The Heart Surgery Forum #2018-2131
22 (2), 2019 [Epub February 2019
doi: 10.1532/hsf.2131

Online address: http://journal.hsforum.com

Determining Which Prosthetic to Use During Aortic Valve Replacement in Patients Aged Younger than 70 Years: A Systematic Review of the Literature

Philip Borger, MD,[1] Eric J. Charles, MD, PhD,[2] Eric D. Smith, MD,[3] J. Hunter Mehaffey, MD,[2] Robert B. Hawkins, MD,[2] Irving L. Kron, MD,[2] Gorav Ailawadi, MD,[2] Nicholas Teman, MD[2]

[1]University of Virginia School of Medicine, Charlottesville, VA; [2]Department of Surgery, University of Virginia, Charlottesville, VA; [3]Department of Medicine, University of Michigan, Ann Arbor, MI

ABSTRACT

Background: The choice of bioprosthesis versus mechanical prosthesis in patients aged less than 70 years undergoing aortic valve replacement (AVR) remains controversial, with guidelines disparate in their recommendations. The objective of this study was to explore outcomes after AVR for various age ranges based on type of prosthesis.

Methods: A systematic review was undertaken according to the Preferred Reporting Instructions for Systematic Reviews and Meta-Analyses (PRISMA) guidelines by using Medline (PubMed), Cochrane, Web of Science, Embase, and Scopus databases. Rates of long-term survival (primary outcome), reoperation, major bleeding, thromboembolism, stroke, structural valve deterioration, and endocarditis were compared between subjects receiving biologic and mechanical prostheses. Findings were grouped into patients aged <60 years, aged ≤65 years, and finally aged <70 years.

Results: A total of 19 studies met inclusion criteria. Seven evaluated patients aged <60 years, 4 of which found mechanical prosthesis patients to have higher long-term survival, whereas the remaining studies found no difference. Eight additional studies included patients aged 65 years or younger, and 9 studies included patients aged <70 years. The former found no difference in survival between prosthesis groups, whereas the latter favored mechanical prostheses in 3 studies. Bleeding, thromboembolism, and stroke were more prevalent in patients with a mechanical prosthesis, whereas reoperation was more common in those receiving a bioprosthesis.

Conclusions: Published literature does not preclude the use of bioprostheses for AVR in younger patients. As new valves are developed, the use of bioprosthetic aortic valves in younger patients will likely continue to expand. Clinical trials are needed to provide surgeons with more accurate guidelines.

Received July 30, 2018; received in revised form October 23, 2018; accepted October 30, 2018.

Correspondence: Nicholas R. Teman, MD, University of Virginia Health System, PO Box 800679, Charlottesville, VA 22908; 1-434-982-4301; fax: 1-434-244-7588 (e-mail: nrt4c@virginia.edu).

INTRODUCTION

In patients undergoing aortic valve replacement (AVR), the choice of prosthesis is delineated into 2 main categories: bioprosthetic (BP) and mechanical prosthetic (MP) (also, in this article, BP can stand for bioprosthesis; and MP, mechanical prosthesis). BP valves are advantageous in that they do not require long-term anticoagulation therapy, although their main drawback is limited durability leading to structural valve deterioration (SVD) and reoperation [Svennsson 2013; Baumgartner 2017; Nishimura 2017]. Conversely, MP valves rarely degenerate structurally over time; however, they have greater thromboembolic potential than BPs and thus require lifetime anticoagulation that increases the risk for bleeding complications [Svennsson 2013; Baumgartner 2017; Nishimura 2017].

For young and middle-aged patients undergoing AVR, current guidelines are variable and evolving (Table 1). Guidelines from the European Society of Cardiology and European Association for Cardio-Thoracic Surgery (ESC/EACTS) (2017) advocate BP for patients aged >65 years, MP for patients aged <60 years, and a choice of either for patients aged 60-65 years [Baumgartner 2017]. Guidelines from the Society of Thoracic Surgeons (STS) (2013) recommend BP in patients aged ≥65 years, but state BP may be reasonable for patients aged <65 years who choose this valve for lifestyle considerations and understand the trade-off between anticoagulation and future reoperation [Svennsson 2013]. Finally, in a recent focused update (2017) to their previous guidelines, the American Heart Association and American College of Cardiology (AHA/ACC) recommend BP for patients aged >70 years, MP for patients aged <50 years, and a choice of either prosthesis type for patients aged 50-70 years who are fully informed of risks and benefits inherent to each [Nishimura 2017].

The above guidelines illustrate the lack of consensus in regard to prosthesis choice in AVR. In addition, new evidence has been published in which mortality and morbidities such as reoperation do not always favor MPs in younger subjects and differs from that which some of the above guidelines were based upon [Nishida 2014; Chiang 2014; Sakamoto 2016; Wang 2016; Zhao 2016; Minakata 2017]. Another complicating issue is that subjects in previous studies have mostly been implanted with older generation valves that are no longer in use. Newer generation valves have the potential to further reduce the rate of SVD [Ruel 2004]. In addition, the emergence

Table 1. Guidelines for Valve Choice in AVR*

	Bioprosthetic	COR	LOE	Mechanical	COR	LOE	Either	COR	LOE
AHA/ACC (2017)	Cannot anticoagulate	I	C	Aged <50 years and can anticoagulate	IIa	B-NR	Aged 50-70 years	IIa	B-NR
	Aged >70 years	IIa	B						
STS (2013)	Cannot anticoagulate	I	C	Aged <65 years	I	C	Aged <65†	IIb	C
	Aged ≥65 years without risk factors for TE	I	C						
	Contemplating pregnancy	IIb	C						
ESC/EACTS (2017)	Desire of informed patient	I	C	Desire of the informed patient with no risk to anticoagulation	I	C	Aged 60-65 years	IIa	C
	Cannot anticoagulate	I	C	At risk for accelerated SVD	I	C			
	Reoperation for MP thrombosis through anticoagulation	I	C	Anticoagulated for valve in another position	IIa	C			
	Low risk of future reoperation	IIa	C	Age <60 years	IIa	C			
	Contemplating pregnancy	IIa	C	Reasonable life expectancy and future high risk for reoperation	IIa	C			
	Aged >65 years or life expectancy shorter than valve durability	IIa	C	Anticoagulated for high risk of TE	IIb	C			

*TE, thromboembolism.

†MP preferred, but BP may be reasonable for these patients with regards to lifestyle considerations after a discussion about future reoperation.

of valve-in-valve (VIV) procedures through transcatheter aortic valve implantation can decrease or eliminate the risk of reoperation for patients implanted with BPs [Dvir 2014; Ye 2015].

The AHA/ACC focused update highlights that uncertainty continues to permeate the choice of prosthesis in young and middle-aged patients undergoing AVR. In the present study, we aimed to perform a thorough systematic review of the literature that includes studies comparing outcomes for BP versus MP in young and middle-aged adult patients (aged <70 years), while paying special attention to patients at the younger end of this spectrum (aged <60 years).

