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Aortic Valve Repair: A Systematic Review and Meta-analysis of Published Literature

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Abstract

Background: **It is widely accepted that aortic valve disease is surgically managed with aortic valve replacement (AVR) using different available prostheses. The long-term survival, durability of the valve, and freedom from reoperation after AVR are well established in published literature. Over the past two decades, aortic valve repair (AVr) has evolved into an accepted surgical option for patients with aortic valve disease. We review and analyze the published literature on AVr.** ***Methods:*** **A systematic review of the current literature was performed through three electronic databases from inception to August 2013 to identify all relevant studies relating to aortic valve repair. Articles selected were chosen by two reviewers. Articles were excluded if they contained a pediatric population or if the patient number was less than 50.** ***Results:*** **Twenty-four studies conformed to the inclusion criteria for inclusion in the systematic review. In total, 4986 patients underwent aortic valve repair. 7 studies represented bicuspid aortic valve (BAV) repair, 5 studies represented cusp prolapse, and 3 studies represented valve repair with root dilation or aneurysm. Overall weighted in-hospital mortality for all studies was low (1.46% ± 1.21). Preoperative aortic insufficiency (AI) ≥ 2+ did not correlate to reoperation for valve failure (Pearson's Rs 0.2705, *P* = 0.2585). AI at discharge was reported in 9 studies with a mean AI ≥ 2+ in 6.1% of patients. Weighted average percentage for valve reoperation following BAV repair was 10.23% ± 3.2. Weighted average reoperation following cusp prolapse repair was 3.83 ± 1.96. Weighted average reoperation in aortic valve sparing procedures with root replacement was 4.25% ± 2.46. Although there are limitations and complications of prosthetic valves, especially for younger individuals, there is ample published literature that confers strong evidence for AVR. On the contrary, aortic valve repair may be a useful option for selected patients, but there is lack of uniformity in data and absence of compelling supporting evidence. An international multi-center study comparing and assessing the results between AVR & AVr is the next step required. Currently, higher levels of evidence do not exist for aortic valve repair.**

Key Words

Aortic valve repair · Aortic valve replacement · Aortic valve surgery · Meta-analysis · Aortic valve

Introduction

It is widely accepted that aortic valve disease is surgically managed with aortic valve replacement (AVR) using different available prostheses. The long-term results and survival, durability of the valve, and freedom from reoperation after AVR are well established in published literature. Over the past two decades, aortic valve repair (AVr) has evolved into an accepted surgical option for patients with aortic valve disease. Current understanding of the mech-

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anisms of valve dysfunction and the etiology of lesions enabled surgeons to modify their techniques in aortic valve repair. Although early results are acceptable, the long-term results, durability of the repair, and freedom from reoperation are still variable. This systemic review and meta-analysis examines the worldwide published literature to draw conclusions on the applicability, durability and outcomes of aortic valve repair as a surgical option to treat aortic valve pathology.

Methods

Search Strategy

Electronic searches were performed in PubMed, Ovid Medline and Cochrane. No limits were placed on dates and included studies from database inception to August 2013. Limits were placed for studies published in the English language. Search terms were charted to Medical Subject Headings and combined using Boolean operations. Search terms included: aortic valve repair OR aortic valve preservation OR aortic valve reconstruction. Reference lists of papers found in the literature search were manually searched to assess suitability for inclusion in this review. Articles were first screened by two reviewers (M.B. and M.F.) based on their titles and abstracts. All identified articles were systematically assessed using the inclusion and exclusion criteria for further study.

Selection Criteria

Articles deemed eligible for inclusion were those in which patient cohorts underwent surgical repair of the aortic valve for any type of pathology, including aortic regurgitation, cusp prolapse, bicuspid aortic valve, root dilation or aneurysm, infective endocarditis, rheumatic disease, or a combination of any of those listed.

Articles were excluded if they contained a pediatric population, defined as patients aged $<$ 18 years, if the patient number was less than 50, if there was less than 100 patient years follow up, if the paper did not report mortality or morbidity, or only included patients operated on an emergency basis.

