Heart Online First, published on March 13, 2018 as 10.1136/heartjnl-2017-312277

ORIGINAL RESEARCH ARTICLE

Subannular reconstruction in secondary mitral regurgitation: a meta-analysis

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► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/heartjnl-2017-312277).

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The abstract was presented at the 46th Annual Meeting of the German Society of Thoracic, Cardiac and Vascular Surgery (DGTHG) in Leipzig (14 February 2017).

Received 8 August 2017
Revised 7 February 2018
Accepted 12 February 2018

ABSTRACT

Objective Mitral valve repair using an undersized complete annuloplasty ring in secondary mitral regurgitation with restricted leaflet motion during systole (Carpentier's surgical classification of mitral valve pathology: type IIIb) only inadequately addresses the underlying left ventricular disease. This may lead to an ongoing ventricular remodelling and progressive papillary muscle displacement with increasing leaflet tethering. Several subannular techniques have been proposed to counteract the reoccurrence of mitral regurgitation after mitral valve repair. We aimed to evaluate the potential additive effect of such subannular techniques on the late reoccurrence rate of secondary mitral regurgitation.

Methods Systematic literature review and meta-analysis were performed on PubMed, Embase and Google Scholar for studies published up to March 2016 and reporting late reoccurrence of mitral regurgitation after mitral valve repair using standard annuloplasty (control group) versus annuloplasty with subannular correction (study group) cohorts. Primary endpoint was late reoccurrence of mitral regurgitation ≥2 after surgical mitral valve repair, as defined by follow-up echocardiography.

Results The cumulative number of 1093 patients in 12 included studies served as our study population. A total of 743 patients underwent combined mitral valve repair including annuloplasty and subannular manoeuvre (ie, study group), while the remaining 350 patients underwent an isolated ring annuloplasty (ie, control group). Secondary mitral regurgitation was caused by ischaemic heart disease in 733/743 patients in the study group and 334/350 patients in the control group. Mean echocardiographic follow-up was 42.7±13.9 months. Pooled outcome analysis demonstrated that the combination of subannular repair with ring annuloplasty was associated with a significantly lower reoccurrence rate of mitral regurgitation ≥2 as compared with annuloplasty alone (OR 0.27, 95% CI 0.19 to 0.38, P=0.0001).

Conclusion The combination of subannular reconstruction and mitral valve annuloplasty is associated with a lower late reoccurrence of mitral regurgitation after surgical mitral valve repair, as compared with annuloplasty alone.

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To cite: Harmel EK, Reichenspurner H, Girdauskas E. *Heart* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/heartjnl-2017-312277

INTRODUCTION

Mitral valve diseases are generally classified using the surgical classification of Alain Carpentier, who was first to describe mitral valve regurgitation in relation to mitral leaflet pathology (type I: normal leaflet motion; type II: leaflet prolapse; type III: restricted leaflet motion). According to Carpentier's classification, regurgitation due to restricted leaflet motion during systole is defined as type IIIb.[1] Surgical treatment of this type IIIb secondary mitral regurgitation (MR) remains highly controversial, mainly due to high reoccurrence rate of MR after standard mitral valve repair.[2 3] The reported reoccurrence rate of MR after standard annuloplasty varies between 15%[4] and 30%,[2 5 6] up to 60%.[7] Until now, there is no consensus regarding how to best address type IIIb secondary MR.[8] In the recent update of the American Association of Thoracic Surgery consensus guidelines on ischaemic mitral valve regurgitation, the level of evidence for mitral valve repair in secondary MR has been downgraded from level A to B, basically due to the lack of large prospective randomised trials.[9] Even though undersized ring annuloplasty is a standard surgical strategy to treat secondary MR, it may only inadequately address the underlying left ventricular (LV) disease. The ongoing LV remodelling causes progressive papillary muscle displacement and thereby increases mitral leaflet tethering. Consequently, there is an ongoing debate regarding mitral valve replacement versus repair strategy in secondary MR. Previous meta-analysis by Vassileva *et al* showed significantly higher short-term and long-term mortality after mitral valve replacement in ischaemic MR, as compared with mitral valve repair subgroup.[10] In contrast, Salmasi *et al* failed to show any significant difference in the long-term mortality in replacement versus repair cohorts.[11] However, mitral valve replacement strategy was associated with a higher in-hospital mortality.[11] Recent randomised trial by Acker *et al* found no significant differences in 1-year mortality and adverse cardiac events when comparing mitral valve repair versus mitral valve replacement cohorts in ischaemic MR.[2] This Cardiothoracic Surgery-Net (CTS-Net) trial focused furthermore on LV reverse remodelling, defined by postoperative changes in left ventricular end-systolic volume index (LVESVI). At 2-year follow-up, the trial failed to show improved reverse remodelling in the mitral repair versus replacement subgroup.[12] Interestingly, a post-hoc analysis of patients with successful repair (ie, no MR recurrence at 2-year follow-up) versus those with recurrence of MR>2 revealed significant difference in reverse LV remodelling (ie, LVESVI 42.7±26.4 mL/m^2 (successful repair) vs 62.6±26.9 mL/m^2 (MR>2 after repair), P<0.0001). This finding indicates the importance of the long-term stability of mitral repair in patients with secondary MR, even though the key message was a significantly lower reintervention rate in the replacement cohort.[2 10]