METHODS

Literature Search Strategy

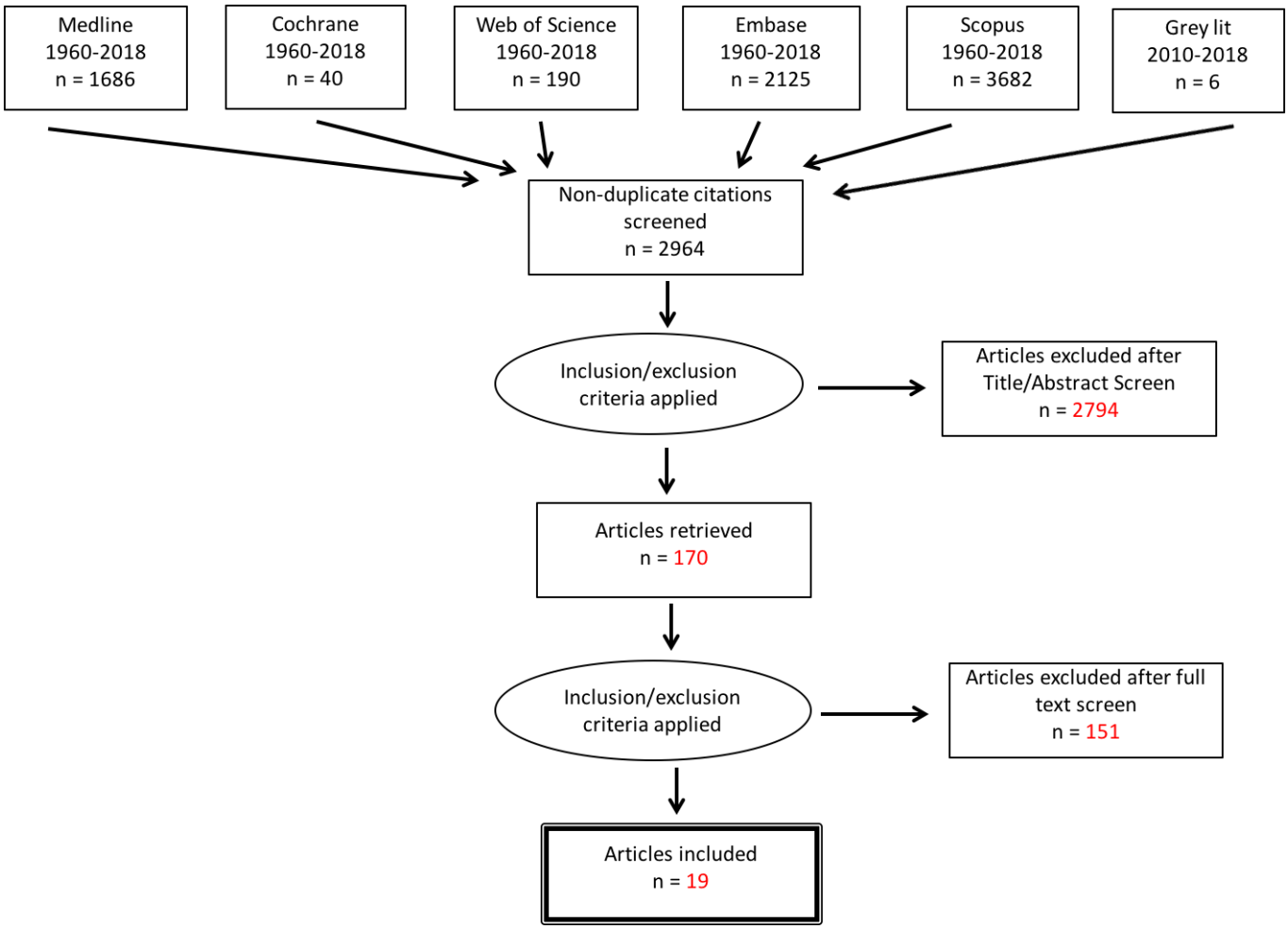
The present study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [Moher 2009]. The PRISMA checklist is available in supplemental Appendix 1. Searches were conducted of Medline (PubMed), Cochrane, Web of Science, Embase, and Scopus from 1960 to February 3, 2018. Terms used in the search were "Bioprosthesis," "Bioprostheses," "Heterograft Bioprosthesis," "Xenograft Bioprosthesis," "Xenograft Bioprostheses," "Glutaraldehyde-Stabilized Grafts," "Glutaraldehyde Stabilized Grafts," "Glutaraldehyde-Stabilized Graft," "mechanical valve," "aortic valve," "Heart Valve Prosthesis," "Heart Valve Prostheses," "Cardiac Valve Prosthesis," "Cardiac Valve Prostheses," "Heart Valve Prosthesis Implantation," "valve," and "replace." The search string from PubMed is available in supplemental Appendix 2.

Eligibility Criteria

Studies were included if they met the following criteria: adult patients aged <70 years who underwent AVR, comparison of BP versus MP outcomes (survival, reoperation, SVD, bleeding, thromboembolism, stroke, endocarditis), follow-up period >5 years postoperatively, English language, and both male and female subjects. Study design was not used to filter results. Studies were excluded if they evaluated outcomes after AVR for patients who were pregnant or were operated on to treat endocarditis.

Data Extraction

Data that included study characteristics and outcomes of interest was extracted from article text, tables, and figures.



Systematic review flow diagram. Names given are the most recent name of the database. Nos. in red are the more pertinent values. Grey lit, grey literature.

The primary outcome was long-term survival, and secondary outcomes were reoperation, major bleeding, thromboembolism, stroke, SVD, and endocarditis. Screening, text review, and data extraction were performed by 2 independent reviewers and then compared. Any discordant results were reviewed and corrected by a third independent reviewer.

Qualitative Synthesis

Outcomes varied in the way they were reported. For example, the primary outcome of survival was listed in some studies as "survival," and in others as "mortality." For reoperation, some studies reported "freedom from reoperation," whereas others reported "risk of reoperation." This heterogeneity in reporting holds true for the other outcomes as well. Thus, each outcome is presented as it was reported in the study it was extracted from.

Risk of Bias Assessment

Because of a paucity of prospective randomized controlled data, qualitative risk of bias assessment was not performed. The majority of the included studies (17 of 19 studies) were retrospective analyses that are limited by significant inherent bias because of study design.

RESULTS

Initial database searches yielded 2964 nonduplicated citations, of which 2794 were excluded after screening the title and abstract for inclusion and exclusion criteria, and an additional 151 were excluded after a full-text screen. This left 19 remaining articles which were included in the present study (Figure).

Study sampling periods ranged from 1969 through 2014, with the number of patients ranging between 56 and 9942. Seventeen studies were designed as retrospective cohorts, whereas one was a prospective cohort and one was a randomized controlled trial. Data analysis methodology also varied and included propensity matching (12 studies), univariate analysis (1 study), multivariate analysis (4 studies), multivariate analysis with inverse probability weighing (1 study), and randomized controlled methodology (1 study) (Table 2).