Data Extraction

All data were extracted from selected articles by two reviewers (M.B. and M.F.). Results were collected on Microsoft Excel for Windows. Statistical analysis was performed using GraphPad Prism. Patient-years (pt-yrs) were either recorded from the article or calculated if not reported by multiplying the number of patients with the mean follow-up time reported. Studies reported from the same center were addressed in data analysis, and if patient cohorts from each study overlapped, the study with the smaller cohort was excluded to prevent patient duplication in the study. Data are presented as mean $\pm$ standard deviation. Weighted means are calculated utilizing either total sample size or patient follow up years.

Results

Identification of Studies

A total of 8761 studies were identified from 3 databases (PUBMED, OVID and COCHRANE) (Fig. 1). After exclusion of duplicates (3982), papers deemed irrelevant from the titles (4518), and papers deemed irrelevant from the abstracts (178), 83 papers remained for full text review. Of these, 59 were excluded as not conforming to the inclusion criteria. The remaining 24 studies were included in the systematic review and meta-analysis [1–24].

Study Characteristics

Study characteristics are displayed in Table 1. In total, 4986 patients underwent aortic valve repair. After excluding studies that may represent overlap of patient cohorts, 15 studies remained: 7 studies representing BAV repair, 5 studies representing cusp prolapse, and 3 studies representing valve repair with root dilation or aneurysm. Studies included were published between 2004 and 2013. The majority of studies originated from 2 centers (Belgium and Germany). All studies bar one were retrospective in nature. There was a single prospective multi-center trial [6].

In all studies, males represented the majority of treated patients (79.8% $\pm$ 10.7) and mean age was 50.8 $\pm$ 5.9 (range 41-65). Average follow up was 4.0 years $\pm$ 1.8 with average follow up-patient years 931.5 $\pm$ 1209.6. Bicuspid valves were present in approximately half of the patient cohort (52.4%). Preoperative AI greater than 2+ was present in 68.2% of patients reported in 58.3% of studies.

Early Outcomes

In-hospital mortality was reported in all studies. Overall weighted in-hospital mortality for all studies was low (1.46% $\pm$ 1.21) (Fig. 2). Cardiopulmonary bypass (CPB) time was reported in 6 studies (Fig. 3), which did not correlate with in-hospital mortality. Preoperative AI $\geq$ 2+ did not correlate to reoperation for valve failure (Pearson's Rs 0.2705, $P = 0.2585$) (Fig. 4). AI at discharge was reported in 9 studies, with a mean AI $\geq$ 2+ in 6.1% of patients (Table 2).

