Aortic Root Replacement With Biological Valved Conduits

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The execution of Bentall procedures using biological valved conduits is expanding owing to the increased incidence of aortic valve and root diseases in the aging population. To review the available data, a systematic search identified 29 studies with a total of 3,298 patients. Although evidence on short-term results suggested favorable outcomes after biological Bentall operations, data beyond 5 years are limited and highlight the urgent need for further investigations with longer follow-up.

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In 1968, Bentall and DeBono [1] first described the technique for complete replacement of the ascending aorta and aortic valve with the reimplantation of the coronary arteries. Since its introduction, this technique, which subsequently became known as the Bentall operation, has been considered the gold standard in the surgical treatment of combined aortic valve and ascending aorta diseases.

The increasing age of patients currently requiring aortic root surgery and excellent long-term durability of newer biological aortic valve prostheses have stimulated an increase in the use of biological valved conduits, such as biological hand-sewn composite grafts, total biological root prostheses, and allografts. Despite this, data on biological Bentall procedures are sparse.

The present systematic review aimed to evaluate early and late clinical outcomes after Bentall operations using biological valved conduits.

Material and Methods

Literature Search Strategy

Electronic searches were performed using PubMed, from the date of inception to February 2014. To achieve the maximum sensitivity of the search strategy and identify all studies, we combined the following terms: "aortic diseases/surgery" [Mesh] AND Bentall [Title] OR stented bioprosthetic valved conduit [Title] OR biological [Title] OR root bioprosthesis [Title] OR biological valved conduit [Title] OR biological root [Title] OR composite graft [Title] AND English [Language]." The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies. All identified articles were systematically assessed using the inclusion and exclusion criteria.

Selection Criteria

Eligible studies for the present systematic review included those in which patient cohorts underwent Bentall procedures with biological prostheses. Primary end points included in-hospital (or 30 days) mortality, stroke, renal failure, respiratory failure, myocardial infarction, as well as follow-up survival, freedom from aortic reintervention, freedom from thromboembolic events, and freedom from prosthesis endocarditis. Studies that did not include predetermined primary or secondary end points were excluded. When institutions published duplicate studies with accumulating numbers of patients or increased lengths of follow-up, only the most complete reports were included for quantitative assessment at each time interval. All publications were limited to those involving human subjects and reported in the English language. Abstracts, case reports, conference presentations, editorials, and expert opinions were excluded. Review articles were omitted because of potential publication bias and duplication of results.

Data Extraction and Critical Appraisal

All data were extracted from article texts, tables, and figures and subsequently tabulated by three of the investigators (S.C., G.M., M.C.). Data were reviewed by another investigator (D.H.T.). Discrepancies between the reviewers were resolved by discussion and consensus. The final results were reviewed by the senior investigator (M.D.E.). The quality of studies was assessed using criteria recommended by the National Health Service Centre for Reviews and Dissemination case series quality assessment criteria (University of York, UK) [2].

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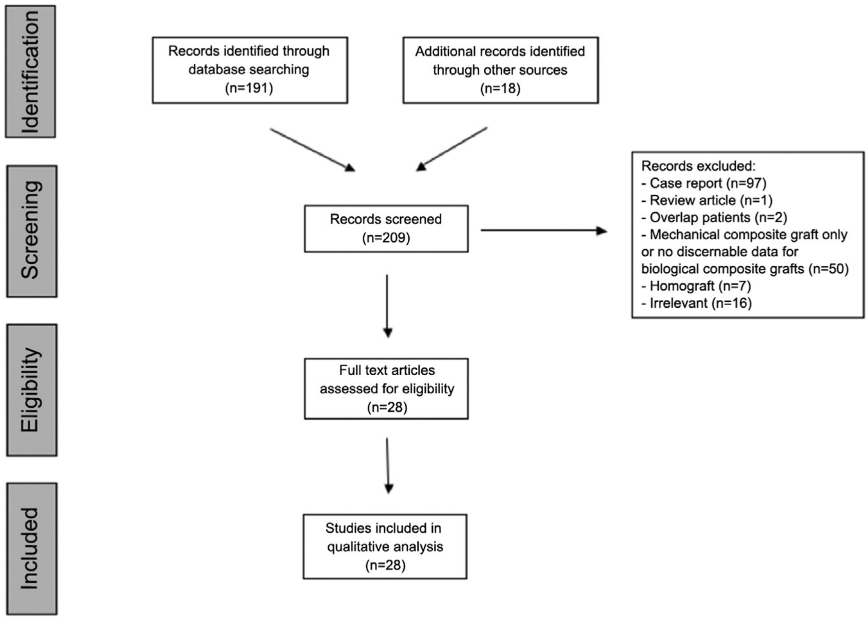

Fig 1. Search strategy of systematic review on Bentall operation using biological valved conduit. From Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA flow-chart [8].

Statistical Analysis

Standard descriptive statistics were used to summarize demographic and baseline data of eligible patients. Data were presented as N (%) or mean ± standard deviation as appropriate. Pooled averages were estimated using the random-effects model as proposed by DerSimonian and Laird [3]. Pooled values were calculated when results were reported by at least 50% of studies and at least 50% of patients. The method of Hozo and colleagues [4] was used to estimate the mean and variance in studies that only reported median and range. Individual patient survival data were reconstructed using an iterative algorithm that was applied to solve the Kaplan-Meier equations originally used to produce the published graphs. This algorithm, as provided by Guyot and colleagues [5], uses digitalized Kaplan-Meier curve data to find numerical solutions to the inverted Kaplan-Meier equations. This algorithm assumed constant censoring (ie, that the censoring mechanism was noninformative), and was implemented in R (v.3.1.0). The reconstructed patient survival data for each study were then aggregated to form combined survival curves. Mixed effects meta-regression was conducted against outcomes on study-level variables. Evidence of publication bias was sought using the methods of Egger and associates [6] and Begg and Mazumdar [7]. If studies appear to be missing in areas of low statistical significance, then it is possible that the asymmetry is a result of publication bias. If studies appear to be missing in areas of high statistical significance, then publication bias is a less likely cause of funnel asymmetry. Intercept significance was determined by the Student's *t* test suggested by Egger and associates [6]. All statistical analyses were conducted with Comprehensive Meta-analysis v2.2 (Biostat Inc, Englewood, NJ) or Stata version 11.0 (Stata Corp, College Station, TX).

Results

Quantity of Studies

A total of 209 studies were identified through PubMed database and other sources. After exclusion of duplicate or irrelevant references, 28 studies remained for assessment. The study selection process is presented in Figure 1 according to the PRISMA statement [8]. One study was separated into two studies because it reported data on two different bioprostheses [9]. A total of 29 series were therefore assessed [9–36]. All of the included studies were retrospective observational studies except one prospective series [16]. Fourteen studies had more than 100 patients (range, 101 to 317 patients) [10, 11, 13, 18, 21, 22, 24, 25, 27, 29, 31, 32, 34, 35], including two multicenter registries [10, 32], and the remaining series had fewer than 100 patients (range, 10 to 80 patients) [9, 12, 14–17, 19, 20, 23, 26, 28, 30, 33, 36].

Fourteen studies reported follow-up greater than 36 months (range, 37 to 92 months) [10, 12, 16, 18, 21, 22, 24, 25, 27, 30, 31, 33–35]. Five studies had follow-up less than 3 years (range, 6 to 24 months) [14, 20, 23, 28, 36], and the remaining studies did not report length of follow-up [9, 11, 13, 17, 19, 26, 29, 32]. The study characteristics are summarized in Table 1. In these 29 series, 3,298 patients underwent the Bentall procedure with a biological prosthesis.

