

## Surgical Management of Patients with Infective Endocarditis: A Systematic Review

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### ABSTRACT

**Introduction:** Replacement of the heart valves has been spread recently with wide variety of types and surgical techniques. There is, however, no consensus regarding the best type and/or techniques of the surgical treatment of infective endocarditis.

**Objective:** The aim of the systematic review was to evaluate the evidence-based published articles dealt with different types of valve replacement in the management of infective endocarditis.

**Methods:** An electronic search was conducted on the electronic search engine PubMed including Medline. Keywords used for this research included; infective endocarditis, bacterial endocarditis, surgery, valve replacement, outcomes, timing, mortality, relapse and death.

**Results:** Among the screened articles there were a total of 11 articles included for this systematic review. Out of which, there were 6 prospective randomized clinical trials and the remaining 5 studies were prospective clinical trials without randomization.

**Conclusion:** From the findings of this review it can be concluded that the infective endocarditis is still a life-threatening disease requires more efforts for prevention and management. Surgical treatment of infective endocarditis with prosthetic or biologic valves does not differ significantly in outcomes or complications with a little bit higher in complications when using biologic valves.

**Keyword:** infective endocarditis, bacterial endocarditis, surgery, treatment, valve replacement.

### INTRODUCTION

Endocarditis, also called infective endocarditis (IE), is an infectious disease affects the heart endocardium. Its effects can be either local or systemic resulting in insufficiency of the valve(s) or a variety of systemic signs and symptoms. Unfortunately, there is increase in the number of individuals with infective endocarditis in the recent years which in turn increase the need for surgical interventions and/or innovations in cardiac devices and prosthetic valves. There is a higher of risk in men than women particularly elders, intravenous drug users, and sometimes associates with systemic diseases such as: diabetes mellitus, cancer, or alcoholism. Some factors have been identified as risk factors including: heart valve disease, replacement of valve, congenital heart disease, and previous infective endocarditis <sup>(1-5)</sup>. IE can either bacterial or non-bacterial disease. For the former, staphylococcus aureus is the most suspected type causing IE. The most affected valves with infective endocarditis are as follows (in descending order): mitral valve, aortic valve, both mitral and aortic valves, tricuspid valve, and with rare frequency the pulmonary valve. Treatment of infective

endocarditis varies according to the cause and type of infection which may be medicinal or surgical <sup>(6,7)</sup>. Surgical treatment of IE differs widely among individuals reflecting that the indication for surgical intervention is depending on many factors and is not absolute issue <sup>(8)</sup>. A number of international guidelines have been published recently based on the evidence-based recommendations regarding valvular heart surgery. The European Society of Cardiology (ESC), however, has published its own guidelines on the management of infective endocarditis. It follows the same guidelines and recommendations of the American Heart Association (AHA) regarding the indications of surgical treatment for infective endocarditis <sup>(9)</sup>.

Surgical treatment of infective endocarditis is considered the most difficult surgeries facing the cardiac specialists. It requires more skills in removing the infected tissue of the endocardium and restoring the function of the heart. Moreover, patients in need for surgical treatment of IE usually present with some other systemic diseases or dysfunction of the cardiac muscles <sup>(10, 11)</sup>. Replacement of the heart valves has been spread recently with wide variety of types and surgical techniques. There is, however, no consensus

regarding the best type and/or techniques of the surgical treatment of infective endocarditis. The aim of the systematic review was to evaluate the evidence-based published articles dealt with different types of valve replacement in the management of infective endocarditis.

## **METHODS**

An electronic search was conducted on the electronic search engine PubMed including Medline. Keywords used for this research included; infective endocarditis, bacterial endocarditis, surgery, valve replacement, outcomes, timing, mortality, relapse and death. The flow of the information through the different stages of the systematic review includes identification of the articles, screening according to the eligibility criteria, and finally the inclusion of the relevant articles for review.

### ***Eligibility Criteria***

All articles published in English language from January 2000 to December 2017 were eligible to be included in this review. Search on PubMed search engine revealed 100 articles. After reading titles and abstracts, irrelevant and duplicated articles were excluded. The resulting articles were read carefully for clinical trial in humans regarding surgical treatment of IE with valvular replacement including detailed data about type of valve(s), outcomes, and complications. The references lists of the resulting articles were screened for additional studies. Review articles and articles without CBCT comparison were excluded. Therefore, the included articles for this review were 11 articles. The study was done after approval of ethical board of Umm Al-Qura university.