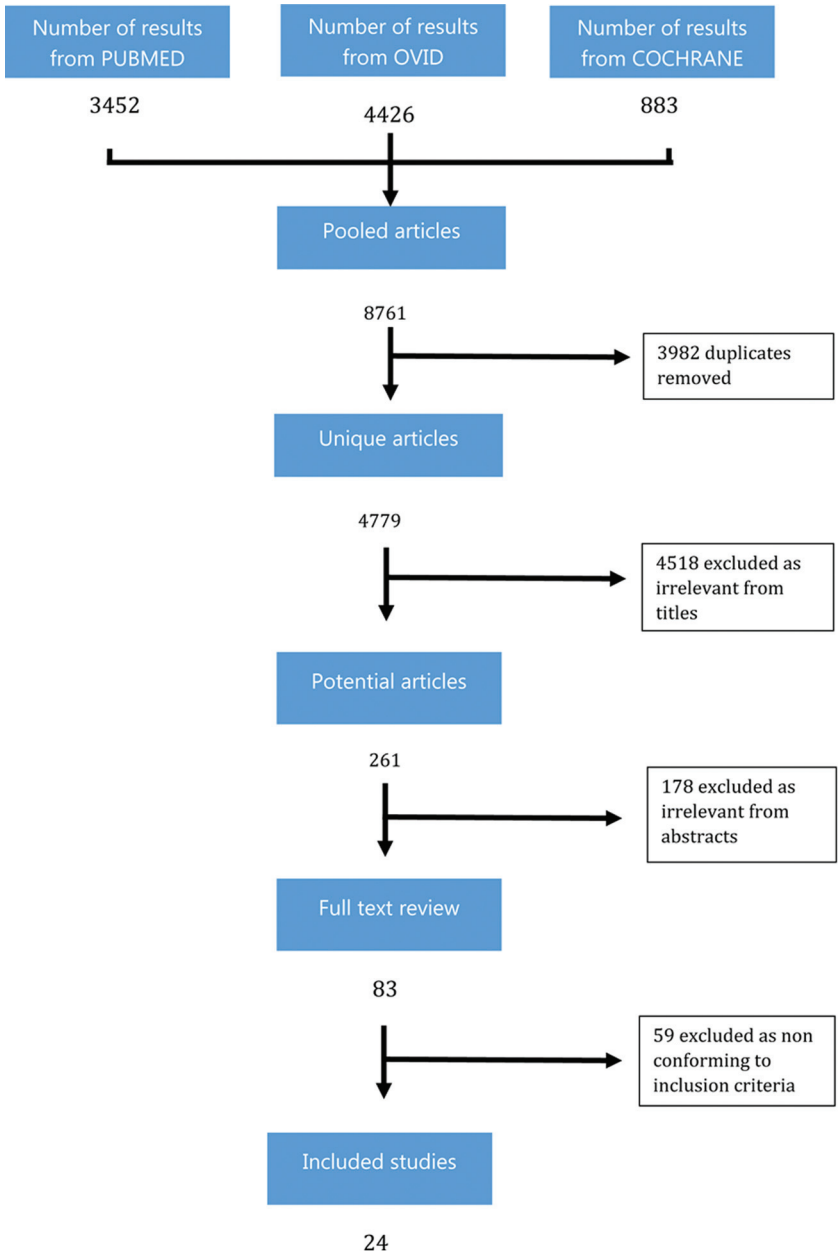

Figure 1. Summary of search strategy, inclusion and exclusion of relevant studies.

Late Outcomes and Valve Related Events

BAV repair represented the majority of patients undergoing aortic valve repair (Table 3). Of all studies, 7 solely assessed BAV repair. Average follow up in this cohort was for one year. In this group, reoperation required due to operated valve failure was reported in all studies. Weighted average percentage for reoperation to valve following BAV repair was 10.23% ± 3.2 (Fig. 5). Valvular endocarditis following BAV repair was reported in 5 studies with a weighted average of 1.72% ± 1.3 (Fig. 6). Other late outcomes such as stroke/TIA (transient ischemic attack) rates were reported in 4 studies with an average rate of 2.7%.

Studies solely investigating cusp prolapse were 5 (Table 4). Average follow up in these studies was 3.72 years ± 0.74. Of these studies, 3 reported reoperation due to valve failure (Fig. 7). Weighted average reoperation following cusp prolapse repair was 3.83 ± 1.96. Negligible rates of TIA and stroke were reported in 3 studies (average 0.53%) (Table 4).

Table 1. Study Characteristics

Authors	Year	Location	Type	No. pts. (n)	Mean age (years)	Male (%)	BAV (%)	Marfan (%)	F/U (years)	F/U pt yrs
Kari et al (1)	2013	Stanford, USA	Retrospective	50	45	80	100	9	3	190
Price et al (2)	2013	Belgium	Retrospective	475	53	81	34	NR	4.6	2152
Aicher et al (3)	2013	Germany	Retrospective	559	47.2	86.8	100	NR	4.6	2559
Vohra et al (4)	2013	Belgium	Retrospective	471	52.1	81.1	34.8	9.3	11.2	5275.2
Luciani et al (5)	2012	Italy	Retrospective case control	58	43	79.3	34.7	NR	3.8	220.4
Fattouch et al (6)	2012	Italy	Retrospective	216	53	76.8	27.7	16.6	3.5	756
Baidu et al (7)	2011	Belgium	Retrospective case control	100	47.2	80	43	3	1.7	167
Boodhwani et al (8)	2011	Belgium	Retrospective	55	65	71	30.9	NR	4.3	237
de Kerchove et al (9)	2011	Germany	Retrospective	106	45.5	93.5	100	NR	4.2	445
Aicher et al (10)	2011	Germany	Retrospective	316	49	84.8	100	NR	4	1253
Boodhwani et al (11)	2011	Belgium	Retrospective	122	44	92	100	NR	5.1	620
Boodhwani et al (12)	2011	Belgium	Retrospective	111	56.5	92	43.1	11	3.8	422
Lansac et al (13)	2010	France	Mulitcentre prospective	187	57.7	NR	21.4	39.7	2.4	455.9
Aicher et al (14)	2010	Germany	Retrospective	640	56	72.7	32	NR	4.7	3035
Ashikhmina et al (15)	2010	Mayo	Retrospective case control	108	41	91	100	NR	5.1	541
David et al (16)	2010	Toronto, Canada	Retrospective	64	46	78.1	NR	NR	4.9	313.6
Schäfers (17)	2010	Germany	Retrospective	111	57	74.6	0	NR	3.5	385
Aicher et al (18)	2010	Germany	Retrospective	427	53	70.3	42.4	2.3	2.9	1238
le Polain de Waroux et al (19)	2009	Belgium	Blinded retrospective	186	55.3	79	37	19	1.5	279
de Kerchove et al (20)	2008	Germany	Retrospective	146	50	93	53	3	3.5	185.5
Jeanmart et al (21)	2007	Belgium	Retrospective	71	51	83.3	46.4	4.2	4.2	298
El Khoury et al (22)	2006	Belgium	Retrospective	68	95.6	43	100	NR	2.8	190.4
Minakata et al (23)	2004	Mayo, USA	Retrospective	160	55	79.3	34	NR	4.2	672
Langer et al (24)	2004	Germany	Retrospective	179	54.5	73.8	44.1	5	2.6	465.4