Demographic Data

Overall, 67.5% of patients were male, with a weighted mean age of 67.1 years. Degenerative aneurysm was the sole surgical indication in one study [20], whereas the rest included a combination of aneurysm, acute aortic dissection, and aortic valve endocarditis. Overall, however, degenerative aneurysm was the primary indication

Table 1. *Summary of Study Characteristics*

Author	Year	Study Period	Institution	Study Type	Prosthesis Type	Patients Number	Follow-Up (mo)
Doty [10]	1998	1992–1997	Multiinstitutional (USA, Europe, New Zealand, Canada)	Retrospective	Full-root Medtronic Freestyle	222	48
Wendler [11]	2001	1997–2000	Homburg, Germany	Retrospective	Full-root Medtronic Freestyle Full-root Edwards Prima Plus	149	…
Ehrlich [12]	2001	1987–1998	New York, USA	Retrospective	Composite graft: Hemashield graft and Carpentier Edwards prosthesis or porcine prosthesis	47	38
Kon [13]	2002	1992–1997	North Carolina, USA	Retrospective	Full-root Medtronic Freestyle	104	…
Muller [14]	2003	1998–2001	Innsbruck, Austria	Retrospective	Full-root Medtronic Freestyle	10	6
Carrel [15]	2003	2000–2003	Berne, Switzerland	Retrospective	Shelhigh BioConduit	35	…
Melina [16]	2004	1997–2004	London, UK	Prospective	Full-root Medtronic Freestyle	80	45
Kunihara [17]	2006	1996–2004	Homburg, Germany	Retrospective	Full-root Medtronic Freestyle Full-root Edwards Prima Plus	60	…
Etz [18]	2007	1993–2005	New York, USA	Retrospective	Composite graft: Carpentier-Edwards Perimount and Dacron graft	275	43
Di Bartolomeo [19]	2008	2007–2008	Bologna, Italy	Retrospective	Vascutek BioValsalva	21	…
Bochenek-Klimczyk [20]	2008	2006–2008	Leicester, UK	Retrospective	Vascutek BioValsalva	17	17
Dapunt [21]	2008	1999–2007	Oldenburg, Germany	Retrospective	Full-root Medtronic Freestyle	317	89
LeMaire [22]	2009	2001–2007	Houston, TX, USA	Retrospective	Full-root Medtronic Freestyle Full-root St. Jude Toronto	132	40
Tabata [23]	2009	2005–2008	New York, USA	Retrospective	Composite graft: Carpentier-Edwards Perimount prosthesis and Gelweave Valsalva graft	68	11
Lehmann [24]	2009	2001–2007	Leipzig, Germany	Retrospective	Full-root St. Jude Toronto	186	50
Urbanski [25]	2010	1998–2008	Bad Neustadt, Germany	Retrospective	Composite graft: St. Jude Toronto stentless prosthesis and InterGard vascular graft	182	48
Stewart [26]	2010	2008–2009	New York, USA	Retrospective	Composite graft: 3f Medtronic Bioprosthesis and Gelweave Valsalva graft	20	…
Etz [27]	2010	1995–2008	New York, USA	Retrospective	Composite graft: pericardial or porcine prosthesis and Hemashield graft	307	79
Moorjani (BioValsalva) [9]	2010	2004–2009	Southampton, UK	Retrospective	Vascutek BioValsalva	21	…
Moorjani (Handsew) [9]	2010	2004–2009	Southampton, UK	Retrospective	Composite graft with hand-sewn Carpentier-Edwards Perimount or St. Jude Epic	18	…
Baraki [28]	2010	2007–2009	Hannover, Germany	Retrospective	Vascutek BioValsalva	50	8

(*Continued*)

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Table 1. Continued

Author	Year	Study Period	Institution	Study Type	Prosthesis Type	Patients Number	Follow-Up (mo)
Desai [29]	2011	1997–2007	Philadelphia, PA, USA	Retrospective	Full-root St. Jude Toronto Full-root Medtronic Freestyle Full-root Edwards Prima-plus	128	…
Galinanes [30]	2011	1999–2008	Leicester, UK	Retrospective	No-React BioConduit	67	85
Kaya [31]	2011	1998–2007	Nieuwegein, The Netherlands	Retrospective	Shelhigh BioConduit	175	37
Ennker [32]	2011	1996–2007	Baden, Lahr, Germany Duesseldorf, Germany Witten, Germany	Retrospective	Full-root Medtronic Freestyle	301	…
Mazzola [33]	2012	2001–2010	L'Aquila, Italy	Retrospective	Full-root Medtronic Freestyle	79	53
Kaya [34]	2012	2008–2011	Nieuwegein, The Netherlands	Retrospective	Vascutek BioValsalva	102	92
Gatti [35]	2013	2001–2012	Trieste, Italy	Retrospective	Composite graft: Hemashield graft and Perimount Edwards prosthesis or Medtronic mosaic prosthesis	101	44
Smith [36]	2013	2005–2009	Michigan, USA	Retrospective	Full-root Medtronic Freestyle	24	24
Total number of patients						3,298	

in 75.1% of patients, acute aortic dissection in 7.5%, and endocarditis in 5.7%. Reoperation procedures were performed in 12% of patients, and 10.8% were urgent or emergent. Only 7 series reported logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation) (range, 15.1 to 48.6) [9, 20, 24, 25, 30, 35]. A summary of preoperative characteristics, indication for surgery, and preoperative clinical status is listed in Tables 2 and 3.

Operative Data

Weighted average cardiopulmonary bypass time and myocardial ischemic time were 185 minutes (range, 112 to 318 minutes) and 124 minutes (range, 76 to 242 minutes), respectively.

The Bentall procedure was performed with a Freestyle stentless aortic root bioprosthesis (Medtronic Inc, Minneapolis, MN) in 12 series [10, 11, 13, 14, 16, 17, 21, 22, 29, 32, 33, 36], with different hand-sewn composite grafts in 8 series [9, 12, 18, 23, 25–27, 35], with BioValsalva conduit (Vascutek Terumo, Renfrewshire, UK) in 5 series [9, 19, 20, 28, 34], with Shelhigh BioConduit model NR-2000C (Shelhigh, Inc, Milburn, NJ) or No-React BioConduit (BioIntegral Surgical, Inc, Mississauga, Ontario, Canada) in 3 series [15, 30, 31], with Prima Plus aortic root bioprosthesis (Edwards Lifesciences, Irvine, CA) in 3 series [11, 17, 29], and with Toronto root bioprosthesis (St. Jude Medical, St. Paul, MN) in 3 series [22, 24, 29].

All but three studies [16, 29, 33] reported the method of coronary reimplantation. In particular, the button technique was described in all of these studies, although a few also practiced the classic inclusion technique and the Cabrol technique [12, 18, 22].

Data pertaining to arch surgery were presented in 18 studies [9, 11, 15, 17–19, 21, 22, 24–28, 31, 34–36]. With regard to the method of brain protection, antegrade selective cerebral perfusion was used in 11 studies [18, 19, 22, 23, 26, 28, 31, 32, 34–36], retrograde cerebral perfusion in 3 studies [22, 35, 36], deep hypothermic circulatory arrest in 14 series [9, 11, 12, 17, 18, 21, 22, 27, 29–31, 34, 35], and a combination of antegrade selective cerebral perfusion and retrograde cerebral perfusion in one study [22]. A summary of operative characteristics (with associated cardiac procedures) is listed in Table 4.

