complication (%)	0 [0–0]	0 [0–31.1]	0 [0–0]
Infectious complication (%)	6.3 [0–12.5]	14.4 [0–20]	0 [0–0]
Cardiovascular complication (%)	0 [0–0]	0 [0–2.2]	0 [0–0]
Hematologic complication (%)	19.8 [6.23–33.3]	2.2 [0–46.7]	0 [0–0]
Cerebrovascular complication (%)	25 [0–50]	1.6 [0–15]	0 [0–5.5]
Renal complication (%)	6.3 [0–12.5]	5.1 [0–22.2]	0 [0–0]
Arrhythmia complication (%)	0 [0–0]	11 [0–20]	0 [0–0]
30-day reoperation (%)	0 [0–0]	2.5 [0–5]	5.8 [4.9–6.7]
30-day mortality (%)	20.8 [16.7–25]	3.8 [0–10]	5.2 [0–10.4]

Data are presented as median [range]. Study IDs matched to the author and publication year of each reference are shown in Table S3. CKD, chronic kidney disease; CPB, cardiopulmonary bypass; ICU, intensive care unit; LOS, length of stay; MAC, mitral annular calcification; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation.

studies had median incidences of infectious, hematologic, cerebrovascular, and renal complications of 14.5%, 2.2%, 1.6%, and 5.1%, respectively. The calcium-avoidant suture group was the only one with postoperative arrhythmia values [median 15%, range, 6.96% (28) to 20% (29)]. Thirty-day reoperation rates were low in all groups (median 0% in hybrid transcatheter, median 2.5% in calcium-avoidant suture, median 5.8% in minimal decalcification). Thirty-day mortality ranged from 16.7% (12) to 25% (21) in the hybrid transcatheter group and from 0.87% (28) to 10% (26) in the calcium-avoidant suture group. The one study that reported 30-day mortality in the minimal decalcification group had a proportion of 10.4% (18).

MAC resect techniques

The "MAC Resect" category was also divided into subgroups [*en-bloc* resection (14,15,17,19,24,25,27,30), partial decalcification (13,16,21-23), resection followed by pericardial patch repair (13,15,16,19,24,27,30), resection followed by primary repair (14,15,17), and resection followed by Teflon repair (23,25)], with aggregate data for each group summarized in *Table 5*. A total of 214 patients (median 50% female) included in this analysis underwent *en-bloc* resection of MAC (14,15,17,19,24,25,27,30), with median age 69.7 [range, 65 (15) to 78 (27)] years, median 35% [range 0% (19,24) to 100% (25,30)] NYHA Functional Class III or IV heart failure, and CKD [prevalence range, 24.6% (27) to 33.3% (24)]. For the *en-bloc* resection group, median CPB time was 204.5 minutes. It is important to note, however, that maximum values from studies including *en-bloc* resection patients were 7.8% (15) for 30-day reoperation and 14.3% (19) for 30-day mortality.

Two hundred and seventy-three patients (median 66.1%

Table 5 Patient characteristics, operative data, and short-term outcomes of "MAC Resect" techniques