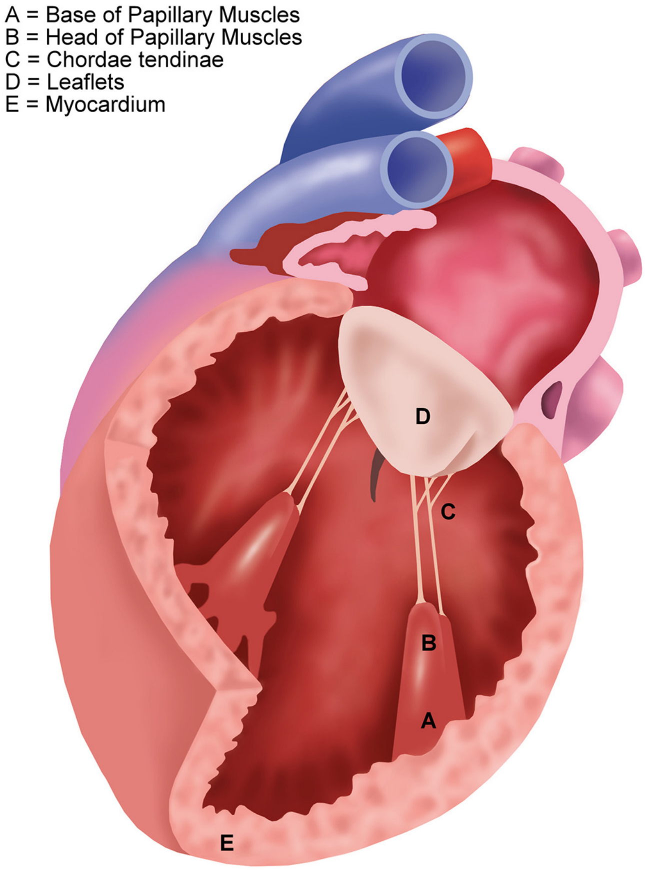

Figure 1 Type IIIb functional mitral regurgitation underlying left ventricular disease which leads to progressive papillary muscle displacement and subsequently increasing leaflet tethering in functional mitral regurgitation. The figure indicates different points of action used in subannular mitral valve reconstruction techniques.

Several subannular repair techniques have been developed to address the limitations of standard annuloplasty in secondary MR, aiming to improve the long-term stability of mitral valve repair.[13] Such techniques can be subdivided (ie, according to the anatomical structure of mitral apparatus being addressed) into papillary muscle relocation (eg, papillary muscle approximation, 'ring and string' technique), correction of chordae tendineae (eg, secondary chordae cutting) and leaflet augmentation techniques (eg, posterior or anterior leaflet augmentation) (figure 1).[14–17] Distinct subannular techniques have been described in detail in the recent systematic review published by Mihos and Santana.[13] However, there is still an ongoing debate regarding the most appropriate subannular technique in secondary MR.

Previous reviews highlighted potential advantages of subannular repair techniques, while pointing out some functional benefits as compared with standard annuloplasty.[8 13 18] However, to the best of our knowledge, no systematic meta-analysis has been conducted. We implemented a meta-analysis designed to answer the question whether adding subannular manoeuvre to a standard ring annuloplasty will improve the long-term stability of mitral valve repair in type IIIb secondary MR.

METHODS

Systematic literature review and meta-analysis were performed according to the Meta-analysis of Observational Studies in Epidemiology guidelines.[19]

Search strategy

A systematic literature search was conducted on PubMed, Embase and Google Scholar, using the terms 'mitral valve annuloplasty', 'functional mitral regurgitation', 'ischemic mitral regurgitation', 'secondary mitral regurgitation', 'subannular mitral valve repair', 'posterior leaflet augmentation' and 'papillary muscle relocation' in various combinations. The search was limited to human, adult studies and original articles, published in the English language. In case of repetitive reports from a single institution, we critically looked at patient cohort details and aimed to select a single article based on the largest number of patients included. In case of similar but not identical patient cohorts, both studies were included, but a sensitivity analysis (exclusion of single trials and recalculation of pooled OR for the remaining studies) was performed to avoid distortion of results. One author (EKH) screened all titles and abstracts to identify publications for full-text review. Potential full-text articles were evaluated independently by two authors (EKH, EG) to confirm the inclusion criteria (*see below*) and to extract the prespecified data using a standardised data abstraction form. All discrepancies were resolved by consensus. The initial search was performed in April 2016. The reference lists of all selected full-text articles were screened to identify additional relevant studies and updates were continued until March 2017 (figure 2).

Inclusion criteria

Original articles reporting on surgical mitral valve repair in secondary MR were identified. A study was considered eligible for inclusion if the following four criteria were all met: (1) pathology of mitral valve disease was defined as secondary MR, (2) longitudinal echocardiographic follow-up was provided, including quantitative information on MR before and after mitral valve repair, (3) echocardiographic follow-up ≥3 years postoperatively was available, and (4) a subgroup of annuloplasty+subannular repair (ie, study group), as well as an isolated ring annuloplasty subgroup (ie, control group), were both included.