Assessment of Safety

All studies reported in-hospital or 30-day mortality [9–36]. Overall, average weighted mortality was 6.4% (range, 0% to 20%). Postoperative stroke was reported in 19 series [9, 11, 17, 18, 20–22, 24, 25, 27–31, 33–36], with an average of 3.7% (range, 0% to 29%). Renal failure was reported in 14 series [9, 18, 20–22, 24, 27, 28, 30, 31, 34–36], respiratory insufficiency was reported in 12 series [9, 18, 19, 22, 26–28, 30, 31, 35, 36], and myocardial infarction was reported in 15 series [9, 11, 14, 18, 20–22, 25, 27, 29, 31, 34–36]. Postoperative renal failure ranged between 0% and 29%, respiratory insufficiency ranged between 3% and 71%, and myocardial infarction was identified in 2.9% of patients (range, 0% to 8%). Atrial fibrillation was reported in only 8 studies (range, 4% to 36%) [16, 17, 20, 22, 25, 30, 35, 36], mediastinitis in 10 series (range, 0% to 6%) [9, 18, 20,

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Table 2. Summary of Preoperative Characteristics[a]

Author	Age (y)	Male, n (%)	DM, n (%)	HT, n (%)	COPD, n (%)	CAD, n (%)	CRF, n (%)	CVD, n (%)	LVEF	NYHA III/IV, n (%)
Doty [10]	…	…	…	…	…	…	…	…	…	…
Wendler [11]	70 ± 9	72 (48.3)	…	…	…	…	…	…	0.58 ± 0.15	…
Ehrlich [12]	75.8 ± 5.5	33 (70.2)	2 (4.3)	29 (61.7)	…	13 (27.7)	…	2 (4.3)	…	…
Kon [13]	72 ± 6.5	47 (45.2)	17 (16.3)	…	19 (18.3)	49 (47.1)	…	12 (11.5)	…	77 (74.0)
Muller [14]	57.8 ± 14	4 (40.0)	1 (10.0)	…	…	2 (20.0)	4 (40.0)	1 (10.0)	…	10 (100)
Carrel [15]	68 ± 7.2	30 (85.7)	…	…	…	…	…	…	…	…
Melina [16]	66 ± 8	55 (68.8)	…	…	…	…	…	…	…	N/A
Kunihara [17]	75 ± 5	9 (15.0)	13 (21.7)	36 (60.0)	10 (16.7)	29 (48.3)	2 (3.3)	4 (6.7)	0.61 ± 0.03	…
Etz [18]	69.3 ± 11.3	202 (73.5)	17 (6.2)	149 (54.2)	8 (2.9)	96 (34.9)	…	24 (8.7)	…	…
Di Bartolomeo [19]	67.8 ± 5.5	16 (76.2)	1 (4.8)	14 (66.7)	2 (9.5)	…	…	…	0.615 ± 0.069	19 (90.0)
Bochenek-Klimczyk [20]	65 ± 10	11 (64.7)	2 (11.8)	11 (64.7)	2 (11.8)	…	…	3 (17.6)	…	8 (47.0)
Dapunt [21]	70.2 ± 10.2	196 (61.8)	41 (12.9)	141 (44.5)	21 (6.6)	…	…	6 (1.9)	…	…
LeMaire [22]	54.8 ± 14	108 (81.8)	…	…	…	41 (31.1)	…	14 (10.6)	…	48 (36.0)
Tabata [23]	66 ± 14.3	49 (72.2)	…	…	…	…	…	…	…	…
Lehmann [24]	62 ± 11.1	148 (79.6)	21 (11.3)	122 (65.6)	31 (16.7)	67 (36.0)	12 (6.5)	9 (5.8)	0.581 ± 0.138	N/A
Urbanski [25]	70 ± 8	119 (65.4)	27 (14.8)	135 (74.2)	16 (8.8)	31 (17.0)	…	17 (9.3)	…	122 (67.0)
Stewart [26]	58 ± 9.8	18 (90.0)	…	…	…	…	…	…	…	…
Etz [27]	71 ± 11	225 (73.3)	19 (6.2)	181 (59.0)	12 (3.9)	105 (34.2)	7 (2.3)	25 (8.1)	…	…
Moorjani (BioValsalva) [9]	70.7 ± 1.7	14 (66.7)	1 (4.8)	15 (71.4)	…	…	…	…	0.509 ± 0.023	N/A
Moorjani (Handsew) [9]	67.6 ± 2.9	13 (72.2)	1 (5.6)	14 (77.8)	…	…	…	…	0.587 ± 0.021	N/A
Baraki [28]	65 ± 7	40 (80.0)	4 (8.0)	23 (46.0)	7 (14.0)	16 (32.0)	4 (8.0)	…	N/A	…
Desai [29]	47.4 ± 9.6	118 (92.2)	68 (53.1)	14 (10.9)	6 (4.7)	…	10 (7.8)	58 (45.3)	…	…
Galinanes [30]	67.9 ± 1.3	40 (59.7)	1 (1.5)	34 (50.7)	11 (16.4)	2 (3.0)	3 (4.5)	5 (7.5)	N/A	30 (45.0)
Kaya [31]	71.1 ± 7.4	102 (58.3)	13 (7.4)	123 (70.3)	23 (13.1)	…	25 (14.3)	21 (12.0)	…	83 (47.0)
Ennker [32]	72 ± 9	133 (44.2)	59 (19.6)	…	54 (17.9)	…	…	21 (7.0)	0.59 ± 0.20	137 (46.0)
Mazzola [33]	73 ± 5.5	48 (60.8)	8 (10.1)	45 (57.0)	12 (15.2)	17 (21.5)	…	…	…	46 (58.0)
Kaya [34]	70.9 ± 7.3	69 (67.6)	12 (11.8)	64 (62.7)	16 (15.7)	…	10 (9.8)	7 (6.9)	…	42 (41.0)
Gatti [35]	68.3 ± 9.2	84 (83.2)	13 (12.9)	79 (78.2)	6 (5.9)	…	2 (2.0)	3 (3.0)	0.563 ± 0.092	21 (21.0)
Smith [36]	57 ± 9.8	15 (62.5)	2 (8.3)	20 (83.3)	1 (4.2)	4 (16.7)	1 (4.2)	1 (4.2)	…	…
Weighted average	67.1	67.5%	11.2%	60.0%	10.5%	…	…	8.4%	…	…
Minimum	47.4	15.0%	1.5%	10.9%	2.9%	3.0%	2.0%	1.9%	0.563	36.0%
Maximum	75.8	90.0%	53.1%	83.3%	17.9%	48.3%	40.0%	45.3%	0.615	100%

[a] Values expressed as number and percentage or mean ± standard deviation.

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; CRF = chronic renal failure; CVD = cerebrovascular disease; DM = diabetes mellitus; HT = hypertension; LVEF = left ventricle ejection fraction; N/A = not applicable; NYHA = New York Heart Association.