Variable	*En-bloc* resection (patient n=214, study n=8) (ID: 5,7,11,14,22,23,25,31)	Partial decalcification (patient n=273, study n=5) (ID: 4,10,18,20,21)	Pericardial patch repair (patient n=281, study n=7) (ID: 4,7,10,14,22,25,31)	Primary repair (patient n=37, study n=3) (ID: 5,7,11)	Teflon repair (patient n=26, study n=2) (ID: 21,23)
Age (years)	69.7 [65–78]	70.9 [62.3–75]	69.7 [65–78]	67 [65–69]	73.3 [71.5–75]
Female sex (%)	50 [0–75]	66.1 [0–86.7]	59.7 [33.3–86.7]	14.3 [0–53.1]	62.5 [50–75]
NYHA class III or IV (%)	35.1 [0–100]	0 [0–69.6]	9.4 [0–100]	50 [18.8–85.7]	50 [0–100]
Preoperative CKD (%)	0 [0–33.3]	26.7 [0–35]	12.3 [0–33]	0 [0–0]	17.5 [0–35]
Preoperative mortality risk (EuroScore or STS calculator, %)	7.5 [6.6–8.4]	6.1 [4.1–8]	8 [6.6–8.4]		
CPB time (minutes)	204.5 [161–240.5]	157 [139–175]	181.5 [139–240.5]	161 [161–161]	
Total hospital LOS (days)	4 [4–4]	12 [10.5–28]	12 [4–28]	4 [4–4]	
Total ICU LOS (days)		3.5 [2–5]	5 [5–5]		
Pulmonary complication (%)	0 [0–1.75]	0 [0–13.3]	0 [0–13.3]	0 [0–0]	0 [0–0]
Infectious complication (%)	0 [0–21.4]	0 [0–0]	0 [0–21.4]	0 [0–0]	0 [0–0]
Cardiovascular complication (%)	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]
Hematologic complication (%)	0 [0–14.3]	1.8 [0–20]	0 [0–20]	0 [0–0]	2.5 [0–5]
Cerebrovascular complication (%)	0 [0–3.5]	0 [0–10]	0 [0–3.5]	0 [0–0]	5 [0–10]
Renal complication (%)	0 [0–16.2]	1.7 [0–6.7]	0.9 [0–16.2]	0 [0–0]	0 [0–0]
Arrhythmia complication (%)	0 [0–16.7]	0 [0–9.3]	0 [0–10.5]	0 [0–16.7]	0 [0–0]
30-day reoperation (%)	0 [0–7.8]	0 [0–0]	0 [0–7.8]	0 [0–7.8]	0 [0–0]
30-day mortality (%)	0 [0–14.3]	4.3 [0–6.3]	0 [0–14.3]	0 [0–3.1]	0 [0–0]

Data are presented as median [range]. Study IDs matched to the author and publication year of each reference are shown in Table S3. CKD, chronic kidney disease; CPB, cardiopulmonary bypass; ICU, intensive care unit; LOS, length of stay; MAC, mitral annular calcification; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons.

female) underwent partial decalcification of MAC. This group had median 0% [range, 0% (13,22,23) to 69.6% (21)] NYHA Functional Class III or IV heart failure and median 29.4% [range, 23.2% (21) to 35% (23)] CKD. Median CPB time in the partial decalcification group was 157 minutes [range, 139 (16) to 175 (13) minutes]. The partial decalcification group had low rates of postoperative complications, 0% 30-day reoperation, and 0% (13) to 6.3% (22) 30-day mortality.

Several techniques for repair after MAC resection were also compared. 281 patients (median 59.7% female, median age 69.7 years) received pericardial patch repair, 37 patients (median 14.3% female, median age 67 years) received primary repair, and 26 patients (median 62.5% female, median age 73.3 years) received Teflon repair. Median CPB time and LOS in the pericardial patch repair group were 181.5 minutes [range, 139 (16) to 240.5 (24) minutes] and 12 days [range 4 (15) to 28 (13) days], respectively. Median rates of postoperative complications, 30-day reoperation, and 30-day mortality were low in all groups (*Table 5*). However, maximum complication rates were highest in the pericardial patch repair group: pulmonary (13.3%) (13), infectious (21.4%) (19), hematologic (20%) (13), renal (16.2%) (30), and arrhythmia (10.5%) (27).