Exclusion criteria

We excluded all case reports, studies reporting on less than 10 patients, as well as all laboratory or experimental works. Moreover, we excluded all publications that insufficiently described mitral valve pathology at the time of mitral valve repair surgery. In case of mixed study population (ie, degenerative and secondary MR), the whole study was excluded from meta-analysis.

Study endpoints

The primary endpoint of the study was the reoccurrence of MR≥2 at the time of last echocardiographic follow-up (defined as ≥3 years after mitral valve repair). The secondary endpoints were comparative analysis of left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVEDD) in both study subgroups.

Statistical analysis

Meta-analysis was conducted using Comprehensive Meta-Analysis V.3 (Biostat, Englewood, New Jersey). Cumulative events were compared as OR with a 95% CI. Inverse variance-weighted random-effects model was used to derive pooled summary estimates. Given the fact that subannular techniques used in the study group (annuloplasty+subannular repair) were heterogeneous (table 1), we decided to use random-effects meta-analysis. We anticipated that the true effect could vary from study to study depending on the exact surgical technique used, and

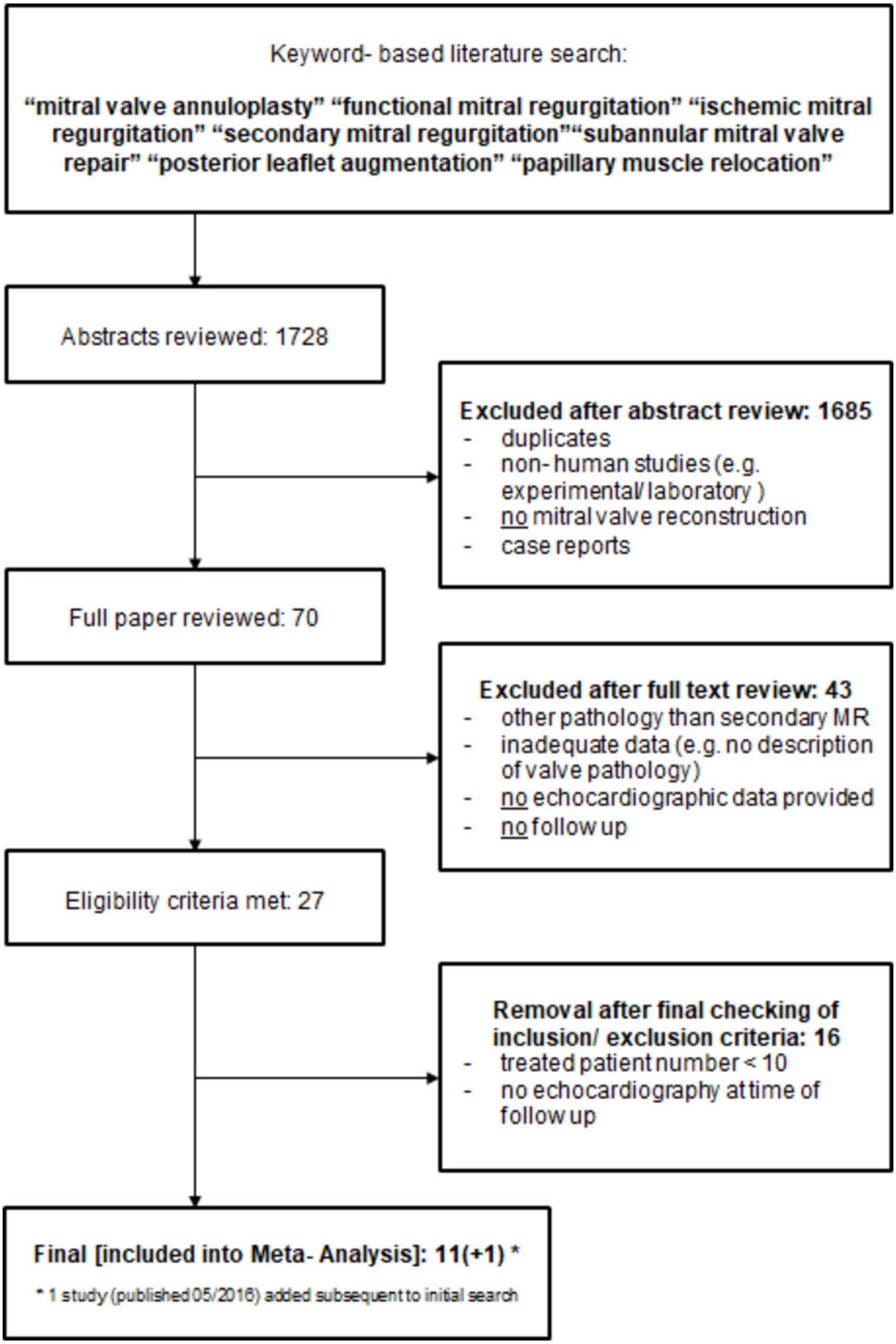

Figure 2 Study flow diagram. Detailed study flow diagram showing identification process of the included studies. MR, mitral regurgitation.