Table 3. Indication to Surgery and Clinical Status[a]

Author	Degenerative Aneurysm, n (%)	Acute Aortic Dissection, n (%)	Endocarditis, n (%)	Redo Cardiac Surgery, n (%)	Urgent/Emergent, n (%)	Logistic EuroSCORE (%)
Doty [10]	211 (95.0)	…	11 (5.0)	…	…	…
Wendler [11]	32 (21.5)	3 (2.0)	24 (16.1)	16 (10.7)	…	…
Ehrlich [12]	30 (63.8)	10 (21.3)	…	10 (21.3)	…	…
Kon [13]	…	…	1 (1.0)	…	…	…
Muller [14]	0	1 (10.0)	10 (100)	0	1 (10.0)	…
Carrel [15]	25 (71.4)	4 (11.4)	6 (17.1)	6 (17.1)	…	…
Melina [16]	…	…	…	16 (20)	…	…
Kunihara [17]	…	…	…	…	…	…
Etz [18]	214 (77.8)	14 (5.1)	13 (4.7)	48 (17.5)	35 (12.7)	…
Di Bartolomeo [19]	17 (81)	2 (9.5)	0	2 (9.5)	2 (9.5)	…
Bochenek-Klimczyk [20]	17 (100)	…	…	…	…	15.1 ± 7.4
Dapunt [21]	139 (43.8)	14 (4.4)	21 (6.6)	…	…	…
LeMaire [22]	130 (98.5)	10 (7.6)	3 (2.3)	26 (19.7)	15 (11.4)	…
Tabata [23]	…	9 (13.2)	…	5 (7.4)	9 (13.2)	…
Lehmann [24]	139 (74.7)	3 (1.6)	60 (32.3)	10 (5.4)	3 (1.6)	16.4 ± 14.8
Urbanski [25]	168 (92.3)	3 (1.6)	3 (1.6)	13 (7.1)	6 (3.3)	15.9 ± 14.3
Stewart [26]	14 (70)	5 (25)	…	1 (5.0)	5 (25)	…
Etz [27]	233 (75.9)	48 (15.6)	…	52 (16.9)	35 (11.4)	…
Moorjani (BioValsalva) [9]	15 (71.4)	0	0	0	8 (38.1)	19.1 ± 0.02
Moorjani (Handsew) [9]	13 (72.2)	0	0	0	4 (22.2)	16.4 ± 0.02
Baraki [28]	…	4 (8.0)	2 (4.0)	4 (8.0)	6 (12.0)	…
Desai [29]	…	8 (6.3)	10 (7.8)	28 (21.9)	…	…
Galinanes [30]	60 (89.6)	…	…	22 (32.8)	…	46.8 ± 19.6
Kaya [31]	110 (62.9)	11 (6.3)	20 (11.4)	33 (18.9)	22 (12.6)	…
Ennker [32]	…	…	2 (0.7)	12 (4.0)	6 (2.0)	…
Mazzola [33]	62 (78.5)	8 (10.1)	2 (2.5)	…	…	…
Kaya [34]	81 (79.4)	4 (3.9)	15 (14.7)	2 (2.0)	12 (11.8)	…
Gatti [35]	81 (80.2)	4 (4.0)	…	9 (8.9)	4 (4.0)	15.5 ± 9.4
Smith [36]	…	24 (100)	…	…	24 (100)	…
Pooled average	75.1%	7.5%	5.7%	12.0%	10.8%	…
Minimum	0%	2.0%	0%	0%	2%	15.1
Maximum	100%	100%	100%	32.8%	100%	46.8

[a] Values expressed as number and percentage or mean ± standard deviation.

EuroSCORE = European System for Cardiac Operative Risk Evaluation.

Table 4. Summary of Operative Characteristics[a]

Author	Coronary Reimplantation Technique	CPB Time (min)	Myocardial Ischemia Time (min)	Associated Arch Surgery, n (%)	Type of Brain Protection	Associated Cardiac Procedures, n (%)
Doty [10]	Button	129	103	N/A	…	N/A
Wendler [11]	Button	118 ± 45	83 ± 26	20 (13.3)	DHCA	CABG: 48 (32.2) MV: 10 (6.7) TV: 0 AF: 0 Other: 0
Ehrlich [12]	Classic Button Cabrol	230 ± 50.3	…	N/A	DHCA	CABG: 15 (31.9) MV: 0 TV: 0 AF: 0 Other: 0
Kon [13]	Button	…	110	0	…	CABG: 46 (44.2) MV: 0 TV: 0 AF: 0 Other: 3 (2.9)
Muller [14]	Button	266 ± 54	177 ± 41	0	…	CABG: 0 MV: 2 (20.0) TV: 1 (10.0) AF: 0 Other: 0
Carrel [15]	Button	…	…	6 (17.1)	N/A	CABG: 5 (14.3) MV: 3 (8.6) TV: 0 AF: 0 Other: 0
Melina [16]	…	136 ± 41	94 ± 22	0	…	CABG: 33 (41.3) MV: 0 TV: 0 AF: 0 Other: 0
Kunihara [17]	Button	112 ± 36	76 ± 21	3 (5.0)	DHCA	CABG: 29 (48.3) MV: 7 (11.7) TV: 0 AF: 0 Other: 0
Etz [18]	Classic Button Cabrol	260 ± 57	181 ± 48	133 (48.4)	DHCA ASCP	CABG: 102 (37.1) MV: 14 (5.1) TV: 0 AF: 0 Other: 11 (4.0)

(*Continued*)

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Table 4. Continued

Author	Coronary Reimplantation Technique	CPB Time (min)	Myocardial Ischemia Time (min)	Associated Arch Surgery, n (%)	Type of Brain Protection	Associated Cardiac Procedures, n (%)
Di Bartolomeo [19]	Button	159 ± 72	119 ± 36	5 (23.8)	ASCP	CABG: 2 (9.5) MV: 0 TV: 0 AF: 3 (14.3) Other: 0
Bochenek-Klimczyk [20]	Button	167 ± 55	112 ± 33	0	…	CABG: 0 MV: 0 TV: 0 AF: 0 Other: 0
Dapunt [21]	Button	190 ± 57	88 ± 27	36 (11.4)	DHCA	CABG: 82 (25.9) MV: 11 (3.5) TV: 0 AF: 0 Other: 0
LeMaire [22]	Classic Button Cabrol Others	190 ± 65	109 ± 37	55 (41.7)	DHCA ASCP RCP ASCP+RCP	CABG: 32 (24.2) MV: 3 (2.3) TV: 0 AF: 3 (2.3) Other: 0
Tabata [23]	Button	139	98	N/A	ASCP	N/A
Lehmann [24]	Button	140.9 ± 52	99.8 ± 28	38 (20.4)	N/A	CABG: 31 (16.7) MV: 26 (14.0) TV: 2 (1.1) AF: 14 (7.5) Other: 8 (4.3)
Urbanski [25]	Button	160 ± 40	106 ± 27	76 (41.8)	N/A	CABG: 31 (17.0) MV: 12 (6.6) TV: 0 AF: 0 Other: 6 (3.3)
Stewart [26]	Button	146 ± 110	110 ± 32	1 (5.0)	ASCP	CABG: 1 (5.0) MV: 2 (10.0) TV: 0 AF: 2 (10.0) Other: 1 (5.0)
Etz [27]	Button	260 ± 58	183 ± 49	136 (44.3)	DHCA	CABG: 109 (35.5) MV: 0 TV: 0 AF: 0 Other: 17 (5.5)

(*Continued*)