MAC intervention techniques

Finally, aggregate data from studies including patients

Table 6 Patient characteristics, operative data, and short-term outcomes of "MAC Intervention" techniques

Variable	CUSA decalcification (patient n=97, study n=4) (ID: 4,12,22,31)	No annular intervention (patient n=312, study n=3) (ID: 12,18,20)
Age (years)	73 [69.4–78]	70.9 [62.3–78.5]
Female sex (%)	75 [33.3–93.3]	66.1 [0–93.3]
NYHA class III or IV (%)	0 [0–35.1]	0 [0–69.6]
Preoperative CKD (%)	24.6 [0–33.3]	0 [0–23.2]
Preoperative mortality risk (EuroScore or STS calculator, %)	7.5 [6.6–8.4]	4.1 [4.1–4.1]
CPB time (minutes)	188 [175–240.5]	180 [180–180]
Total hospital LOS (days)	20.5 [13–28]	10.5 [10–13]
Total ICU LOS (days)	–	2 [2–2]
Pulmonary complication (%)	0 [0–13.3]	0 [0–0]
Infectious complication (%)	0 [0–5.3]	0 [0–0]
Cardiovascular complication (%)	0 [0–0]	0 [0–0]
Hematologic complication (%)	0 [0–20]	0 [0–1.8]
Cerebrovascular complication (%)	0 [0–3.5]	0 [0–5.5]
Renal complication (%)	0 [0–6.7]	0 [0–5.4]
Arrhythmia complication (%)	0 [0–10.5]	0 [0–0]
30-day reoperation (%)	–	–
30-day mortality (%)	–	–

Data are presented as median [range]. Study IDs matched to the author and publication year of each reference are shown in Table S3. CKD, chronic kidney disease; CPB, cardiopulmonary bypass; CUSA, cavitron ultrasonic surgical aspirator; ICU, intensive care unit; LOS, length of stay; MAC, mitral annular calcification; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons.

who underwent MAC intervention via CUSA (13,18,24,27) or MAC intervention without subsequent annular reconstruction (18,21,22) is included in *Table 6*. Ninety-seven patients (median 75% female, median age 73 years) received CUSA decalcification. The CUSA decalcification group had a median CPB time of 188 minutes [range, 175 (13) to 240.5 (24) minutes], and median LOS of 20.5 days [range, 13 (18) to 28 (13) days]. Patients who received MAC intervention without subsequent annular reconstruction (N=312, median 66.1% female, median age 70.9 years) had median CPB time of 180 minutes, median LOS 10.5 days and median ICU LOS of two days. Median rates of all postoperative complications in both groups were 0%, although maximum rates reached 20% for hematologic complications in the CUSA decalcification group.

Discussion

Our findings corroborate prior studies characterizing the natural history of MAC pathogenesis. Although MAC is often diagnosed incidentally, female sex, increased age, systemic inflammation (e.g., CKD), and concomitant cardiovascular disease or metabolic syndrome have all been identified as associated risk factors for MAC (32,33). Mirroring these trends, the patients in the cohort of studies we analyzed were predominantly female, and MAC risk factors were consistently prevalent across the patient populations of all included studies. Propensity-matched analyses demonstrate that MAC independently predicts the incidence of major adverse cardiac events (MACEs) and all-cause mortality (4,5). Although functional insults to valvular function secondary to MAC are equally distributed between MV regurgitation, stenosis, or mixed disease, the presence of any dysfunction is associated with poor outcomes (34).

In conjunction with the high morbidity and mortality associated with the natural history of MAC, interventional management of MAC remains complex. Historically, surgical management of MAC was only considered when MV degeneration reached a symptomatic threshold, due to surgical complexity. However, advancements in preoperative characterization of MAC burden and intraoperative techniques have dramatically improved outcomes of MAC interventions. When indicated, interventions on the MV are broadly categorized as surgical MV repair, surgical MV replacement, or transcatheter replacement.

Surgical interventions remain the gold-standard therapy for severe MAC, especially with concomitant MV dysfunction; nevertheless, MAC has been consistently associated with poor postoperative outcomes due to increased surgical complexity (35). Moreover, approaches to surgical management of MAC remain heterogeneous, with no standardized criteria available to guide MAC interventions within the overarching dichotomy of "MAC Respect" or "MAC Resect."