random-effect model would therefore allow for a more appropriate calculation of combined effect estimate. Between-study heterogeneity was evaluated using the index of heterogeneity I^2 test and was deemed to be relevant when $I^2 > 50\%$. Given the substantial potential for heterogeneity in meta-analysis of observational studies due to residual confounding, we collected information on potential confounders for each of the included studies. Sensitivity analysis was performed by exclusion of single trials and recalculating the pooled OR for the remaining studies. Results are presented as forest plot, including each individual OR as well as the overall composite effect estimate. The contribution of each included study to the final pooled estimate is presented as a study weight (W). An OR with 95% CI <1 indicates a significant benefit of combined surgical procedure (annuloplasty+subannular manoeuvre) as compared with annuloplasty alone regarding the primary study endpoint (ie, the reoccurrence

Table 1 Overview of subannular techniques: detailed overview describing the various surgical techniques used in subannular reconstruction, including the different points of action

Paper	Subannular technique	Point of action	Description
20	Papillary muscle approximation (PMA)	Base of papillary muscles (PM)	Gathering of anterior+posterior PM, using pledgetted mattress sutures (3–0 polypropylene)[20]
	PMA+left ventriculoplasty	Base of PM+ventricle	PMA as described+overlapping left ventriculoplasty or partial left ventriculectomy for an anteroseptal or inferoposterior scar lesion, respectively[20]
21	Posterior leaflet duplication	Posterior leaflet (PML)	PML duplication, to abolish the tethering at PML segments 2+3 and to decrease the distance between anterior+posterior PM at the leaflet level, to obtain a good apposition zone with the anterior leaflet (AML) by reducing the free edge of the PML[21]
14 22 24 26	PM relocation	Head of PM	Technique as described by Kron *et al*[28] Suture placement (polytetrafluoroethylene) at the head of each PM+subsequently through ipsilateral mitral annulus (arrested heart); relocation of both PM to minimise tenting; usually, relocation of 1 head of the anterior PM + 2 heads (anterior+posterior) among the 3 heads of the posterior PM
23	PM sling	Base of PM	A blunt dissector is worked through the trabeculations at the base of the posterior PM, ensuring that the tube (4 mm polytetrafluoroethylene) will not be able to later migrate towards the head of the PM. The tube is then drawn around the base of the anterior PM. The loop is progressively tightened until the two PMs are in close contact, without any residual gap between the bases of the two PMs, but not squeezed tight to avoid any ischaemia. The tube forms an intraventricular ring that is secured with strong sutures, but no sutures are placed on the PMs themselves.[23]
15	Ring and string	Head of posterior PM	A combination between ring annuloplasty and posterior PM repositioning A Teflon-pledgeted suture (3–0 polytetrafluoroethylene) is anchored in the head of the posterior PM and then passed through the fibrosa (mid-septal annular saddle horn) underneath the commissure, between non-coronary and left coronary aortic cusps and exteriorised through the aortic wall. The suture is finally tied under echocardiographical guidance in the loaded beating heart to reposition the displaced posterior PM towards the fibrosa.[15]
17	Posterior leaflet extension	PML	PML extension (bovine pericardial patch) extending the medial half of P2 and all of P3; detachment of PML at its base (middle of P2 to posterior commissure); preparation of a bovine pericardial patch (rinsed thoroughly+cut in an oblong fashion (1×3.5–4.5 cm)); patch placement to the edge of the PML defect and the posterior mitral annulus with a running suture (5–0 polytetrafluoroethylene)[17]
16	Secondary chordal cutting	Chordae tendineae	Division of secondary chords to the AML, PML and the commissure that arise from the PM or muscles affected by the infarcted myocardium; identification of affected PM by preoperative echocardiography and/or ventriculography; separation of secondary chords from primary chords with a nerve hook, confirming their attachment to the belly of the leaflets rather than to the free edge; division and cutting of all secondary chords from the affected PM[16]
25	Posterior leaflet shortening	PML	A pericardium-pledgeted suture (3–0 polypropylene) is placed through the fibrous body of the trigone and then tied, after which it is run continuously along the annulus from one trigone towards the mid-section of the posterior annulus. The same is done on the opposite trigone. These sutures are then tied over the valve sizer to prevent overnarrowing of the valve orifice. When competence is assured, both sutures using the same needles are passed onto an untreated autologous pericardial strip, which is then attached to the posterior annulus (mid-segment to trigone) by continuous sutures in a through-and-through fashion. Through posterior annulus augmentation by the pericardial strip tissue, the coaptation area, which the PML offers to the AML, is enhanced.[25]
27	PMA	Base of PM	The PM approximation is performed with 4 mm Gore-Tex tube encircling the bodies of posterior-medial and anterolateral PMs, which are drawn together. In the presence of two independent heads of PM (morphology type IV/V), both posteromedial PMs are approximated to minimise mitral valve tenting.[27]

of MR≥2). Publication bias was evaluated graphically using a funnel plot and determined mathematically using Egger regression and the Begg-Mazumdar rank correlation test.