Table 4. Continued

Author	Coronary Reimplantation Technique	CPB Time (min)	Myocardial Ischemia Time (min)	Associated Arch Surgery, n (%)	Type of Brain Protection	Associated Cardiac Procedures, n (%)
Moorjani (BioValsalva) [9]	Button	141 ± 6	113 ± 6	3 (14.3)	DHCA	CABG: 2 (9.5) MV: 0 TV: 0 AF: 1 (4.8) Other: 0
Moorjani (Handsew) [9]	Button	170 ± 17	115 ± 7	3 (16.7)	DHCA	CABG: 2 (11.1) MV: 1 (5.6) TV: 0 AF: 1 (5.6) Other: 0
Baraki [28]	Button	178 ± 30	106 ± 7	20 (40.0)	ASCP	CABG: 15 (30.0) MV: 2 (4.0) TV: 3 (6.0) AF: 1 (2.0) Other: 0
Desai [29]	…	…	…	…	DHCA	…
Galinanes [30]	Button	183 ± 86	130 ± 45	…	DHCA	CABG: 17 (25.4) Other: 9 (13.4)
Kaya [31]	Button	190 ± 54	125 ± 30	91 (52.0)	DHCA ASCP	CABG: 47 (26.9) MV: 5 (2.9) TV: 0 AF: 0 Other: 7 (4.0)
Ennker [3]	Button	…	…	N/A	ASCP	N/A
Mazzola [33]	…	…	…	0	…	CABG: 17 (21.5) MV: 5 (6.3) TV: 0 AF: 0 Other: 0
Kaya [34]	Button	194 ± 79	133 ± 46	38 (37.3)	DHCA ASCP	CABG: 29 (28.4) MV: 4 (3.9) TV: 0 AF: 0 Other: 3 (2.9)
Gatti [35]	Button	206 ± 58	163 ± 45	60 (59.4)	DHCA ASCP RCP	CABG: 31 (30.7) MV: 7 (6.9) TV: 5 (5.0) AF: 9 (8.9) Other: 0

(*Continued*)

Table 4. Continued

Author	Coronary Reimplantation Technique	CPB Time (min)	Myocardial Ischemia Time (min)	Associated Arch Surgery, n (%)	Type of Brain Protection	Associated Cardiac Procedures, n (%)
Smith [36]	Button	318 ± 120	242 ± 97	24 (100)	ASCP RCP	CABG: 2 (8.3) MV: 1 (4.2) TV: 1 (4.2) AF: 0 Other: 1 (4.2)
Pooled average	…	185	124		…	
Minimum	…	112	76		…	
Maximum	…	318	242		…	

[a] Values expressed as number and percentage or mean ± standard deviation.

AF = atrial fibrillation procedure; ASCP = antegrade selective cerebral perfusion; CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass; DHCA = deep hypothermic circulatory arrest; MV = mitral valve procedure; N/A = not applicable; RCP = retrograde cerebral perfusion; TV = tricuspid valve procedure.

25, 27, 30, 34–36], and pacemaker implantation in 9 series (range, 0% to 20%) [9, 14, 17, 18, 22, 28, 30, 31]. Reoperation for bleeding was reported by all but 8 studies [10, 12–15, 24, 29, 32] and occurred in 7.6% of patients (range, 0% to 28%). Intensive care unit stay ranged between 1.5 and 4.9 days, whereas in-hospital stay ranged between 8.9 and 18.3 days. A summary of early outcomes is listed in Table 5. No statistical correlation between mean age and mortality or the incidence of stroke was identified.

Assessment of Long-Term Efficacy

Long-term survival was reported in 14 studies [12, 14, 18, 20–22, 24, 29–32, 34–36] with 1,882 patients: at 1, 2, 3, 5, and 10 years survival was 88%, 86%, 82%, 76%, and 58%, respectively (Fig 2). Ten studies (1,216 patients) reported freedom from reoperation [12, 13, 16, 20, 21, 28, 29, 31, 34, 36]: at 1, 2, 3, and 5 years, freedom from reoperation was 96%, 94%, 93%, and 90%, respectively (Fig 3). Only 3 studies [12, 24, 29] reported freedom from thromboembolic events (361 patients): at 1, 2, 3, and 5 years, freedom from thromboembolic events was 97%, 97%, 95%, and 94%, respectively (Fig 4). Moreover 3 studies [21, 24, 29] reported freedom from prosthesis endocarditis (631 patients): at 1, 2, 3, and 5 years, freedom from prosthesis endocarditis was 99%, 98%, 96%, and 94%, respectively (Fig 5).

Publication Bias

The funnel plot of Begg and Mazumdar [7] and the test of Egger and colleagues [6] were performed to assess publication bias in the literature. The funnel plot (Fig 6) appears asymmetric, although there is evidence for bias using Begg and Mazumdar's rank correlation method ($p = 0.001$) but not using the weighted regression method of Egger and colleagues ($p = 0.238$).

Comment

The reported use of biological prostheses in aortic valve replacement operations has increased markedly in the past decade [37]. This trend might be justified by the increasing incidence of aortic valve diseases in the aging population [38], the mounting evidence for improved long-term durability of newer valve models [39], and the need for long-term anticoagulation for mechanical prostheses [40], as well as by the recent development of minimally invasive transcatheter valve-in-valve procedures [41]. Additionally, age cutoff and major medical contraindications to anticoagulant therapy are no longer considered the only major selection criteria for tissue valves; in fact, the most recent guidelines for the management of patients with heart valve diseases also recommend the placement of a biological prosthesis in patients of any age who are reluctant to receive lifelong anticoagulant therapy [38, 42]. Together, these data support the extended use of bioprosthetic valves, not only in patients with isolated aortic valve diseases but also in those with combined aortic valve and root diseases.

In the past decade, aortic valve-sparing techniques have gained significant interest. However, compared with

Table 5. Summary of Early Outcomes[a]