We subclassified purely surgical interventions (including both repair and replacement procedures) under "MAC Respect" into two major methodologies: "calcium-avoidant sutures" and "partial or absent decalcification". "MAC Respect" techniques focus on either avoiding or suturing through the calcium bar while placing annular sutures (calcium-avoidant sutures), with little to no direct surgical intervention on the annulus (9-11). Although such approaches may not be able to fully excise the complete burden of annular calcification, they carry the benefit of a reduced risk of damaging surrounding structures, particularly the atrioventricular groove and left circumflex coronary artery. In comparison, extensive resection in a "MAC Resect" approach may be able to adequately treat the complete burden of valvular disease, but carries an increased risk of calcium embolization and thromboembolic complications (5,12).

Our analysis was limited by inconsistent reporting of preoperative demographics and postoperative complications. However, limited comparisons suggest that preoperative characteristics of the patient cohorts of the two primary surgical "MAC Respect" approaches ("Calcium-Avoidant Sutures" and "Partial Annular Decalcification") were equivalent in median age and preoperative complication burdens (as assessed by maximum reported prevalence). In alignment with the theoretical risks of increased annular decalcification, qualitative postoperative outcomes analysis suggests a larger maximum prevalence of cerebrovascular complications and longer hospital stays in patients undergoing "Partial Annular Decalcification".

Despite the conservative approach of "MAC Respect" annular interventions, we found equivalent outcomes to non-MAC patients for cohorts undergoing MV replacement (10,11,15). Approaches of partial decalcification remain under development, and continued refinement of surgical techniques may reduce the theoretical risk of thromboembolic complications we observed in our qualitative analysis.

"MAC Resect" techniques involve complete removal of the calcified mitral annulus, followed by reconstruction of any removed or weakened annular segments. In comparison to "MAC Respect" techniques, the complete resection and removal of the calcium bar avoids the under-sizing of a mitral prosthesis; it also allows for the placement of solid sutures to hold the prosthesis in place without running the risk of going through unstable calcium that can lead to prosthesis dehiscence. Another benefit of "MAC Resect" approach entails the ability to execute durable MV repair by re-attaching the MV leaflet to a healthy annulus. "MAC Resect" approaches are also able to augment the size of the posterior MV leaflet, by attaching its base to a pericardial patch used to repair the AV groove.

To encompass all possible techniques within the "MAC Respect" category, we defined two methods of annular decalcification ("En-Bloc" and "Partial Decalcification") and three methods of subsequent annular repair ("Primary Repair", "Pericardial Patch Repair", and "Teflon Repair"). The first MV repair procedures on MAC pathology were "En-Bloc" approaches, with complete removal of the calcium bar and primary closure with an atrial tissue flap as reported by Carpentier *et al.* (36) with favorable patient outcomes. More recent iterations of "En-Bloc" techniques have utilized Teflon, bovine pericardial, or autologous pericardial patches for repair of the disrupted annulus. In general, "En-Bloc" approaches to MAC surgical management are indicated in patients with severe MV dysfunction but lower surgical risk, as extensive annular resection may improve long-term function of a repaired MV or implanted MV prosthesis (9,17-23). Such patients should also exhibit physiological reserve to compensate for higher operative complexity, exhibited by longer ischemic and CPB times (12). Another alternative method is "Partial Decalcification", in which only certain areas of the annulus are systematically and completely decalcified to facilitate replacement or repair procedures. Such approaches could balance the advantages of improved long-term MV function in “En-Bloc” decalcification, with fewer postoperative complications from reduced operative complexity. “Partial Decalcification” approaches are also conceivably more flexible and can accommodate differences in leaflet repair or MV replacement in different MV pathologies (15,24-27). However, direct comparisons of surgical approach, short-term, and long-term outcomes between “Partial Decalcification” and “En-Bloc” approaches remain sparse in the literature.