NR = not reported.

Aortic valve sparing procedures with root replacement were reported in 3 studies (Table 5). Of these 3 studies 2 used the remodeling technique with the other using the reimplantation technique. Average follow up in this group was 3.2 years ± 0.97. Reoperation in these studies for valve failure was reported in all 3, with a weighted average of 4.25% ± 2.46 (Fig. 8). Stroke and TIA rates were reported in all 3 studies with an average of 0.98% (Table 5).

Discussion

Every diseased aortic valve may ultimately require replacement. There are few, if any, medical procedures

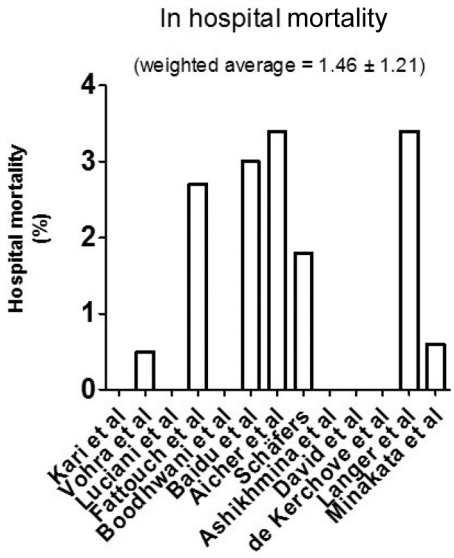

Figure 2. In hospital mortality per study. (Weighted average is based on study size. Average follow up for all studies was four years. Studies originated from the same center were assessed and if potential overlap in patient populations was discovered, the smaller cohort was removed to avoid duplicate patients.)

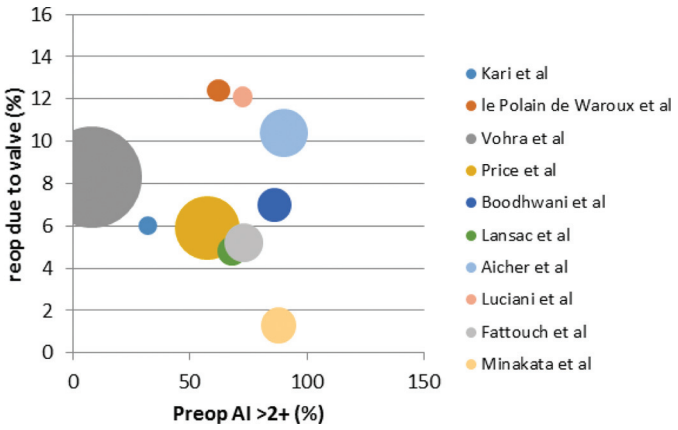

Figure 4. Bubble chart displaying the percentage of patients in each study with AR ≥2+ against reoperation rate for valve failure. (Size of bubble is weighted with patient follow up years for each study. Studies from the same center that may represent similar or overlapping patients are removed to avoid duplication, Pearson's r 0.2705, $P = 0.2585$.)