Author	In-Hospital Mortality, n (%)	Stroke, n (%)	Renal Failure, n (%)	Respiratory Insufficiency, n (%)	Myocardial Infarction, n (%)	Reoperation for Bleeding, n (%)	Atrial Fibrillation, n (%)	Mediastinitis, n (%)	Pacemaker, n (%)	ICU Stay (days)	In-Hospital Stay (days)
Doty [10]	26 (11.7)	…	…	…	…	…	…	…	…	…	…
Wendler [11]	10 (6.7)	1 (0.7)	…	…	1 (0.7)	9 (6)	…	…	…	3.6 ± 4.7	13 ± 10
Ehrlich [12]	2 (4.3)	…	…	…	…	…	…	…	…	…	…
Kon [13]	4 (3.9)	…	…	…	…	…	…	…	…	…	…
Muller [14]	2 (20.0)	…	…	…	0	…	…	…	2 (20.0)	…	…
Carrel [15]	1 (2.7)	…	…	…	…	…	…	…	…	…	…
Melina [16]	4 (5.0)	…	…	…	…	4 (5)	15 (18.8)	…	…	…	…
Kunihara [17]	3 (5.0)	4 (6.7)	…	…	…	2 (3.3)	9 (15)	…	0	2.3 ± 1.7	8.9 ± 3.1
Etz [18]	17 (6.2)	7 (2.5)	6 (2.2)	43 (15.6)	9 (3.3)	16 (5.8)	…	3 (1.1)	2 (0.7)	…	…
Di Bartolomeo [19]	1 (4.7)	…	…	2 (9.5)	…	1 (4.8)	…	…	…	…	12
Bochenek-Klimczyk [20]	0	0	1 (5.9)	…	0	1 (5.9)	4 (23.5)	1 (5.9)	…	1.5 ± 1	12.8 ± 7.7
Dapunt [21]	25 (7.9)	10 (3.2)	5 (1.6)	…	3 (0.9)	30 (9.5)	…	…	…	4.9 ± 8.1	9.8 ± 8.1
LeMaire [22]	10 (7.6)	9 (6.8)	8 (6.1)	28 (21.2)	2 (1.5)	17 (12.9)	45 (34.1)	…	9 (6.8)	…	…
Tabata [23]	2 (2.9)	…	…	…	…	2 (2.9)	…	…	…	2	6
Lehmann [24]	11 (5.9)	4 (2.2)	14 (7.5)	…	…	…	…	…	…	2.7 ± 5.6	…
Urbanski [25]	1 (0.5)	4 (2.2)	…	…	1 (0.5)	8 (4.4)	7 (3.8)	1 (0.5)	…	…	…
Stewart [26]	0	…	…	1 (5.0)	…	1 (5.0)	…	…	…	…	…
Etz [27]	15 (4.9)	9 (2.9)	6 (2)	37 (12.1)	15 (4.9)	11 (3.6)	…	11 (3.6)	…	…	…
Moorjani (BioValsalva) [9]	0	0	0	1 (4.8)	0	0	…	0	0	…	13.6 ± 2.62
Moorjani (Handsew) [9]	0	2 (11.1)	0	1 (5.6)	0	1 (5.6)	…	0	0	…	14.6 ± 1.27
Baraki [28]	4 (8.0)	0	0	2 (4.0)	…	7 (14.0)	…	…	5 (10.0)	2.3 ± 7	10.3 ± 3.5
Desai [29]	3 (2.3)	0	…	…	3 (2.3)	…	…	…	…	…	…
Galinanes [30]	8 (11.9)	3 (4.5)	5 (7.5)	2 (3.0)	…	2 (3.0)	17 (25.4)	1 (1.5)	3 (4.5)	…	…
Kaya [31]	24 (13.7)	19 (10.9)	7 (4)	31 (17.7)	14 (8.0)	48 (27.4)	…	…	17 (9.7)	6	…
Ennker [3]	15 (5.0)	…	…	…	…	…	…	…	…	…	…
Mazzola [33]	2 (2.5)	1 (1.3)	…	…	…	0	…	…	…	…	…
Kaya [34]	5 (4.9)	0	1 (1.0)	…	2 (2.0)	20 (19.6)	…	1 (1.0)	…	…	…
Gatti [35]	5 (5.0)	1 (1.0)	15 (14.9)	16 (15.8)	2 (2.0)	17 (16.8)	36 (35.6)	2 (2.0)	…	2	10
Smith [36]	6 (25.0)	7 (29.2)	7 (29.2)	17 (70.8)	3 (12.5)	2 (8.3)	6 (25.0)	1 (4.2)	…	…	18.3 ± 11
Pooled average	6.4%	3.7%	…	…	2.9%	7.6%	…	…	…	…	…
Minimum	0%	0%	0%	3.0%	0%	0%	4.0%	0%	0%	1.5	8.9
Maximum	25.0%	29.2%	29.2%	70.8%	12.5%	27.4%	35.6%	5.9%	20.0%	4.9	18.3

[a] Values expressed as number and percentage or mean ± standard deviation.

ICU = intensive care unit.

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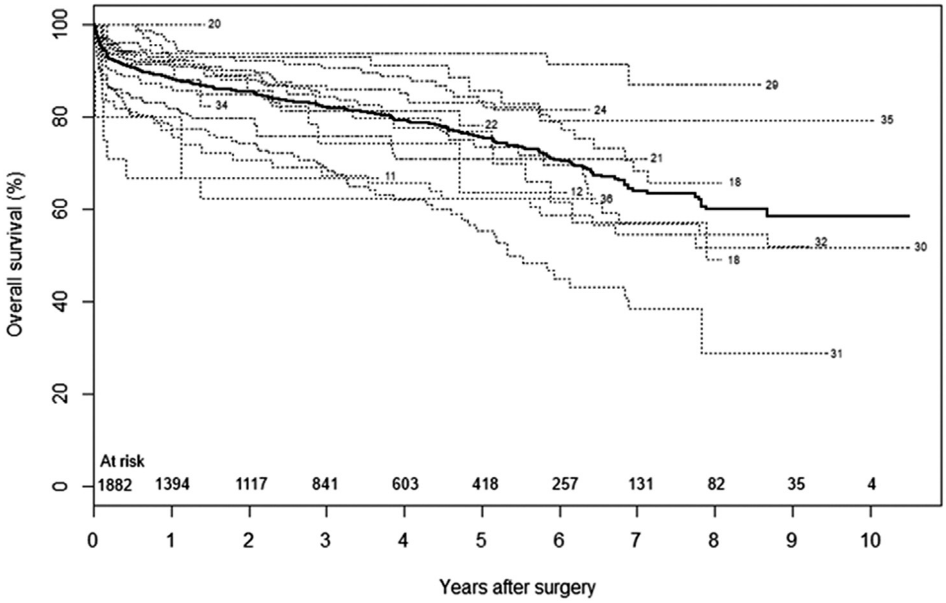

Fig 2. Overall survival based on reconstructed individual patient data. Data of 1,882 patients from 15 studies were reconstructed and presented. Dotted lines represent Kaplan-Meier curves of individual studies, and the solid line represents aggregated survival data of the 15 included studies. Numbers within the figure represent the study reference from which the corresponding curve was reconstructed.

Bentall interventions, valve-sparing root replacements are less appealing for the elderly as a result of frequent aortic leaflet disorders, increased technical complexity, longer operational duration, and not excludable greater durability of biological valve prostheses [43] (Fig 7). Therefore, the present systematic review was conducted, with emphasis on early- and long-term outcomes, to evaluate the existing evidence for aortic root replacement with a biological valved conduit.

In our data, a degenerative aneurysm (75.1%) was the predominant disease that required a biological root replacement, followed by acute aortic dissection (7.5%) and aortic valve endocarditis (5.7%). This distribution was not different from that observed in studies assessing Bentall surgery with mechanical valves [44–46]. The low proportion of patients presenting with acute aortic dissection may be because the majority of aortic dissections can be successfully treated with a conservative approach involving simple supracoronary ascending aorta and hemiarch replacement with commissural resuspension, particularly in the elderly. Composite graft replacement, either biological or mechanical, is most frequently performed in patients presenting with severe involvement or dilatation of the aortic root, in whom