Table 2. Study Characteristics

Study*	Patient Age Range (Years)	Number of Patients	Design	Sampling Period
[Alex 2018]	55-65	n = 236	Retrospective cohort (propensity matched)	1995-2014
[Badhwar 2012]	≤65	n = 98	Retrospective cohort (propensity matched)	2003-2007
[Brown 2008]	50-70	n = 440	Retrospective cohort (propensity matched)	1991-2000
[Carrier 2001]	55-65	n = 526	Prospective cohort (multivariate analysis)	1982-1999
[Chiang 2014]	50-69	n = 2002	Retrospective cohort (propensity matched)	1997-2004
[Glaser 2016]	50-69	n = 2198	Retrospective cohort (propensity matched)	1997-2013
[Goldstone 2017]	45-54; 55-64	n = 9942	Retrospective cohort (multivariate analysis with inverse probability weighting)	1996-2013
[Kulik 2006]	50-65	n = 388	Retrospective cohort (multivariate analysis)	1977-2002
[McClure 2014]	<65	n = 722	Retrospective cohort (propensity matched)	1992-2011
[Minakata 2017]	<60; 60-69	n = 1002	Retrospective cohort (propensity matched)	BP: 1985-2000; MP: 1991-2001
[Nishida 2014]	<60; 60-69	n = 459	Retrospective cohort (univariate analysis)	1981-2013
[Prasongsukarn 2007]	61-65; 66-70	n = 922	Retrospective cohort (multivariate analysis)	1982-1998
[Roumieh 2015]	55-65	n = 120	Retrospective cohort (propensity matched)	1996-2008
[Ruel 2007]	<60	n = 314	Retrospective cohort (multivariate analysis)	1969-2004
[Sakamoto 2016]	60-70	n = 56	Retrospective cohort (propensity matched)	1995-2014
[Stassano 2009]	55-70	n = 310	Randomized controlled	1995-2003
[Suri 2013]	<70	n = 820	Retrospective cohort (propensity matched)	1993-2009
[Wang 2016]	<60	n = 224	Retrospective cohort (propensity matched)	2002-2009
[Weber 2012]	<60	n = 206	Retrospective cohort (propensity matched)	2000-2009

*Study names are indicated by citation of references in this article.

Aged <60 years

In long-term follow-up of subjects aged <60 years (Table 3), 3 studies found no difference in survival between BP and MP [Ruel 2007; Wang 2016; Minakata 2017], whereas 4 found survival to be superior in patients with MPs [Weber 2012; Nishida 2014; Glaser 2016; Goldstone 2017]. However, in the study by Weber and colleagues (2012), this advantage disappeared upon multivariate analysis of additional variables (ie, age, HTN, renal failure, active endocarditis, CABG, etc.) different from those used for propensity matching [Weber 2012].

Four studies favored MP in reducing the risk of reoperation [Ruel 2007; Nishida 2014; Minakata 2017; Goldstone 2017], whereas 2 found no difference [Weber 2012; Wang 2016].

Major bleeding was found to be similar in 3 studies that explored this [Weber 2012; Nishida 2014; Wang 2016], but favored BP in the study by Goldstone and colleagues (2017) [Goldstone 2017].

Only Nishida and colleagues (2014) evaluated SVD, and found it to be more prevalent in subjects with BP [Nishida 2014].

Stroke risk was found to be lower in patients with BP in the study by Goldstone and colleagues (2017) [Goldstone 2017],17 whereas Nishida and colleagues (2014) found no difference [Nishida 2014].

Valve type did not influence occurrence of thromboembolism [Nishida 2014; Wang 2016] or endocarditis [Weber 2012; Nishida 2014] in studies that reported on these complications. It should be noted that results by Nishida and colleagues (2014) were based on univariate analysis without adjustment for disparate patient characteristics [Nishida 2014].

Aged ≤65 years

When the age threshold for inclusion was expanded to patients 65 or younger (Table 4), none of the 8 studies that were added found a difference in survival between valve types [Carrier 2001; Kulik 2006; Prasongsukarn 2007; Badhwar 2012; McClure 2014; Roumieh 2015; Alex 2018; Goldstone 2017].

Four reported higher rates of reoperation in subjects with a BP [McClure 2014; Roumieh 2015; Alex 2018, Goldstone 2017], whereas one found no difference [Prasongsukarn 2007].

One study reported a lower incidence of stroke in patients with MPs [Roumieh 2015], whereas 2 found valve type did not impact this [McClure 2014; Goldstone 2017].

Two studies found an increased risk of bleeding among MP subjects [McClure 2014; Goldstone 2017], whereas one found no interaction between valve type and bleeding [Roumieh 2015].

Table 3. Outcomes after Bioprosthetic (BP) and Mechanical (MP) Aortic Valve Replacements in Patients Aged <60 Years*

Study†	Age (Years)	Outcome	HR (BP versus MP)	95% CI	Percentage (BP versus MP)	*P*
Survival						
[Goldstone 2017]	45-54	Multivariate-adjusted long-term mortality	1.25	1.03-1.52	30.6% versus 26.4%	.02
[Minakata 2017]	<60	20-Year survival	0.75	0.30-1.99	—	.54
[Glaser 2016]	50-59	15-Year survival	0.60‡	—	—	.026
[Wang 2016]	<60	10-Year survival	—	—	88.7% versus 87.9%	.860
[Nishida 2014]	<60	20-Year survival	—	—	37.2% ± 1% versus 71.9% ± 3.7%	.0035
[Weber 2012]	<60	Crude mortality	0.243	0.064-0.923	—	.038
		Multivariate-adjusted mortality	0.277	0.038-1.997	—	.203
[Ruel 2007]	<60	Multivariate-adjusted long-term mortality	0.95	0.7-1.3	—	.7
Reoperation						
[Goldstone 2017]	45-54	Multivariate-adjusted long-term reoperation risk	2.6	1.91-3.40	—	S
[Minakata 2017]	<60	20-Year FFR	0.16	0.06-0.46	—	<.01
[Wang 2016]	<60	10-Year FFR	—	—	90.2% versus 96.3%	.296
[Nishida 2014]	<60	20-Year FFR	—	—	17.8% ± 10% versus 94.2% ± 2.1%	<.0001
[Weber 2012]	<60	FFR at late follow-up (>90 days)	—	—	100% versus 98%	.231
[Ruel 2007]	<60	Multivariate-adjusted long-term reoperation risk	3.9	2.6-6.3	—	<.001
Major bleeding						
[Goldstone 2017]	45-54	Multivariate-adjusted long-term bleeding risk	0.63	0.51-0.75	—	S
[Wang 2016]	<60	10-Year FFB	—	—	96.9% versus 91.5%	.128
[Nishida 2014]	<60	20-Year FFB	—	—	88.1% ± 7.9% versus 94.0% ± 2.2%	.214
[Weber 2012]	<60	FFB at late follow-up (>90 days)§	—	—	100% versus 99%	.482
Thromboembolism						
[Wang 2016]	<60	10-Year FFT	—	—	94.3% versus 91.0%	.528
[Nishida 2014]	<60	20-Year FFT	—	—	87.4% ± 8.2% versus 89.8% ± 2.6%	.9294
Stroke						
[Goldstone 2017]	45-54	Multivariate-adjusted long-term stroke risk	0.64	0.46-0.86	—	S
[Weber 2012]	<60	FFS at late follow-up (>90 days)	—	—	97% versus 94%	.316
Structural Valve Deterioration						
[Nishida 2014]	<60	20-Year FFSVD	—	—	29.5% ± 15% versus 100%	<.0001
Endocarditis						
[Nishida 2014]	<60	20-Year FFE	—	—	78.9% ± 10% versus 93.7% ± 2.4%	NS
[Weber 2012]	<60	FFE at late follow-up (>90 days)	—	—	97% versus 98%	1