RESULTS

Identification of studies

The keyword-based search, performed on 21 April 2016, revealed a total of 1728 potential publications. After removal of duplicate studies and exclusion of experimental and laboratory studies, abstract screening was conducted and yielded 70 relevant papers. Full-text review revealed 27 eligible manuscripts, while long-term echocardiographic data (ie, >3 years postoperatively) were available only in 11 (40.7%) of them.[14–17 20–26] Continuous updates on the literature search were performed until March 2017 and identified one additional paper, which was included in the meta- analysis.[27]

Study population

The cumulative number of 1093 patients in 12 included studies served as our study population. A total of 743 patients underwent combined mitral valve repair including annuloplasty and subannular manoeuvre (ie, study group), while the remaining 350 patients underwent an isolated ring annuloplasty (ie, control group). Since the underlying ventricular

Table 2 Baseline characteristics of study subgroups

Variable	Group A Annuloplasty+subannular repair	Group B Isolated annuloplasty	P value
Patients (n)	743	350	
Age (years)	60.8±10.5	62.1±9.0	0.1
Male, % (n)	64.9 (455)*	63.2 (221)	0.8
LVEF, %	35.2±7.9	40.1±8.4	0.06
LVEDD (mm)	61.8 ± 6.6†	57.5 ± 5.1†	0.05
AF, % (n)	13.7 (36)‡	17.2 (40)‡	0.8
Left ventricular disease, % (n)	ICM 98.2 (733) DCM 1.8 (10)	ICM 95.4 (334) DCM 4.6 (16)	0.6

No significant differences were found between the two study groups.
*Gender unknown in 4.98% (n=37) in group A.
†No data available in 14.3% (n=106) in group A and 19.7% (n=69) in group B.
‡No data available in 49.3% (n=366) in group A and 33.7% (n=118) in group B.
AF, atrial fibrillation;DCM, dilated cardiomyopathy; ICM, ischaemic cardiomyopathy; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction.

disease was ischaemic cardiomyopathy in 733/743 patients in the study group and in 334/350 patients in the control group, in most procedures, concomitant coronary artery bypass grafting (CABG) was performed. In group A (ie, study group), concomitant CABG was performed in 91.4% of patients (679/743) and in 98.6% (345/350) of patients in group B (ie, control group). The mean age at time of surgery was 61.2±10.0 years, and 64.3% (676/1056) were male. Gender had not been reported in 3.4% (37/1093). Baseline characteristics were comparable between both study subgroups (ie, control vs study group) (table 2) and supplementary table).

The underlying LV disease leading to secondary MR was ischaemic cardiomyopathy in most patients (ie, 1067/1093, 97.6%), while non-ischaemic cardiomyopathy was diagnosed in the remaining 26 patients (2.4%). The mean preoperative LVEF was 36.9%±8.1% and the mean LVEDD was 60.3±6.1 mm in the whole study cohort. There was a tendency towards larger preoperative LVEDD and lower preoperative LVEF in the study group, however without reaching statistical significance (table 2). Subannular techniques used in the study group (n=743) were heterogeneous and included papillary muscle relocation (306/743, 41.2%), papillary muscle reapproximation (105/743, 14.1%), posterior leaflet duplication (136/743, 18.3%), posterior annulus shortening (75/743, 10.1%), posterior leaflet extension (44/743, 5.9%), secondary chordal cutting (43/743, 5.8%) and LV remodelling (34/743, 4.6%). A more detailed overview of the different subannular techniques is given in table 1.[28]

Rate of MR reoccurrence after mitral valve repair

The mean echocardiographic follow-up was 42.7±13.9 months. Pooled outcome analysis demonstrated that the combination of subannular repair with ring annuloplasty was associated with a fourfold lower reoccurrence rate of MR ≥2 as compared with annuloplasty alone (OR 0.27, 95% CI 0.19 to 0.38, P=0.0001) (figure 3). Cumulative reoccurrence rate of MR≥2 was 9.8% (73/743 patients) in the study group vs 24% (84/350 patients) in the control group (P=0.0001).

No evidence of clinical between-study heterogeneity ($I^2=0$, tau-squared=0, P=0.691) could be shown. Furthermore, significant publication bias was excluded by the funnel plot of pooled studies, Egger regression (intercept=−2.1, 95% CI (−7.3 to 12.1), t-test=−0.78, P=0.571) and the adjusted Begg-Mazumdar rank correlation test (Δx-y= −5, Kendall's tau a=−0.09, z=−0.48, P=0.393) (figure 4). Furthermore, the exclusion of any single study from the meta-analysis did not alter the pooled effect result. Meta-regression coefficients were not significant for LVEF (P=0.3) and LVEDD (P=0.1).