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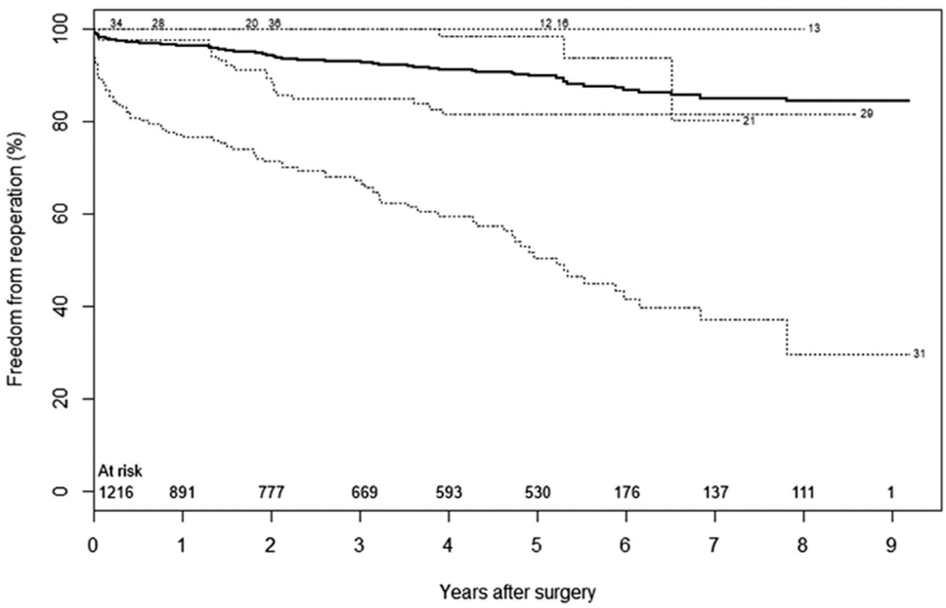

Fig 3. Freedom from reoperation based on reconstructed individual patient data. Data of 1,216 patients from 10 studies were reconstructed and presented. Dotted lines represent Kaplan-Meier curves of individual studies, and the solid line represents aggregated survival data of the 10 included studies. Numbers within the figure represent the study reference from which the corresponding curve was reconstructed.

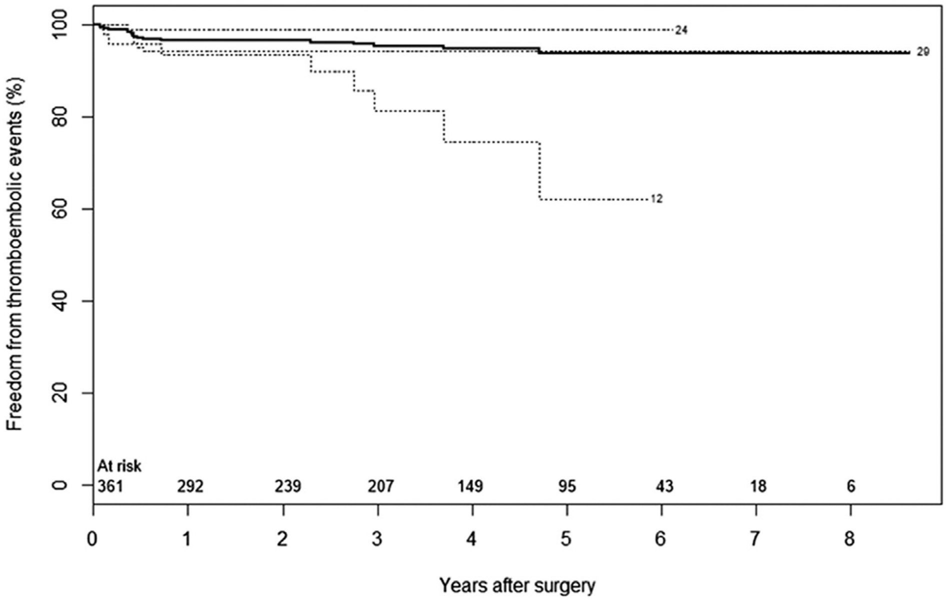

Fig 4. Freedom from thromboembolic events based on reconstructed individual patient data. Data of 361 patients from 3 studies were reconstructed and presented. Dotted lines represent Kaplan-Meier curves of individual studies, and the solid line represents aggregated survival data of the 3 included studies. Numbers within the figure represent the study reference from which the corresponding curve was reconstructed.

repair is assumed to be associated with poorer short- and mid-term results [47, 48].

Historically, earlier operations that required a biological Bentall operation used intraoperative hand-sewn composite graft constructions. The use of stentless xenografts [49, 50] and pre-sewn biological valved conduits [51, 52] has increased in recent years.

Hand-sewn composite grafts still represent the most frequently used. This is because of the possibility of combining different valves with different conduits on

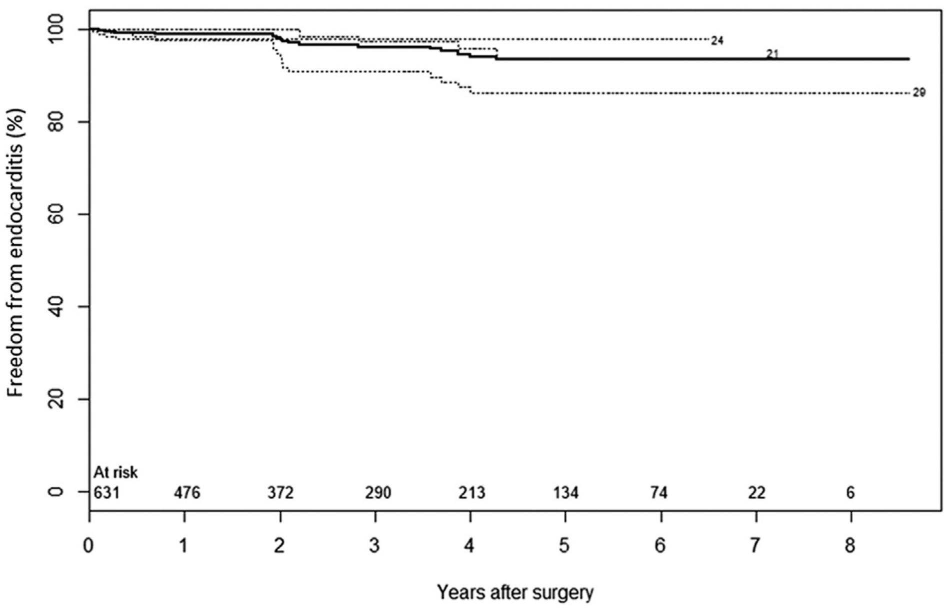

Fig 5. Freedom from endocarditis based on reconstructed individual patient data. Data of 631 patients from 3 studies were reconstructed and presented. Dotted lines represent Kaplan-Meier curves of individual studies, and the solid line represents aggregated survival data of the 3 included studies. Numbers within the figure represent the study reference from which the corresponding curve was reconstructed.

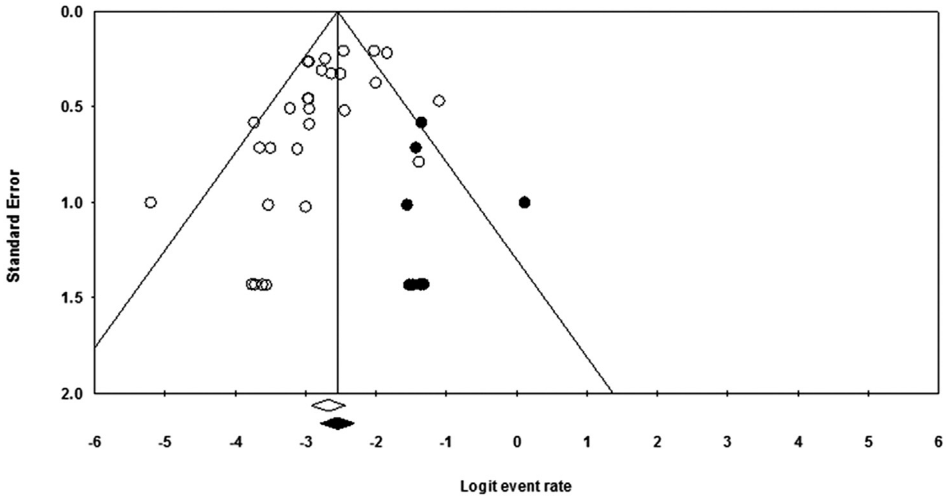

Fig 6. Funnel plot for systematic review of Bentall procedures using biological roots. The logit event rate for mortality (horizontal axis) is presented against the standard error of the log of the logit event rate (vertical axis). The standard error inversely corresponds to the study size. Asymmetry of the plot can indicate publication bias. Open circles indicate included studies, and filled circles represent imputed studies identified through Trim and Fill analysis.

which the operating surgeons rely. Nevertheless, the implantation is less handy, especially when the annular sutures have to be passed through the sewing ring of the assembled device, which may translate into somewhat prolonged operative times.