*FFR, freedom from reoperation; FFB, freedom from major bleeding/hemorrhage; FFT, freedom from TE; FFS, freedom from stroke; FFSVD, freedom from structural valve deterioration; FFE, freedom from endocarditis; S, significant; NS, not significant. Italicized P value indicates significance.
†Study names are indicated by citation of references in this article.
‡Reciprocal value, reported as MP versus BP HR 1.67 (95% CI: 1.06-2.61).
§Cerebral hemorrhage only.

Table 4. Additional BP versus MP Outcomes in AVR When Age Cutoff Expanded to ≤65 Years*

Study†	Age (years)	Outcome	HR (BP versus MP)	95% CI	Percentage (BP versus MP)	*P*
Survival						
[Goldstone 2017]	55-64	Multivariate-adjusted long-term mortality	1.11	0.98-1.25	36.1% versus 32.1%	.12
[Alex 2018]	55-65	Multivariate-adjusted 15-year survival	1.16	0.69-1.94	—	.58
[Roumieh 2015]	55-65	15-Year survival	—	—	54% ± 13% versus 53% ± 8%	.95
[McClure 2014]	<65	15-Year survival	—	—	65 ± 5 versus 75 ± 4%,	.752
[Badhwar 2012]	≤65	8-Year survival	—	—	83% versus 100%	.04
[Prasongsukarn 2007]	61-65	15-Year survival	—	—	—	NS
[Kulik 2006]	50-65	Multivariate-adjusted 10-year survival	0.76‡	—	—	.77
[Carrier 2001]	55-65	10-Year mortality	—	—	—	NS
Reoperation						
[Goldstone 2017]	55-64	Multivariate-adjusted long-term reoperation risk	2.46	1.93-3.20	—	S
[Alex 2018]	55-65	Multivariate-adjusted 15-year reoperation risk	4.16§	—	—	<.01
[Roumieh 2015]	55-65	15-Year FFR	—	—	73% ±11% versus 91% ±5%	.04
[McClure 2014]	<65	15-Year survival	—	—	55% versus 95%	.002
[Prasongsukarn 2007]	61-65	Multivariate-adjusted valve-related reoperation	1.30	—	—	.67
Major bleeding						
[Goldstone 2017]	55-64	Multivariate-adjusted long-term bleeding risk	0.66	0.58-0.75	—	S
[Roumieh 2015]	55-65	15-Year FFB	—	—	88% ± 6% versus 77% ± 10%	.98
[McClure 2014]	<65	18-Year FFB	—	—	98% versus 78%	.002
Stroke						
[Goldstone 2017]	55-64	Multivariate-adjusted long-term stroke risk	0.92	0.73-1.13	—	NS
[Roumieh 2015]	55-65	15-Year FFS||	—	—	83% ± 8% versus 97% ± 3%	.03
[McClure 2014]	<65	15-Year FFS	—	—	91% versus 95%	.332
SVD						
[Roumieh 2015]	55-65	15-Year FFSVD	—	—	64% ± 12% versus 93% ± 5%	.003
Endocarditis						
[Roumieh 2015]	55-65	15-Year FFE	—	—	83% ± 8% versus 98% ± 2%	.05

*FFR, freedom from reoperation; FFB, freedom from major bleeding/hemorrhage; FFS, freedom from stroke; FFSVD, freedom from structural valve deterioration; FFE, freedom from endocarditis; S, significant; NS, not significant. Italicized P value indicates significance.
†Study names are indicated by citation of references in this article.
‡Reciprocal value, reported as MP versus BP HR 1.3 (CI not reported).
§Reciprocal value, reported as MP versus BP HR 0.24 (95% CI: 0.09-0.68).
||Includes TIA.

Roumieh and colleagues (2015) reported higher rates of SVD and endocarditis in BP subjects [Roumieh 2015].

Aged ≤70 years

When the age threshold for inclusion was expanded to patients 70 or younger (Table 5), 3 of 9 studies favored MP in long-term survival [Brown 2008; Suri 2013; Glaser 2016]. However, in the study by Glaser and colleagues (2016), this difference was not present in a subgroup of patients aged 60-69 years [Glaser 2016]. Because MPs were favored for survival in a separate subgroup of patients aged 50-59 years, this suggests these younger subjects may be responsible for the observed difference in survival. The remaining 6 studies did not find a significant relationship between prosthesis type and survival [Prasongsukarn 2007; Stassano 2009; Chiang 2014; Nishida 2014; Sakamoto 2016; Minakata 2017]. The investigation by Stassano and colleagues (2009) is notable in that it represents the only recent randomized trial to investigate

Table 5. Additional BP versus MP Outcomes in AVR When Age Cutoff Expanded to <70 Years*