Echocardiographic outcome parameters at time of follow-up

Even though our meta-analysis was not powered to analyse the most appropriate subannular reconstruction technique, table 3 provides a systematic overview of MR recurrence rates in the different studies included in our meta-analysis. The postoperative

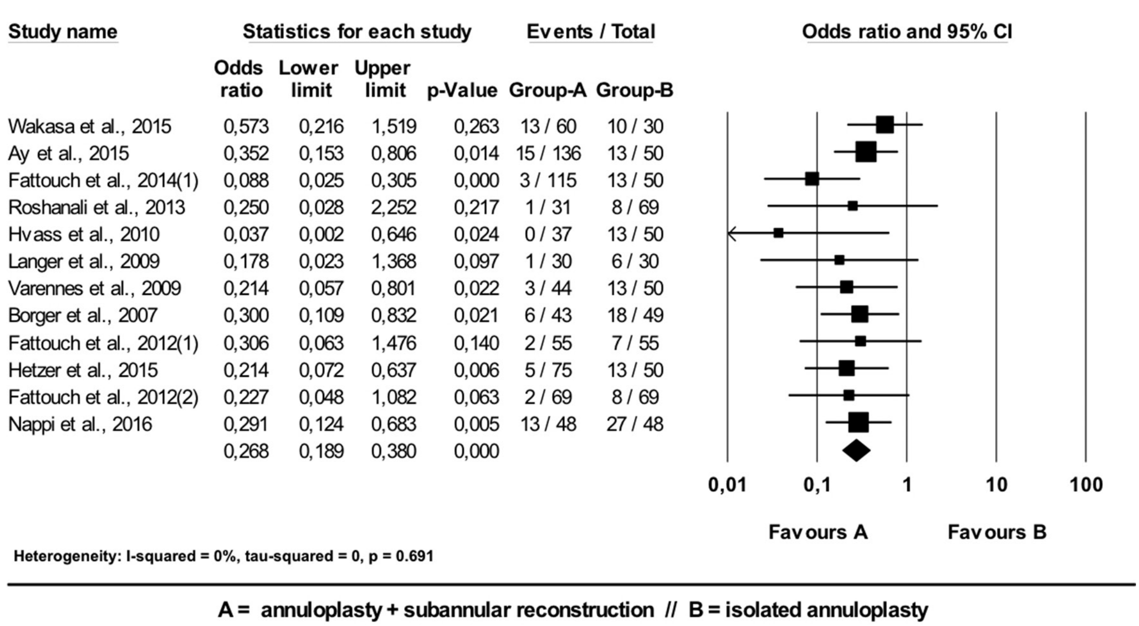

Figure 3 Meta-analysis of late reoccurrence of mitral regurgitation after surgical mitral valve repair. Our data demonstrate a significant association between lower late reoccurrence rate of mitral regurgitation ≥2 and the treatment strategy of annuloplasty in combination with subannular reconstruction (group A), as compared with annuloplasty alone (group B) (OR 0.27, 95% CI 0.19 to 0.38, P=0.0001).

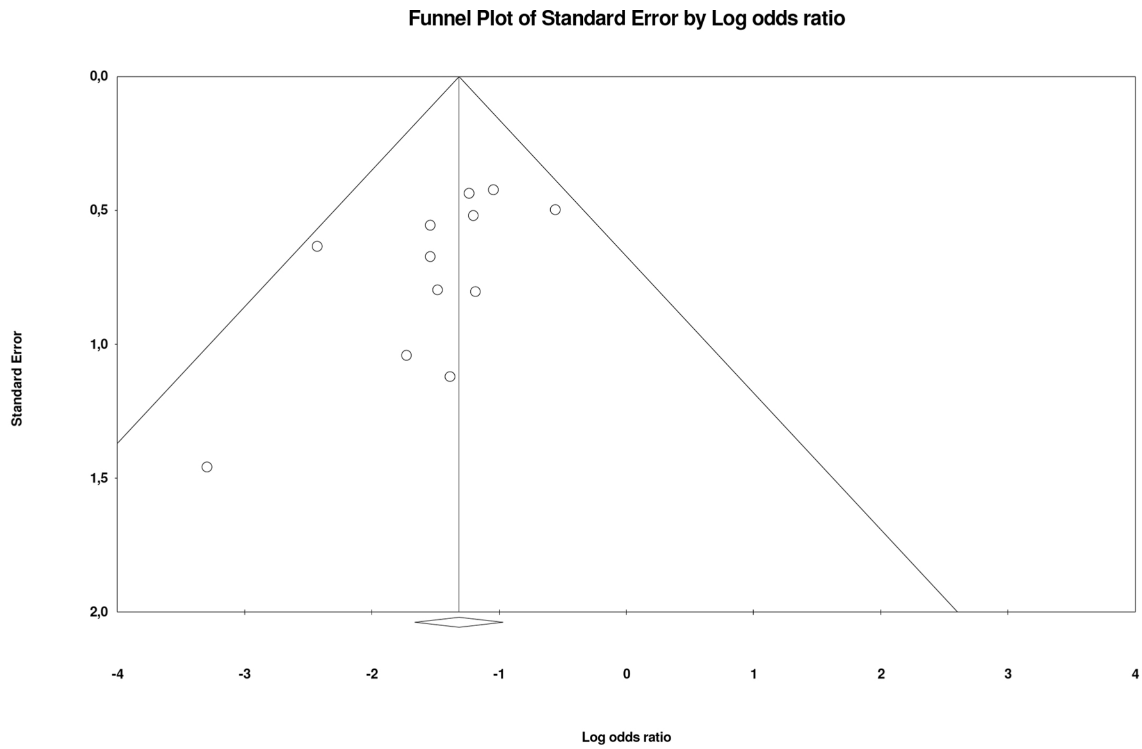

Figure 4 Analysis of publication bias: funnel plot of SE by log OR.

changes of LVEF and LVEDD in isolated annuloplasty versus annuloplasty+subannular repair subgroups are summarised in table 4.