Stentless xenografts have been widely used owing to improved flow pattern, durability, and excellent long-term clinical results; possible disadvantages include difficult handling, limited durability compared with mechanical valve conduits [53], and severe conduit calcification with time [22].

Among pre-sewn valved conduits, the BioValsalva conduit, which combines a Valsalva graft with a stentless porcine valve [52, 54], allows the separate excision of the diseased cups, facilitating reoperative interventions as a result of structural valve deterioration; however, its triple-layered graft reduces both pliability and handling.

Finally, the pre-sewn Shelhigh BioConduit, a bovine pericardial straight graft with an incorporated stentless valve [51], is favored for its complete biological characteristics, particularly in elderly patients with degenerative aortic root disease or those with aortic valve endocarditis. However, early structural degeneration has been reported as a serious concern by some authors [55, 56].

The lack of comparative studies and the heterogeneity of the reported study populations did not permit comparative analyses of short- and long-term outcomes with different biological valved conduits; as a result, the surgeon's confidence with specific materials still plays a major role in graft selection.

Another important issue is the coronary reimplantation procedure, with the classic inclusion, aortic button, and Cabrol techniques representing the three most commonly used methods. The original Bentall operation [1] with the inclusion technique and direct reanastomosis of the coronary ostia was abandoned in the early 1990s in favor of the button technique [57, 58], which has several features that may reduce the incidence of early and late complications. In particular, to obviate the problem of false aneurysms associated with wrapping in the inclusion technique, some surgeons advocate excision of the coronary ostial buttons,

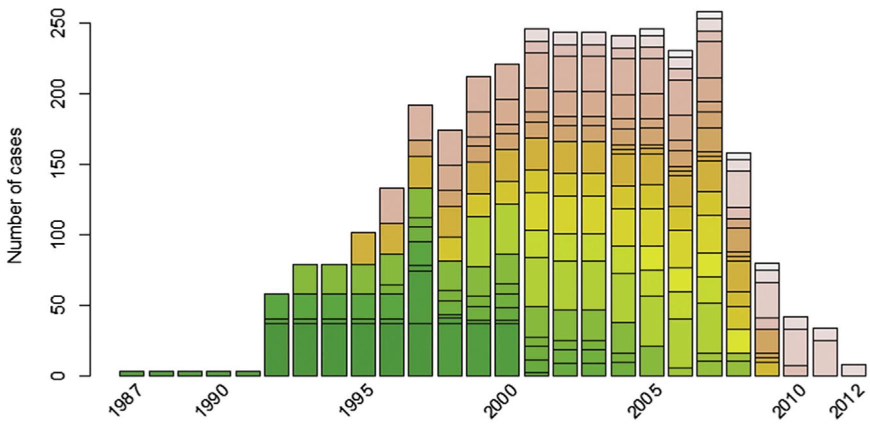

Fig 7. Temporal trend of biological Bentall cases. The number of cases per year is averaged over the duration of each study. Each bar is subdivided into the contributions of individual studies. For example, in 2010, there were 3 studies with data presented. Color scheme identifies individual studies across the study period.

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mobilization of the proximal coronary arteries, and then reattachment of the ostia to the composite valve graft. This allows an increased length of artery that should bridge the gap between the aneurysm wall and the graft with minimal tension on the anastomoses. Thereafter, Cabrol and colleagues [59] developed a technique in which a 10-mm interposition tube graft was looped between the two coronary ostia and then the loop was attached to the ascending aortic composite valve graft with a side-to-side anastomosis. This technique was used mainly for patients who had undergone root reoperation or for extreme aortic dilatation because of difficult mobilization and approximation of the coronary arteries to the aortic graft. It is likely that the increasing use of grafts recreating the sinuses of Valsalva will further reduce the use of the Cabrol technique for coronary ostia reimplantation. In fact, by recreating the sinuses of Valsalva, these grafts may reduce the distance between the coronary ostia and the graft itself and reduce the complications at the anastomotic site.

Operative times are very different among the series; cardiopulmonary bypass time and myocardial ischemic time ranged between 112 and 318 and 76 and 242 minutes, respectively. This discrepancy is attributable to the different associated procedures, particularly the aortic arch surgery.

The present review found acceptable operative mortality, stroke, and myocardial infarction rates (6.4%, 3.7%, and 2.9%, respectively). Our relatively high operative mortality reflects an unselected patient population because patients with acute aortic dissections or active endocarditis were included in these reviewed series, a subgroup in which operative mortality may approach 30% [60].

In our review, overall survival at 1, 2, 3, and 5 years was 88%, 86%, 82%, and 76%, respectively. These survival rates are low in comparison with mechanical Bentall operation presented in other series [61, 62]; the explanation may be that our patients are older (average age, 67.1 years) than those in the mechanical Bentall series. However, 5-year survival was reported in few studies, and more long-term data are required.

Freedom from thromboembolic events at 1, 2, 3, and 5 years was 97%, 97%, 95%, and 94%, respectively. This is lower than reported in most studies involving mechanical aortic valve replacement [63, 64], probably owing to the fact that the patients receive anticoagulation therapy for a limited postoperative period.

Freedom from reoperation at 1, 2, 3, and 5 years was 96%, 94%, 93%, and 90%, respectively. The increased risk of reoperation with a biological Bentall procedure must be weighed against the life-long risk of anticoagulant-related bleeding with a mechanical Bentall procedure. Reoperations in general can be performed with acceptable mortality and good mid- and long-term outcomes, in particular when carried out on an elective basis [65].

Freedom from endocarditis at 1, 2, 3, and 5 years was 99%, 98%, 96%, and 94%, respectively.

Altogether, these excellent results encourage the implant of biological valved conduits.

Limitations

The present findings are limited by several constraints. First, all the series (except one) were retrospective observational studies, and significant variations in several critical surgical variables (such as preoperative characteristics, indication for surgery, methods of coronary artery reimplantation, associated surgical procedure such as arch surgery) have lessened the general applicability of the results. Second, outcomes were unable to be stratified according to underlying diseases, especially when it relates to the difference between acute disease (such as aortic dissection) and chronic (such as degenerative aneurysm). Third, several kinds of prostheses have been used, each with different characteristics and different postoperative management, especially with regard to oral anticoagulant therapy. Finally, statistical aggregation of long-term survival data were conducted under the assumption that censorship was constant, and only a selected portion of studies presented such survival data.

Conclusions

The execution of biological root replacement interventions is expanding, likely as a result of the increasing incidence of aortic valve diseases in the aging population and mounting evidence of improved long-term durability of the newer valve models. Although data on short-term results suggest favorable outcomes, the shortage of long-term follow-up beyond 5 years highlights the urgent need for further investigations with longer follow-up.

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