Study†	Age (years)	Outcome	HR (BP versus MP)	95% CI	Percentage (BP versus MP)	*P*
Survival						
[Minakata 2017]	60-69	20-Year survival	0.88	0.56-1.39	—	.59
[Sakamoto 2016]	60-70	15-Year survival	—	—	85% ± 9% versus 88% ± 8%	.734
[Glaser 2016]	50-69	Multivariate-adjusted 15-year survival	0.75‡	—	50% versus 59%	.006
	60-69		0.93§	—	—	.539
[Chiang 2014]	50-69	Multivariate-adjusted 15-year survival (post–propensity matched)	0.97	0.83-1.14	60.6% versus 62.1%	.74
[Nishida 2014]	60-69	20-Year survival	—	—	26.0% ± 12% versus 28.7% ± 6.9%	.7404
[Suri 2013]	<70	Multivariate-adjusted 15-year mortality	1.27	—	—	.03
[Stassano 2009]	55-70	Survival at late follow-up	—	—	69.4% versus 72.5%	.06
		Multivariate-adjusted late mortality	1.37‖	—	—	.2
[Brown 2008]	50-70	10-Year survival	—	BP 52-58, MP 62-76	50% versus 68%	<.01
		Multivariate-adjusted late mortality	2.1¶	—	—	<.01
[Prasongsukarn 2007]	66-70	BP 15-year survival versus MP 12-year survival	—	—	28.5% ±3.3% versus 44.2% ± 9.6%	.10
Reoperation						
[Sakamoto 2016]	60-70	15-Year FFR	—	—	85% ± 8% versus 100%	.110
[Glaser 2016]	50-69	Multivariate-adjusted risk of reoperation at maximum follow-up (BP 16.0 years versus MP 15.9 years)	2.36	1.71-2.79	—	.001
[Chiang 2014]	50-69	Multivariate-adjusted 15-year reoperation risk	1.92#	—	—	.001
[Nishida 2014]	60-69	20-Year FFR	—	—	63.2% ± 16% versus 95.9% ± 2.1%	.0559
[Brown 2008]	50-70	10-Year FFR	—	—	91% versus 97.5%	.13
[Prasongsukarn 2007]	66-70	Multivariate-adjusted valve-related reoperation	3.28	—	—	.2684
Major bleeding						
[Minakata 2017]	60-69	20-Year FFB	0.93	0.39-2.23	—	.88
[Sakamoto 2016]	60-70	Hemorrhage rate (% patients per year)	—	—	0.12% versus 0.34%	<.001
[Glaser 2016]	50-69	Risk of bleeding at maximum follow-up (BP 16 years versus MP 15.8 years)	0.49	0.34-0.70	—	.001
[Chiang 2014]	50-69	Multivariate-adjusted 15-year risk of major bleeding	0.57**	—	—	.001
[Nishida 2014]	60-69	20-Year FFB	—	—	98.4% ± 1.6% versus 73.0% ± 7.9%	.1735
[Brown 2008]	50-70	10-Year FFB	—	—	93.6% versus 86.3%††	.06
Thromboembolism						
[Minakata 2017]	60-69	Multivariate-adjusted 20-year FFT	7.55	0.98-58.0	—	.05
[Sakamoto 2016]	60-70	TE rate (% patients per year)	—	—	0.35% versus 0.58%	<.001
[Nishida 2014]	60-69	20-Year FFT	—	—	98.0% ± 2.1% versus 71.3% ± 6.2%	.033

Table 5. Additional BP versus MP Outcomes in AVR When Age Cutoff Expanded to <70 Years*

Studyb	Age (years)	Outcome	HR (BP versus MP)	95% CI	Percentage (BP versus MP)	*P*
Stroke						
[Glaser 2016]	50-69	Multivariate-adjusted stroke risk at maximum follow-up (BP 15.9 years versus MP 15.8 years)	1.04	0.72-1.50	—	.848
[Chiang 2014]	50-69	Multivariate-adjusted 15-year stroke risk	0.96‡‡	—	—	.84
[Brown 2008]	50-70	10-Year FFS	—	BP 85.8-95.8, MP 88.9-97.4	91.4% versus 93.2%	.07
SVD						
[Nishida 2014]	60-69	20-Year FFSVD	—	—	54.2% ± 18% versus 100%	<.0001
Endocarditis						
[Nishida 2014]	60-69	20-Year FFE	—	—	98.3% ± 2.4% versus 90.7% ± 6.4%	NS
[Brown 2008]	50-70	FFE at late follow-up (>30 days)	—	—	96.4% versus 97.1%***	.72

*FFR, freedom from reoperation; FFB, freedom from major bleeding/hemorrhage; FFT, freedom from TE; FFS, freedom from stroke; FFSVD, freedom from structural valve deterioration; FFE, freedom from endocarditis; NS, not significant. Italicized P value indicates significance.
†Study names are indicated by citation of references in this article.
‡Reciprocal value, reported as MP versus BP HR 1.34 (95% CI: 1.09-1.66).
§Reciprocal value, reported as MP versus BP HR 1.08 (95% CI: 0.85-1.36).
||Reciprocal value, reported as MP versus BP HR 0.73 (95% CI: 0.47-1.20).
¶Reciprocal value, reported as MP versus BP HR 0.48 (95% CI: 0.35-0.67).
#Reciprocal value, reported as MP versus BP HR 0.52 (95% CI: 0.36-0.75).
**Reciprocal value, reported as MP versus BP HR 1.72 (95% CI: 1.27-2.43).
††Reported as bleeding, BP 6.4% (95% CI: 1%-12.3%) versus MP 13.7% (95% CI: 8.3%-19.2%).
‡‡Reciprocal value, reported as MP versus BP 1.04 (95% CI: 0.75-1.43).
***Reported as endocarditis, BP 3.6% versus MP 2.9%.

BP vs MP in younger patients. With the trial taking place at 2 Italian centers in subjects aged 55-70, after an adequate discussion of the risks and benefits of each valve type, subjects requested that their surgeon make a decision for them. Because ACC/AHA guidelines at that time did not make a definitive recommendation for these patients, clinical equipoise enabled randomization [Stassano 2009].

In regards to reoperation risk, 2 studies favored MPs [Chiang 2014; Glaser 2016], whereas 4 studies found no difference between prostheses [Prasongsukarn 2007; Brown 2008; Nishida 2014; Sakamoto 2016].

Major bleeding was found to be more prevalent in MPs by 3 studies [Chiang 2014; Glaser 2016; Sakamoto 2016], whereas 3 found no association with valve type [Brown 2008; Nishida 2014; Minakata 2017].

Three publications that evaluated thromboembolism rate found it to be lower in patients with BPs [Nishida 2014; Sakamoto 2016; Minakata 2017].

Stroke risk was not different in 3 studies that evaluated this [Brown 2008; Chiang 2014; Glaser 2016].

Consistent with other age groups, Nishida and colleagues found a higher rate of SVD in patients with a BP valve [Nishida 2014].

Endocarditis did not differ in 2 publications that evaluated this outcome [Brown 2008; Nishida 2014].

DISCUSSION

The present systematic review illustrates the variability of results from investigations into long-term mortality and morbidity in young and middle-aged patients undergoing AVR with either MP or BP. Our findings expand upon the results published by Head and colleagues (2017), by including morbidities' outcomes and additional relevant studies. For the subgroup that extended to individuals aged 65 years, all studies found no association between valve type and survival. Four of the 5 investigations that evaluated reoperation favored MPs, whereas findings regarding bleeding and stroke were variable in the few studies that reported on these. All

guidelines reported allow for individualized choice regarding prosthesis type in patients aged 60-65 years.

For the subgroup with age threshold expanded to 70 years, the majority found no difference in mortality related to valve type. Findings for bleeding and reoperation varied, whereas thromboembolic risk was found to be increased in MPs in all 3 investigations that quantified this. For patients aged 60-70 years, the recent ACC/AHA update allows for a choice of either prosthesis, whereas the STS and ESC/EACTS recommend BP for patients in the second half of this decade, and allow a choice of either for those in the first half.