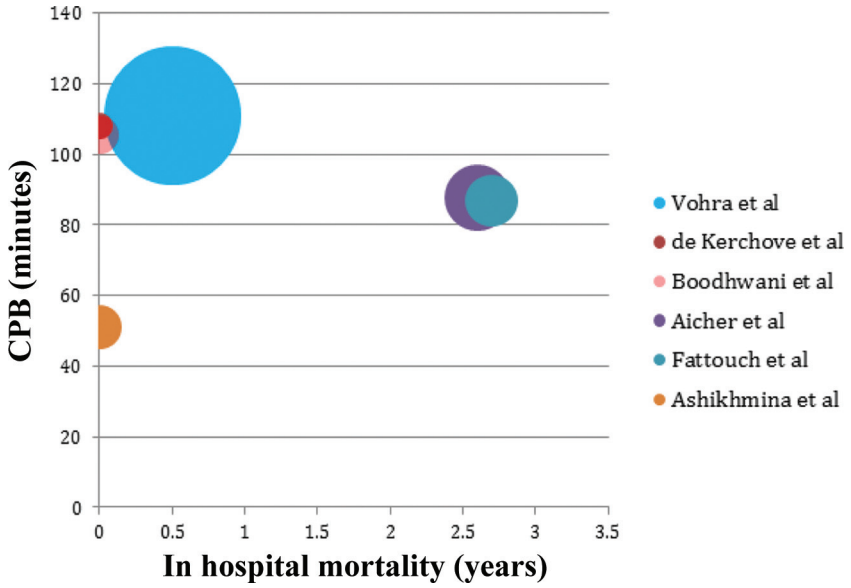

Figure 3. Bubble chart displaying the average cardiopulmonary bypass (CPB) time (where available) per study and in hospital mortality. (Size of bubble is weighted with patient follow up years for each study. Studies from the same center that may represent similar or overlapping patients are removed to avoid duplication.)

Table 2. Study AI Characteristics Preoperative and At Discharge

Authors	Year	No. pts.	Mean age	F/U	F/U pt yrs	LVEF >50	Preop AI (≥2+)	Discharge AI (≥2+)	Reop due to valve (%)
Kari et al	2013	50	45	3	190	NR	32	NR	6
Vohra et al	2013	471	52.1	11.2	5275.2	NR	7.9	5.7	8.3
Aicher et al	2013	559	47.2	4.6	2559	NR	NR	NR	10
Price et al	2013	475	53	4.6	2152	88.4	57.5	NR	5.9
Luciani et al	2012	58	43	3.8	220.4	NR	72.4	NR	12.1
Fattouch et al	2012	216	53	3.5	756	NR	73	NR	5.2
Boodhwani et al	2011	55	65	4.3	237	NR	NR	7	1.8
Baidu et al	2011	100	47.2	1.7	167	69	NR	NR	8
de Kerchove et al	2011	106	45.5	4.2	445	88.7	80.2	4	8.5
Aicher et al	2011	316	49	4	1253	NR	90.2	NR	10.4
Boodhwani et al	2011	122	44	5.1	620	NR	86	7	7
Boodhwani et al	2011	111	56.5	3.8	422	NR	91	12	8
Lansac et al	2010	187	57.7	2.4	455.9	NR	67.9	NR	4.8
Aicher et al	2010	640	56	4.7	3035	NR	NR	NR	5.6
Ashikhmina et al	2010	108	41	5.1	541	NR	NR	NR	17.6
David et al	2010	64	46	4.9	313.6	NR	NR	NR	1.5
Aicher et al	2010	427	53	2.9	1238	NR	NR	3	3
Schäfers	2010	111	57	3.5	385	NR	NR	NR	4
le Polain de Waroux et al	2009	186	55.3	1.5	279	NR	62.2	NR	12.4
de Kerchove et al	2008	146	50	3.5	185.5	NR	NR	8	4
Jeanmart et al	2007	71	51	4.2	298	NR	90.1	NR	3.1
El Khoury et al	2006	68	95.6	2.8	190.4	NR	56.5	0	10
Langer et al	2004	179	54.5	2.6	465.4	NR	NR	NR	2.8
Minakata et al	2004	160	55	4.2	672	NR	88	8	1.3

NR = not reported.

that are as effective in relieving symptoms, improving quality of life, and also increasing long-term survival as much as AVR for aortic stenosis (AS) or aortic regurgitation (AR). AVR is associated with low perioperative morbidity and mortality. The average perioperative mortality in the Society of Thoracic Surgeons database is 3.0% to 4.0% for isolated AVR and 5.5% to 6.8% for AVR plus coronary artery bypass grafting (CABG) [25,26]. A review of Medicare data, involving 684 US hospitals and more than 142,000 patients, indicates that the average in-hospital mortality for AVR in patients over the age of 65 years is 8.8% [27,28].