It is notable that after application of our exclusion criteria, we did not analyze studies addressing all possible combinations of decalcification and repair approaches. Nevertheless, qualitative assessment of preoperative study cohort characteristics between decalcification methods suggests equivalent age and gender distributions, but a higher maximum prevalence of hypertension and dyslipidemia in the partial decalcification cohort. Increased morbidity from an extensive surgical intervention during *en-bloc* excision of MAC may be particularly exacerbated in the setting of preexisting cardiovascular pathologies like coronary artery disease. Corroborating these findings, intraoperative parameters suggest shorter CPB times in the “Partial Decalcification” cohort, compared to the “En-Bloc” cohort. However, the “Partial Decalcification” cohort displayed longer median postoperative hospital stays and greater median prevalence of renal or hemodynamic complications, with greater variability across all postoperative complications. Such findings could be explained by a more heterogenous patient population in the “Partial Decalcification” cohort, leading to a wide spectrum of MAC pathology and subsequent variations in postoperative recovery.

In conjunction with “MAC Resect” decalcification, annular reconstruction is often required to repair resected annular regions, provide a contiguous annular surface for prosthesis or annuloplasty ring seating, and reinforce the atrioventricular groove. Primary repair using endogenous tissue may be the most straightforward approach to annular reconstruction, with conceivable advantages of reduced foreign body reactions and favorable biomechanical properties. When primary repair may not be feasible (e.g., extensive resection leading to a wide hollow trench in the annulus), use of exogenous patches is common. In studies on MAC MV replacement, fixed bovine pericardium was preferred due to its favorable mechanical properties (24,28). Reports of autologous patch repair techniques for other MV interventions (e.g., endocarditis) have described reoperations due to patch degeneration leading to reemergence of MV dysfunction (29). In these cases, Gor-Tex/Teflon patches have been successfully utilized due to the material’s favorable durability (30). In some reports, autologous patches have been reported to exhibit superior biocompatibility and less severe foreign body reactions compared to bovine pericardium (32,33). A direct comparison of patient outcomes between patch-based or primary repair approaches has not been completed in the literature.

Stratifying by annular/AV groove repair approach, qualitative assessment of preoperative patient characteristics suggests relatively comparable cohorts by age, sex, and preoperative disease burden. The “Primary Repair” and “Teflon Repair” cohorts suffered from high missingness of postoperative complications, which limited analysis. However, longer CPB times and increased durations of hospital stay in the pericardial patch cohort suggests that patients undergoing “Primary Repair” after “MAC Resect” approaches may exhibit less complex anatomical patterns of MAC calcification that may be amenable to simple primary closure. When reported, rates of reoperation appeared to be equivalent between pericardial patch repair and primary closure. Nevertheless, further research is warranted to examine the course of degeneration for various patch materials following “MAC Resect” surgical approaches.

When comparing “MAC Resect” techniques to their “MAC Respect” counterparts, our findings suggest that Resect-oriented operative methods may be preferred for patients with few systemic comorbidities. Conversely, shorter CPB and duration of ICU or hospital stay in the MAC Respect cohort suggests that Respect-oriented operative approaches incur lower overall surgical burden on patient physiology. Thus, clinician decision-making after preoperative patient evaluation may explain the inter-cohort differences we qualitatively observed in our analysis. The lower maximum reported rate of short-term postoperative mortality (30-day) in the “MAC Resect” cohort could be due to a selection bias towards patients with fewer comorbidities, who may be able to tolerate extensive annular reconstruction.

Another emerging method to address MAC includes various transcatheter interventions. Methods of transcatheter replacement generally proceed through transseptal puncture, laceration or displacement of the anterior leaflet, followed by deployment of an inverted transcatheter aortic valve prosthesis (TAVI) or dedicated mitral valve prosthesis (TMVR) in more recent studies (37).