In the most controversial age group—young subjects aged under 60 years—there was disagreement among publications regarding the association of valve type with mortality and risk of reoperation. Of 7 studies, 4 favored survival in MP patients, whereas 3 found no difference. Although the study by Goldstone and colleagues (2017) favored MP patients, it should be noted that this study stratified patients into 2 age groups, 45-54 and 55-64 [Goldstone 2017].17 Thus, in analyzing patients aged <60 years it differs among the other studies in that it leaves out patients aged 55-59. It would be interesting to analyze outcomes in these patients in an additional group, aged 45-59. Four studies favored freedom from reoperation in MP patients, whereas 2 found no difference. This makes it difficult to reach a consensus opinion, and consequently to validate or invalidate guidelines on prosthesis choice for patients aged between 50 and 60 years. The AHA/ACC focused update and STS guidelines allow for an informed individualized choice, whereas ESC/EACTS maintains a recommendation for MPs.

It is well documented that the proportion of BPs being implanted in younger patients has continued to increase, despite some of the current clinical guidelines that would advise MP implantation in many of these individuals. In a large cohort of Swedish patients aged 50-69, BPs were used in 58% of patients in the years 2006-2013, whereas between 1997 and 2002 they were implanted in only 17% of cases. The average age of these patients remained constant during this time, which supports that other factors are responsible for this rise [Glaser 2016]. Similarly, in the United States, BP use increased from 37.7% in 1998-2001, to 63.6% in 2007-2011. Notably, this change was highest in younger patients aged 55 to 64 years [Isaacs 2015].

One explanation for the rise in BP implantation is likely related to concern for quality of life and future complications. Compared with BP patients, patients with MP have been shown to have significantly greater anxiety over the prospect of thromboembolism [Myken 1995]. They also have a higher likelihood of feeling bothered by the sound of their valve, the possibility of bleeding, and the frequency of blood work and office visits. Also, they were more likely to express doubt in their valve choice at follow-up [Korteland 2016]. MPs have also been associated with lower physical function, higher prevalence of disability, and worsened disease perception [Ruel 2005].

The main detractor from BP implantation in younger individuals is the prospect of future SVD and reoperation. Contemporary rates of early operative mortality from redo conventional aortic valve replacement (cAVR) are 3-7%, approximately [Akins 1998; Jones 2001; Jamieson 2003; Potter 2005]. When compared with primary AVR, redo cAVR has been shown to have higher rates of operative mortality (4.6% versus 2.2%, P <.0001), postoperative stroke, aortic insufficiency, and pacemaker requirement [Kaneko 2015]. Contributing to increased reoperative risk is that although patients may be good surgical candidates at their index procedure, upon redo AVR many will be septua- or octogenarians with major comorbidities, placing them at higher surgical risk [Kirsch 2004; Maganti 2009]. Transcatheter VIV implantation has emerged as a less invasive and possibly safer alternative to cAVR [Webb 2010; Webb 2013] and to this point has mainly been utilized in patients at intermediate or high risk for reoperation [Webb 2010; Ye 2015].

A recent metaanalysis of VIV implantation by Phan and colleagues (2016) found VIV and cAVR to have similar rates of 30-day all-cause mortality (6.4% versus 6.5%, P = .353), as well as comparable hemodynamic outcomes. Occurrence of stroke and bleeding was lower in VIV, whereas incidence of moderate paravalvular leaks was higher. Notable was that patients receiving VIV implantation were of more advanced age (77.5 versus 66.7 years) and were more than twice as likely to have hypertension, peripheral vascular disease, and chronic kidney disease. Although these results are encouraging, the authors point out that many of the included studies were of small sample size, lacked long-term follow-up, and lacked direct comparison between VIV and cAVR, highlighting the need for large randomized controlled trials [Phan 2016].

The principle VIV technologies studied to date are the self-expandable CoreValve (Medtronic, Minneapolis, MN, USA) devices and balloon-expandable Edwards SAPIEN (Edwards Lifesciences, Irvine, CA, USA) devices. In any new guidelines, patient heterogeneity must be taken into account. For example, it has been shown that in patients that require implantation with small-orifice valves (≤21 mm), the use of the balloon-expandable Edwards SAPIEN device resulted in higher postprocedural gradients than with CoreValve technology [Dvir 2012]. High postprocedural gradients increase risk of patient–prosthesis mismatch, a complication which is associated with worse mortality and morbidity [Pibarot 2006]. A separate study that utilized multiple generations of balloon-expandable transcatheter valves, most of which were Edwards SAPIEN, demonstrated small valve size (19 and 21 mm) was a risk factor for decreased midterm survival (HR 6.2; 95% CI: 1.0-22.8, P = .013) [Ye 2015]. This concern is reflected in the recent AHA/ACC focused update, which discourages VIV implantation of smaller-sized valves. However, a later generation self-expandable valve, the CoreValve Evolut, was shown to reliably lower the postprocedural gradient in patients who undergo VIV implantation with a small-orifice valve. The success of these valves in patients with small annuli is believed to be due to their "low profile, optimized radial force, and supra-annular positioning" [Diemert 2014].

As noted in the study by Phan and colleagues (2016), patients receiving VIV implantation were older and less healthy than patients undergoing surgery [Phan 2016]. This bias towards treating such patients with a transcatheter

approach, and younger and healthier patients surgically, extends to transcatheter aortic valve replacement (TAVR) as whole and is supported by current guidelines [Ponikowski 2016]. However, evidence is now emerging that supports the use of TAVR in younger and healthier patients. Whereas historically clinical trials for TAVR have evaluated octogenarians, a recent retrospective cohort study analyzed intermediate- to prohibitive-risk patients that were aged <75 years (average age 69) in 2 high volume Italian hospitals. A composite score of clinical efficacy that took into account mortality, valve positioning, prosthesis–patient mismatch, regurgitation, and valve gradient found that 30-day efficacy was 90%, with a 2% overall death risk. Valve efficacy at 1 year was 83% overall and was significantly higher in intermediate-risk patients at 95% (P = .004) [Fraccaro 2018]. In addition, a recent metaanalysis comparing TAVR to surgical AVR in low- to moderate-risk patients found no difference at one year in mortality, myocardial infarction, or length of hospital stay after surgery, as well as a lower incidence of life-threatening bleeding and acute kidney injury [Elmaraezy 2017].