DISCUSSION

Pathophysiological background of secondary MR

Type IIIb secondary MR, defined as secondary MR with reduced systolic leaflet motion, is a disease of the left ventricle and results from a complex remodelling process of the whole 'ventriculo-mitral unit'.[8] The European Society of Cardiology guidelines on the management of valvular heart disease define secondary MR as a sequel of geometrical distortion of the subvalvular mitral apparatus, caused by LV dilatation and remodelling in dilated/ischaemic cardiomyopathy.[29] From the pathophysiological point of view, type IIIb secondary MR results from progressively increasing distance between the tips of papillary muscles and the mitral annular plane (figure 1). Keeping this in mind, standard surgical technique that addresses 'only' mitral valve annulus is unable to adequately treat the underlying mechanism of secondary MR. This correlates well with the clinical data indicating that standard annuloplasty leads to high reoccurrence rate of secondary MR after mitral valve repair.[2 4–7] Therefore, additional subannular manoeuvres that address LV disease seem to be reasonable. Several subannular techniques were developed to correct distorted subvalvular geometry by reducing the distance between papillary muscles tips and mitral annular plane. Recent randomised trial by Acker *et al* showed that reverse LV remodelling was strongly dependent on the functional result of mitral valve repair. Those patients who had postoperative MR recurrence of grade 2 and more showed no significant reduction of their LVESVI at 2-year follow-up.[2 12] Furthermore, a recent study revealed a significant correlation between reverse LV remodelling and the improvement in survival of patients with secondary MR.[30] Therefore, in our current meta-analysis, we aimed to evaluate the long-term effect of subannular techniques in combination with the standard ring annuloplasty.

Table 3 MR recurrence rates in different subannular techniques

Point of action	Subannular technique	Paper	Patients (n)		Freedom from MR>2 at time of >3 years of follow-up (%)		Effect size (Cohen's d)
Base of PM	PM approximation	20 27	108	145	75.6	81.8	0.15
	PM sling	23	37		100		
Head of PM	PM relocation	14 22 24 26	270	300	96.7	96.6	0.47
	Ring and string	15	30		96		
PML	PML extension	17	44	255	93	91.9	0.28
	PML duplication	21	136		89.6		
	PML shortening	25	75		93		
Chordae tendineae	Secondary chordal cutting	16	43		85	85	0.08

Freedom from MR>2 at time of >3 years of follow up. Studies included in the meta-analysis are summarised according to the point of action of the specific subannular reconstruction techniques used.
MR, mitral regurgitation; PM, papillary muscle; PML, posterior mitral leaflet.

Table 4 Echocardiographic follow-up parameters of study subgroups

	Group A	Group B	
Variable	Annuloplasty+subannular repair	Isolated annuloplasty	P value
n*	636	301	
LVEF* %	44.1±7.5	45.9±9.0	0.1
Δ LVEF %	+8.9	+5.8	
LVEDD* (mm)	55.2±7.0	56.1±7.4	0.3
Δ LVEDD (mm)	−6.6	−1.4	

Even though no significant difference in LVEDD/LVEF was found between the two study groups, a tendency of greater LVEDD reduction/recovery of LVEF can be noted in the study group (Δ LVEDD/Δ LVEF).
n*=number of patients at time of follow-up.
LVEF*=mean LVEF±SD at time of follow-up.
LVEDD*=mean LVEDD±SD at time of follow-up.
ΔLVEDD (mm)=LVEDD (mm) baseline–LVEDD (mm) follow-up.
ΔLVEF %=LVEF% baseline–LVEF % follow-up.
LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction.

Reoccurrence of secondary MR

The main finding from our meta-analysis is that adding subannular manoeuvre to the standard ring annuloplasty is associated with a significant reduction of the late reoccurrence rate of secondary MR. Given the fact that secondary MR reoccurrence is mostly reported after the initial 'silent' interval of 6–12 months postoperatively,[2 7] we considered the time interval of at least 3 years after mitral valve repair to be adequate for primary endpoint analysis. Although reoccurrence rate of MR>2 was still in the range of 10% in the study group, such early 'feasibility' studies reflect a wide range of distinct surgical manoeuvres and often include 'learning curve' experience. Nonetheless, regardless of the subannular technique used, functional result after mitral valve repair was significantly better in the study group, which indicates the importance of subannular correction when treating type IIIb secondary MR.