These techniques were not the primary topic of this review. Historically, transcatheter methods have been preferred in MAC patients with prohibitively high surgical risk and large comorbidity burdens due to the reduced overall morbidity of the operation (38). Nevertheless, outcomes of transcatheter interventions in MAC vary significantly by center. In general, 30-day mortality rates, left ventricular outflow tract obstruction, device embolism, and reoperation rates are high following transcatheter interventions in MAC patients (34). In addition, transcatheter interventions are associated with increased rates of hemolysis, which is otherwise rare in surgical procedures (39). Underlying mechanisms include flow disruption due to paravalvular leak (PVL), or high-flow hemolysis around the stent used during device deployment.

Hybrid surgical-TMVR (H-TMVR) mirrors conventional surgical interventions, proceeding through left atrial entry via Sondegaard's groove, followed by resection of the anterior leaflet and deployment of a transcatheter MV prosthesis directly into the annulus. H-TMVR procedures do not directly intervene on the calcified annulus, and we thus classified them under the overarching category of "MAC Respect". Conceivably, surgical resection of the anterior leaflet and direct visualization of prosthesis deployment could improve seating of the replaced valve, reducing complications of PVL and hemolysis (12). Moreover, obstruction of the left ventricular outflow tract can be reduced through resection or complete removal of the anterior leaflet (40).

Due to the novelty of H-TMVR procedures, we only identified two cohorts of patients undergoing H-TMVR which were ultimately excluded from our study. Nevertheless, preliminary qualitative comparisons suggests that H-TMVR may exert a reduced insult on patient physiological reserve: despite comparable prevalence ranges of preoperative comorbidities, prevalence ranges for pulmonary and infectious postoperative complications were qualitatively lower in H-TMVR, compared to "MAC Respect" studies. However, H-TMVR procedures appeared to be associated with higher burdens of hemodynamic and cerebrovascular complications. This suggests that the complications associated with transcatheter prostheses are not completely eliminated by a hybrid surgical procedure.

The findings of this systematic review highlight the complexity of MAC pathogenesis, and surgical management. Variability in the presentation of MAC and burden of disease necessitates individualized surgical approaches. Our analysis corroborates the extensive variation in current clinical practices to manage MAC, and highlights the need for extensive preoperative characterization MAC and a collaborative, multi-specialty approach to preoperative planning.

We observed that different surgical approaches of "MAC Resect" and "MAC Respect" lead to different possible profiles of postoperative complications. We suggest that the postoperative management of MAC patients should thus be closely informed by the chosen method of MAC intervention and the patient's intraoperative course. For example, the postoperative blood pressure target of patients undergoing extensive annular decalcification and patch reconstruction may be lower than other operative approaches. Similarly, debridement of the calcium bar increases the risk for calcium embolization, warranting close postoperative neuromonitoring.

The strengths of our systematic review originate from the use of a systematic method of study selection across multiple different databases, ensuring that we captured a wide range of surgical interventions for MAC in our analysis. Moreover, systematic methods of quality assessment, data extraction, and evaluation of surgical technique enhances the external validity of our review.

Limitations of this systematic review originate from methodological differences between studies. Heterogeneity in patient populations and differences in center volume or surgeon experience precluded the execution of a robust meta-analysis, limiting our conclusions to qualitative studies only. Moreover, missingness and variations in reported statistics may have been obscured by manual categorization of intraoperative techniques and postoperative complications. Notably, there was especially high missingness for data on atrioventricular groove disruption, which is a particularly serious complication in MAC patients.

Conclusions

It is clear that surgical interventions remain the gold standard of treatment for MAC, despite increased morbidity and mortality when compared to non-MAC patients. Our systematic review identified that thorough characterization of MAC burden, meticulous preoperative planning, and procedure-informed postoperative monitoring could improve patient outcomes. We also demonstrate the advantages and disadvantages of the primary approaches in MAC surgical interventions. Future research should continue to refine surgical techniques, especially in newer approaches of H-TMVR or ultrasonic decalcification. In addition, future multi-center prospective studies could examine head-to-head comparisons of established (e.g. "En-Bloc" decalcification) and emerging (ultrasonic decalcification, H-TMVR) techniques to further reduce postoperative morbidity and improve postoperative outcomes.

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