An additional principle that continues to evolve is that of postoperative anticoagulation in patients with BP implantation. Prescribing practices are currently varied, with a global registry of 48 centers showing that in the first 3 months following hospital discharge after BP AVR without CABG, only 63% of centers prescribe a vitamin K antagonist with or without aspirin [Colli 2008]. In a randomized clinical trial of 55 patients undergoing BP AVR, 4-dimensional CT administered 30 days postoperatively showed reduced leaflet motion in 40% of subjects. This rate was reduced in patients receiving therapeutic anticoagulation versus those receiving dual antiplatelet therapy and those receiving subtherapeutic or no anticoagulation. Following imaging, leaflet motion was eventually restored in all patients that continued or started therapeutic anticoagulation, whereas this was not the case in patients that remained free of anticoagulation. Despite differences in leaflet motion, there were no significant changes in short-term hemodynamics or clinical outcomes. Conversely, in a cohort taken from 2 single-center registries, rates of stroke or TIA were found to be higher in patients not receiving anticoagulation [Makkar 2015]. A separate study by Brennan and colleagues (2012) found that compared to aspirin only, a combination of warfarin and aspirin lowered both mortality and risk of embolic events in the first 3 months following surgery, although this came at the cost of a higher risk of bleeding [Brennan 2012]. Finally, an analysis of the Danish National Patient Registry found a decreased risk of cardiovascular death when warfarin was administered for 6 months postoperatively [Mérie 2012]. These findings are reflected in the recent AHA/ACC update that recommends anticoagulation for 3-6 months after AVR with tissue prostheses.3

This analysis does have several limitations, primarily related to the underlying studies. Comparisons between studies were limited by heterogeneity between age populations. A metaanalysis was not possible owing to the lack of homogeneity between study populations, as well as variability in the outcomes evaluated between studies. Additionally, all retrospective studies (17 of 19 in this review) are limited by significant inherent bias due to study design. Finally, the studies included encompass a 16-year time period, during which there were significant change in valve technology, indications for valve selection, and frequency of TAVR placement. Future research should focus on randomized controlled trials comparing valve type (bioprosthetic versus mechanical) for well-matched patients within various age ranges (ie, aged <60, 60-70, >70 years). Additionally, surgical AVR should be compared with transcatheter AVR for low-, moderate-, and high-risk populations.

CONCLUSION

The optimal choice of prosthesis in young and middle-aged patients undergoing AVR remains unclear. The present data highlight the heterogeneity of evidence that informs clinical guidelines and practice. These guidelines currently vary, especially in patients aged 50-60 years. Although classically MPs have been recommended for such patients, lifestyle concerns and new technology such as VIV implantation have led to an increase in the proportion of BPs implanted in younger individuals. Currently, long-term data are lacking for patients undergoing VIV procedures, as well as for patients implanted with current generation valves. As new evidence continues to emerge, it remains to be seen whether clinical guidelines will fully endorse the currently observed shift towards the use of bioprosthetic aortic valves in younger patients.

ACKNOWLEDGMENTS

This work was supported by the National Institutes of Health grants T32 HL007849, and UM1HL088925. The authors had full control of the design of the study, methods used, results, data analysis, and production of the written manuscript. None of the authors report any financial conflicts of interest.

G.A. reports a consulting relationship with Edwards Life Sciences, St. Jude, Atricure, Abbott, and Mitralign.

The authors extended their appreciation to librarians Megan Nunemaker, Karen Knight, and Whitney Townsend for their assistance with the databases' queries.

REFERENCES

Akins CW, Buckley MJ, Daggett WM, et al. 1998. Risk of reoperative valve replacement for failed mitral and aortic bioprostheses. Ann Thorac Surg 65:1545-51; discussion 1551-2.

Alex S, Hiebert B, Arora R, Menkis A, Shah P. 2018. Survival and long-term outcomes of aortic valve replacement in patients aged 55 to 65 years. Thorac Cardiovasc Surg 66:313-21.

Badhwar V, Ofenloch JC, Rovin JD, van Gelder HM, Jacobs JP. 2012. Noninferiority of closely monitored mechanical valves to bioprostheses overshadowed by early mortality benefit in younger patients. Ann Thorac Surg 93:748-53.

Baumgartner H, Falk V, Bax JJ, et al. 2017. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 38:2739-91.

Brennan JM, Edwards FH, Zhao Y, et al. 2012. Early anticoagulation of bioprosthetic aortic valves in older patients: results from the Society of Thoracic Surgeons Adult Cardiac Surgery National Database. J Am Coll Cardiol 60:971-7.

Brown ML, Schaff HV, Lahr BD, et al. 2008. Aortic valve replacement in patients aged 50-70 years: improved outcome with mechanical versus biologic prostheses. J Thorac Cardiovasc Surg 135:878-84; discussion 884.

Carrier M, Pellerin M, Perrault LP, et al. 2001. Aortic valve replacement with mechanical and biologic prosthesis in middle-aged patients. Ann Thorac Surg 71(5 suppl):S253-6.

Chiang YP, Chikwe J, Moskowitz AJ, Itagaki S, Adams DH, Egorova NN. 2014. Survival and long-term outcomes following bioprosthetic vs mechanical aortic valve replacement in patients aged 50 to 69 years. JAMA 312:1323-9.

Colli A, Verhoye JP, Heijman R, et al. 2008. Antithrombotic therapy after bioprosthetic aortic valve replacement: ACTION Registry survey results. Eur J Cardiothorac Surg 33:531-6.

Diemert P, Seiffert M, Frerker C, et al. 2014. Valve-in-valve implantation of a novel and small self-expandable transcatheter heart valve in degenerated small surgical bioprostheses: the Hamburg experience. Catheter Cardiovasc Interv 84:486-93.

Dvir D, Barbanti M, Tan J, Webb JG. 2014. Transcatheter aortic valve-in-valve implantation for patients with degenerative surgical bioprosthetic valves. Curr Probl Cardiol 39:7-27.

Dvir D, Webb J, Brecker S, et al. 2012. Transcatheter aortic valve replacement for degenerative bioprosthetic surgical valves: results from the global valve-in-valve registry. Circulation 126:2335-44.

Elmaraezy A, Ismail A, Abushouk AI, et al. 2017. Efficacy and safety of transcatheter aortic valve replacement in aortic stenosis patients at low to moderate surgical risk: a comprehensive meta-analysis. BMC Cardiovasc Disord 17:234.

Fraccaro C, Testa L, Schiavo A, et al. 2018. Transcatheter aortic valve implantation in patients younger than 75 years: guidelines-based patients selection and clinical outcome. Int J Cardiol 272:273-8.

Glaser N, Jackson V, Holtzmann MJ, Franco-Cereceda A, Sartipy U. 2016. Aortic valve replacement with mechanical vs. biological prostheses in patients aged 50-69 years. Eur Heart J 37:2658-67.

Goldstone AB, Chiu P, Baiocchi M, et al. 2017. Mechanical or biologic prostheses for aortic-valve and mitral-valve replacement. N Engl J Med 377:1847-57.

Head SJ, Çelik M, Kappetein AP. 2017. Mechanical versus bioprosthetic aortic valve replacement. Eur Heart J 38:2183-91.

Isaacs AJ, Shuhaiber J, Salemi A, Isom OW, Sedrakyan A. 2015. National trends in utilization and in-hospital outcomes of mechanical versus bioprosthetic aortic valve replacements. J Thorac Cardiovasc Surg 149:1262-1269.e3.

Jamieson WR, Burr LH, Miyagishima RT, et al. 2003. Re-operation for bioprosthetic aortic structural failure – risk assessment. Eur J Cardiothorac Surg 24:873-8.