The use of a mechanical valve exposes the patient to lifelong need for anticoagulation and the risks of anticoagulant-related bleeding. Thromboembolic events and valve thrombosis can occur, especially if anticoagulation therapy is altered or suboptimally delivered. The risk of major bleeding with long-term anticoagulation is approximately 1% per year; however, this significantly increases with increasing age [27]. Anticoagulation in females of reproductive age poses its own complexities and risks. There are several advantages to aortic valve replacement, including ease of insertion, safety, durability, excellent hemodynamic and long-term track record of performance. However, aortic valve replacement inherently is associated with certain disadvantages, in addition to the aforementioned. These include issues of durability, infection, valve degeneration and patient-prosthesis mismatch. Banbury et al confirmed that younger age decreases durability of biological prostheses [29]. They found that freedom from explant due to structural valve damage (SVD) was 99%, 94%, and 77% at 5, 10, and 15 years. Studies analyzing factors influencing structural valve damage (SVD) post AVR conclude that SVD is promoted by the age at implantation (younger age), site of implantation (mitral position), gender (male), and valve type (porcine) [30–33]. Also, not all patients with SVD undergo reoperation within the time frame of the 15-year follow-up.

Table 3. Outcomes in BAV Repair

Authors	Year	No. pts. (n)	F/U (years)	F/U pt yrs	Reimplantation (%)	Remodeling (%)	In-hosp mortality (%)	Reop due to valve (%)	Valve post op endocarditis (%)	TIA (%)	Stroke (%)
Kari et al	2013	50	3	190	100	0	0	6	2	2	0
Aicher et al	2013	559	4.6	2559	NR	NR	0.50	10	NR	NR	NR
de Kerchove et al	2011	106	4.2	445	74	26	0	8.5	2.8	NR	8
Aicher et al	2011	316	4	1253	NR	NR	0.63	10.4	0.6	NR	NR
Boodhwani et al	2011	122	5.1	620	34	10	0	7	1.6	0.8	2.5
Ashikhmina et al	2010	108	5.1	541	NR	NR	0	17.6	3.8	NR	2.8
El Khoury et al	2006	68	2.8	190.4	NR	NR	0	10	NR	NR	NR

NR = not reported.

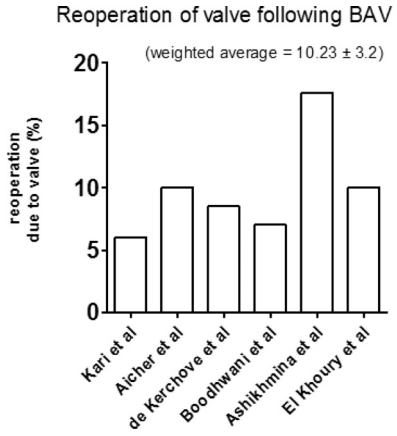

Figure 5. Graph displaying the percentage of patients in each study requiring reoperation due to valve failure. (Average follow up 4.1 ± 0.93 years.)

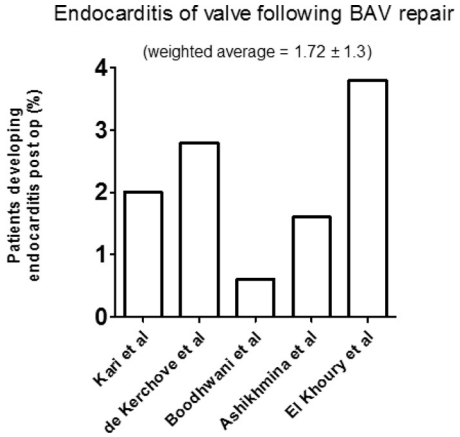

Figure 6. Graph displaying the percentage of patients in each study reported with endocarditis following BAV repair. (Average follow up 4.1 ± 0.93 years.)