A systematic overview of MR recurrence rates in the different studies, included in our meta-analysis, is provided in table 3. Considering marked between-study heterogeneity (eg, number of patients, combination of subannular techniques used, severity of cardiomyopathy, time of the last follow-up), no definite conclusions might be drawn from these data. Although 'papillary muscles techniques' were the most commonly used manoeuvres in the included studies (ie, 411/743 (55.3%) patients), our meta-analysis was not powered to analyse the most appropriate subannular manoeuvre in secondary MR treatment.

This technical issue should be addressed in the subsequent prospective studies designed to compare the effectiveness and reproducibility of different subannular manoeuvres.

Reverse remodelling

The main argument for additional use of subannular manoeuvres (eg, papillary muscle relocation) might be that these may improve reverse LV remodelling by restoring normal LV geometry. On the other hand, some subannular manoeuvres, such as secondary chordae cutting, may further aggravate LV remodelling, which is well known in the mitral valve replacement surgery. Given a strong association between reverse LV remodelling and success of mitral valve repair (MR<2),[12] one may hypothesise that even though chordal cutting might initially deteriorate LV geometry, a stable repair result (ie, less MR recurrence) might outweigh this limitation in the long term. Therefore, the prospective comparison of LV remodelling parameters among different subannular repair techniques would be of major interest. Unfortunately, those LV remodelling variables were strongly under-reported in the included retrospective studies. Given the fact that detailed follow-up information regarding the actual number of patients submitted to echocardiographic follow-up was available for a limited number of studies, even mean values of LVEDD and LVEF should be interpreted with caution. This precluded any further comparison of LV geometry between subannular repair techniques.

Study limitations

Most of the included studies were observational, with the exception of one prospective randomised trial.[27] Therefore, our analysis contains all the limitations of retrospective study design. We aimed to overcome this limitation by combining meta-analysis design with the sensitivity analyses and the evaluation of publication bias. Second, several studies[14 17 21 23 25] reported specifically on the study group (ie, combination of annuloplasty with subannular repair) only.

Additionally, a number of confounding variables (ie, medical therapy, location of myocardial ischaemia, biventricular pacing and presence of atrial fibrillation) which have a well-established impact on ventricular remodelling might account for differences in outcome between the two groups. Given the fact that medical therapy was reported in only one-third of the whole study population (group A (study): 18.7% (139/743 patients), group B (control): 42% (147/350 patients)), no valuable conclusions can be drawn from these data. Since subannular procedures were performed in the study group only, and information on the specific location of myocardial infarction was only available

Key messages

What is already known on this subject?

- In secondary mitral regurgitation (MR) with restricted systolic leaflet motion, long-term outcome of surgical mitral valve repair by isolated annuloplasty is accompanied by a high MR reoccurrence rate, which varies between 15% and 60% in different studies. Mitral valve replacement has been suggested to improve the durability of mitral surgery, however potentially at the price of increased perioperative mortality and prosthesis-related complications.

What might this study add?

- Our study demonstrates that mitral annuloplasty with simultaneous subannular repair is associated with significantly better long-term stability (freedom from MR reoccurence >2) in secondary MR with restricted systolic leaflet motion, as compared with annuloplasty alone (OR 0.27, 95% CI 0.19 to 0.38, P=0.0001).

How might this impact on clinical practice?

- The proof of improved durability of mitral valve repair when using simultaneous subannular repair in secondary MR might have an important impact on the clinical practice. The most important positive effects would be the increased rate of mitral valve repair in secondary MR and thereby prevention from the prosthesis-associated risks of mitral valve replacement, including bleeding events, thromboembolic complications, endocarditis and structural valve degeneration.

in 4 out of 12 included studies (28.1% (209/743 patients)), the question which location best responds to subannular procedures cannot be answered. Unfortunately, only a single trial reported on the presence of pacemaker devices.[16] However, even in this publication no information regarding biventricular pacing was provided. While the reporting on preoperative atrial fibrillation was similarly limited in both groups (table 2), only a single study included follow-up data on the persistence of AF,[16] which is obviously insufficient to draw any valuable conclusion.

Furthermore, some baseline characteristics were under-reported in the originally published data (ie, quantitative LV measurements such as LVEDD, Left ventricular end-systolic diameter (LVESD), left ventricular end-systolic diameter index (LVESDI) and surgical risk stratification scores). These lacking data may limit the comparability between study subgroups to some extent.

Finally, due to the heterogeneity of subannular manoeuvres used, we are unable to address the question whether all of them would lead to improved long-term mitral valve stability after surgical mitral valve repair.

CONCLUSION

Mitral valve annuloplasty with simultaneous subannular repair was associated with a significant reduction of late reoccurrence of secondary MR after mitral valve repair, as compared with annuloplasty alone. Prospective cohort studies are needed to determine when and what subannular technique should be best integrated in the standard secondary MR treatment.

Contributors EKH and EG planned the meta-analysis. EKH did the primary literature research. EKH und EG did the detailed review of all eligible papers. Statistical analyses were performed by EKH and reviewed by EG. The manuscript was written by EKH and EG. HR did the proof reading of the manuscript and was a valuable contributor for the introduction and discussion. HR, EG and EKH are responsible for the overall content as guarantors.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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