Jones JM, O'Kane H, Gladstone DJ, et al. 2001. Repeat heart valve surgery: risk factors for operative mortality. J Thorac Cardiovasc Surg 122:913-8.

Kaneko T, Vassileva CM, Englum B, et al. 2015. Contemporary outcomes of repeat aortic valve replacement: a benchmark for transcatheter valve-in-valve procedures. Ann Thorac Surg 100:1298-304; discussion 1304.

Kirsch M, Nakashima K, Kubota S, Houël R, Hillion ML, Loisance D. 2004. The risk of reoperative heart valve procedures in octogenarian patients. J Heart Valve Dis 13:991-6; discussion 996.

Korteland NM, Top D, Borsboom GJ, Roos-Hesselink JW, Bogers AJ, Takkenberg JJ. 2016. Quality of life and prosthetic aortic valve selection in non-elderly adult patients. Interact Cardiovasc Thorac Surg 22:723-8.

Kulik A, Bédard P, Lam BK, et al. 2006. Mechanical versus bioprosthetic valve replacement in middle-aged patients. Eur J Cardiothorac Surg 30:485-91.

Maganti M, Rao V, Armstrong S, Feindel CM, Scully HE, David TE. 2009. Redo valvular surgery in elderly patients. Ann Thorac Surg 87:521-5.

Makkar RR, Fontana G, Jilaihawi H, et al. 2015. Possible subclinical leaflet thrombosis in bioprosthetic aortic valves. N Engl J Med 373:2015-24.

McClure RS, McGurk S, Cevasco M, et al. 2014. Late outcomes comparison of nonelderly patients with stented bioprosthetic and mechanical valves in the aortic position: a propensity-matched analysis. J Thorac Cardiovasc Surg 148:1931-9.

Mérie C, Køber L, Skov Olsen P, et al. 2012. Association of warfarin therapy duration after bioprosthetic aortic valve replacement with risk of mortality, thromboembolic complications, and bleeding. JAMA 308:2118-25.

Minakata K, Tanaka S, Tamura N, et al. 2017. Comparison of the long-term outcomes of mechanical and bioprosthetic aortic valves: a propensity score analysis. Circ J 81:1198-1206.

Moher D, Liberati A, Tetziaff J, Altman DG, PRISMA Group. 2009. Preferred reporting items for systematic reviews and meta-analysis: the PRISMA statement. PLoS Med 6:e1000097.

Myken P, Larsson P, Larsson S, Berggren H, Caidahl K. 1995. Similar quality of life after heart valve replacement with mechanical or bioprosthetic valves. J Heart Valve Dis 4:339-45.

Nishida T, Sonoda H, Oishi Y, et al. 2014. Long-term results of aortic valve replacement with mechanical prosthesis or Carpentier-Edwards Perimount bioprosthesis in Japanese patients according to age. Circ J 78:2688-95.

Nishimura RA, Otto CM, Bonow RO, et al. 2017. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Taste Force on Clinical Practice Guidelines. J Am Coll Cardiol 70:252-89.

Phan K, Zhao DF, Wang N, Huo YR, Di Eusanio M, Yan TD. 2016. Transcatheter valve-in-valve implantation versus reoperative conventional aortic valve replacement: a systematic review. J Thorac Dis 8:E83-93.

Pibarot P, Dumesnil JG. 2006. Prosthesis-patient mismatch: definition, clinical impact, and prevention. Heart 92:1022-9.

Ponikowski P, Voors AA, Anker SD, et al. 2016. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 18:891-975.

Potter DD, Sundt TM 3rd, Zehr KJ, et al. 2005. Operative risk of reoperative aortic valve replacement. J Thorac Cardiovasc Surg 129:94-103.

Prasongsukarn K, Jamieson WR, Germann E, Chan F, Lichtenstein SV. 2007. Aortic and mitral prosthetic valve replacement in age groups 61-65

& 66-70 years. Asian Cardiovasc Thorac Ann 15:127-33.

Roumieh M, Ius F, Tudorache I, et al. 2015. Comparison between biological and mechanical aortic valve prostheses in middle-aged patients matched through propensity score analysis: long-term results. Eur J Cardiothorac Surg 48:129-36.

Ruel M, Chan V, Bédard P, et al. 2007. Very long-term survival implications of heart valve replacement with tissue versus mechanical prostheses in adults <60 years of age. Circulation 116(11 suppl):I294-300.

Ruel M, Kulik A, Lam BK, et al. 2005. Long-term outcomes of valve replacement with modern prostheses in young adults. Eur J Cardiothorac Surg 27:425-33.

Ruel M, Kulik A, Rubens FD, et al. 2004. Late Incidence and determinants of reoperation in patients with prosthetic heart valves. Eur J Cardiothorac Surg 25:364-70.

Sakamoto Y, Yoshitake M, Matsumura Y, Naruse H, Bando K, Hashimoto K. 2016. Choice of aortic valve prosthesis in a rapidly aging and long-living society. Ann Thorac Cardiovasc Surg 22:333-9.

Stassano P, Di Tommaso L, Monaco M, et al. 2009. Aortic valve replacement: a prospective randomized evaluation of mechanical versus biological valves in patients ages 55 to 70 years. J Am Coll Cardiol 54: 1862-8.

Suri RM, Schaff HV. 2013. Selection of aortic valve prostheses: contemporary reappraisal of mechanical versus biologic valve substitutes. Circulation 17:1372-80.

Svennsson LG, Adams DH, Bonow RO, et al. 2013. Aortic valve and ascending aorta guidelines for management and quality measures: executive summary. Ann Thorac Surg 95:1491-505.

Wang Y, Chen S, Shi J, Li G, Dong N. 2016. Mid- to longer-term outcome comparison of the Medtronic Hancock II and bi-leaflet mechanical aortic valve replacement in patients younger than 60 years of age: a propensity-matched analysis. Interact Cardiovasc Thorac Surg 22:280-6.

Webb JG, Dvir D. 2013. Transcatheter aortic valve replacement for bioprosthetic aortic valve failure: the valve-in-valve procedure. Circulation 127:2542-50.

Webb JG, Wood DA, Ye J, et al. 2010. Transcatheter valve-in-valve implantation for failed bioprosthetic heart valves. Circulation 121:1848-57.

Weber A, Noureddine H, Englberger L, et al. 2012. Ten-year comparison of pericardial tissue valves versus mechanical prostheses for aortic valve replacement in patients younger than 60 years of age. J Thorac Cardiovasc Surg 144:1075-83.

Ye J, Cheung A, Yamashita M, et al. 2015. Transcatheter aortic and mitral valve-in-valve implantation for failed surgical bioprosthetic valves: an 8-year single-center experience. JACC Cardiovasc Interv 8:1735-44.

Zhao DF, Seco M, Wu JJ, et al. 2016. Mechanical versus bioprosthetic aortic valve replacement in middle-aged adults: a systematic review and meta-analysis. Ann Thorac Surg 102:315-27.