The alternative option to aortic valve replacement is aortic valve repair. This was even attempted before the advent of cardiopulmonary bypass using different techniques like circumclusion [34] and bicuspidization [35]. Lillehei in 1958 [36], using cardiopulmonary bypass, also applied the bicuspidization technique as well as single cusp enlargement using Ivalone sponge. Later, other techniques were developed, such as plication of the aortic annulus [37] and annuloplasty [38,39]. Mulder described in 1960 a variety of techniques referred to as valvuloplasty [40]. Later, Starr [41] and Spencer [42] described their techniques to repair aortic valve prolapse concomitant with VSD. Surgeons became more involved with the concept of aortic valve repair after annular disruptions and other balloon-induced injuries that caused acute insuffi-

Table 4. Outcomes in Cusp Prolapse Repair

Authors	Year	Location	No. pts.	Mean age	Male %	% BAV	F/U	F/U pt yrs	In-hosp mort	Valve post op endocarditis	TIA	Stroke	CPB	AXC
David et al	2010	Toronto, Canada	64	46	78.1	NR	4.9	313.6	0	NR	NR	NR	NR	NR
de Kerchove et al	2008	Belgium	146	50	93	53	3.5	185.5	0	0.7	0	2.1	108	88
Boodhwani et al	2011	Belgium	111	56.5	92	43.1	3.8	422	0	0	0.9	0.9	105.5	NR
Aicher et al	2010	Germany	427	53	70.3	42.4	2.9	1238	2.6	0.5	NR	NR	87.7	62.7
Schäfers	2010	Germany	111	57	74.6	0	3.5	385	1.8	4	0.9	0	NR	NR

NR = not reported.

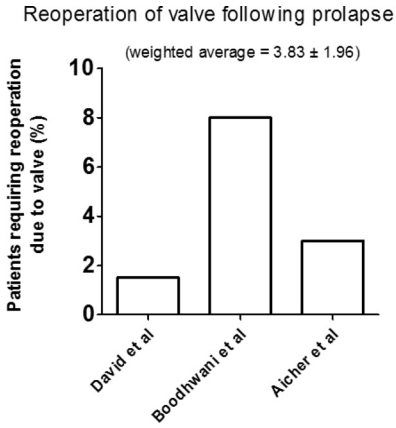

Figure 7. Graph displaying the percentage of patients per study requiring reoperation due to valve failure following prolapse repair. (Average follow up 3.72 ± 0.74 years.)

ciency in young patients requiring immediate repair [43].

The techniques of aortic valve repair have been modified since those early times. Modern techniques have been grouped into the following categories: 1) Nonaneurysmal related annular dilation of the valve may be corrected with circular annuloplasty, commissural annuloplasty (commissural plication), and complex valve extension using pericardium. 2) Cusp prolapse is dealt with using techniques of triangular resection, leaflet resuspension, and plication of the free edge of the leaflet. 3) Valve stenosis is corrected via commissurotomy. 4) Cusp perforation is directly patch repaired.

The key questions that need to be clarified in aortic valve repair include the following.

1) What is the durability of aortic valve repair?

Given the variable strategies, the different techniques, and the short term results, the answer remains ambiguous. Initially, aortic valve repair was reserved for young patients, thus avoiding major risks related to anticoagulation and allowing better quality of life. This trend has changed and extended. AVr is now an option to be considered in a wider range of patients, with reported clinical results now extending to the early midterm stage. Our meta-analysis revealed that reoperation is 10.2% for repair of bicuspid aortic valve. BAV repair makes up the mainstay of patients undergoing aortic valve repair despite a relatively small number of studies with a relative small average follow up time. Studies looking primarily at cusp prolapse

Table 5. Outcomes of Studies Evaluating Aortic Valve Repair in Patients with AR Secondary to Root Dilation or Aneurysm

Authors	Year	No. pts. (n)	Mean age (n)	F/U (years)	F/U pt yrs	Reimplantation (%)	Remodeling (%)	in-hosp mort	reop due to valve	Valve post op endocarditis	TIA	Stroke
Kari et al	2013	50	45	3	190	100	0	0	6	2	2	0
Boodhwani et al	2011	55	65	4.3	237	0	100	0	1.8	1.8	0	1.8
Lansac et al	2010	187	57.7	2.4	455.9	0	100	NR	4.8	1.1	1.60	0.5

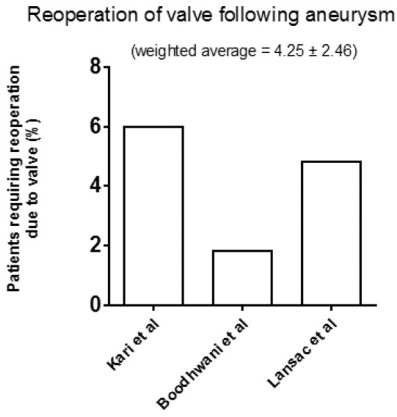

Figure 8. Percentage of patients requiring reoperation due to valve failure following aortic valve repair with concomitant aneurysm repair. (Average follow up 3.2 ± 0.97 years.)

repair and root dilation with aortic valve repair represent a smaller number with reoperation rates between 3-4%. However, these studies include a much smaller average follow up.

There are no clear indications on when repair should be applied, and data showing its safety and durability are limited. AVr is confounded because most reports describe mixed groups of patients, including those with tricuspid and bicuspid valve repairs, as well as valve repair performed during procedures for aortic root reconstruction. Long-term survival data are scarce, and comparison is currently made with no control group undergoing aortic valve replacement. In the published literature, the incidence of valve-related complications is low, with recurrent aortic regurgitation being the most frequent late complication of repair. While surgical mortality is low, reoperation rates are high.

During our study, aortic insufficiency was not always reported in a standardized way. Thus comments on only a small number of studies can be made.

The majority of studies operated on patients with AI $\geq$ 2+. However, there was significant variation and reoperation rates were analyzed to see if there was a correlation with degree of preoperative AI. No correlation was seen between preoperative AI and reoperation rates. At discharge AI $\geq$ 2+ was 6.1%. AI at follow up was not reported in a standardized way, in grading technique or time, and was therefore not included in this study. However, future studies addressing both these factors would be of considerable interest in assessment of the durability of the repair.

2) What are the reasons for valve repair failure?

Our meta-analysis found a reoperation rate of 10.3% for repair of bicuspid aortic valve. Ashikhmina et al. (15) report the potential risk factors related to BAV repair failure, which are: time of operation: age at original BAV repair; sex; body mass index; year of operation; era of operation (before 2000 or after 2000); left ventricular function; concomitant cardiac pathologic factors (eg, coarctation); AV morphologic characteristics as described by the operating surgeon, including calcification; AV repair techniques; concomitant procedures; and mean AV gradient at follow-up transthoracic echocardiographic analysis.

Conclusion

Although there are limitations and complications of prosthetic valves, especially for younger individuals, there is ample published literature that provides strong evidence for AVR. On the contrary, aortic valve repair may be a useful option for selected patients, but there is lack of uniformity in data and lack of compelling long-term evidence in its favor. An international multi-center study comparing results between AVR and AVr is the next step required.

Limitations

Primarily, this study is limited due to the small number of published reports available. Furthermore, the majority of available studies are observational in nature. Currently, higher levels of evidence do not exist for aortic valve repair. Only a select number of centers and surgeons perform aortic valve repair. In this study, we identified only one prospective trial. Single-centered studies mean that patient numbers remain relatively small reducing the potential to draw definitive conclusions even when studies are combined. Analysis of type of repair is complicated by surgeon preference and valve dysfunction etiology.

There is a process and a learning curve in aortic valve repair and the relation to morbidity and mortality is a function of time and case load. . This may imply that studies published earlier do not reflect the current practice. Importantly, there are limited data on long term follow up available, particularly in regards to the need for aortic valve reoperation following repair, valve related events, and mortality. Average follow up in this study was only four years.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

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EDITOR'S COMMENT

The reoperation rate for aortic valve repair is 10%. A tremendous amount of surgical experience, talent, and creativity has gone into achieving this level of success. But, we find ourselves now in a "glass half full or glass half empty" situation. Is a 10% reoperation rate a triumph or a tragedy? It is a triumph in terms of surgical science. But, for those unfortunate young people in the 10% who need an early reoperation, that is a rather tragic outcome. One's overall take on this is all a matter of point of view. Each reader needs to decide this for himself.