### ***Data Extraction***

Extraction of the data in relation to the required information was ensured by two reviewers. The data extraction form included: study design, number of included patients, age of patients, indication(s) for surgery, name of the involved valve(s), type of the valve (prosthetic or biologic), outcome of the surgery including survival rate, and complications of

the surgery including early mortality, late mortality, relapse, or any other complications.

## **RESULTS**

Among the screened articles there were a total of 11 articles included for this systematic review (Table 1). Out of which, there were 6 prospective randomized clinical trials and the remaining 5 studies were prospective clinical trials without randomization. The number of the included subjects varied considerably among studies ranging from 40 to 569. Two studies included > 50 subjects, two studies included > 100 and < 200 subjects, and seven studies included > 200 and < 600 subjects. The age of the participants ranged from 8 years to 89 years. Two studies reported the age without means (> 60 years and > 75 years). Indications for surgery differed widely including valvular diseases, myocardial infarction, ventricular dysfunction, ischemic heart disease, congestive heart failure, and re-replacement of the valve. The infected valves which were replaced in the included studies were, aortic, mitral, both aortic and mitral, pulmonary, and tricuspid valve. Nine studies replaced aortic valve, four studies replaced mitral valve, 3 studies replaced both aortic and mitral valves, one study replaced pulmonary valve, and one study replaced tricuspid valve.

Some studies replaced more than one types of valves. Different types of valves were used to replace the infected ones.

There were three studies used porcine bioprosthetic valve, five studies used mechanical prosthetic valve, one study used mechanical prosthesis valve with Maze procedure, three studies used biological valves, 1 study used pulmonary autograft valve, one study used Melody valve, and 1 study used silzone valve. The outcome of the surgery was presented in different ways including survival rate, hemodynamic performance, New York Heart Association (NYHA) classification, and left ventricle function. More details about outcomes and subsequent complications such as early and late mortality and other localized and systemic complications are presented in Table 1.

**Table (1):** Summary of the findings of the included studies

Reference of article	Study design	Sample size	Age of patients	Indication of surgery (congestive heart failure, pulmonary edema)	Name of valve	Type of valve	Outcomes of surgery	Complications
					(aortic, pulmonary)	(prosthetic, native)	(Success rate)	(early death, late death, rapture, relapse)
<b>Eichinger et al.</b> <sup>(18)</sup>	Pros. CT	561	70 (23-89)	Valvular heart disease	- Aortic  - Mitral	Porcine bioprosthesis	After 1 year evaluation 91% aortic group and 83% of mitral group had improvement in NYHA classification.  After 6 years evaluation 100% of both group had improvement.	- Early mortality rate was 2.4% for aortic and 1% for mitral.  - Late mortality rate was 3.7% per patient-year in aortic group and 3.6% per patient-year in the mitral group.  - Other complications include thromboembolism and valve thrombosis.
<b>Lim et al.</b> <sup>(12)</sup>	Pros. RCT	485	61 (10-82)	Valve relapse and dysfunction (stenosis / regurgitation)	- Aortic	Mechanical prosthesis	Survival rate was 82.4±2.6% for CarboMedics group and 79.9±2.8% for St Jude Medical group.	- Early mortality rate was 6% for CarboMedics group and 4.4% for St Jude Medical group.
					- Mitral			- Late mortality rate was 0.7% per patient-year for CarboMedics group and 1% per patient-year for St Jude Medical group.
					- Both			- Other complications include Thromboembolism and hemorrhage.

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Reference of article	Study design	Sample size	Age of patients	Indication of surgery (congestive heart failure, pulmonary edema)	Name of valve	Type of valve	Outcomes of surgery	Complications
					(aortic, pulmonary)	(prosthetic, native)	(Success rate)	(early death, late death, rapture, relapse)
<b>Reiss et al.</b> <sup>(19)</sup>	Pros. CT	88 young	58 for young	- Atrial fibrillation.	- Aortic	Porcine bioprosthesis	- Systolic gradient increased significantly.	- Valve-related death was 0.1% per patient-year for young group and 0.2% per patient-year for old group.
		167 old	72 for old	- Severely impaired left ventricular fraction.			- Effective orifice area values decreased significantly.	- Cardiac death was 0.1% per patient-year for young group and 0.2% per patient-year for old group.
<b>Stassano et al.</b> <sup>(13)</sup>	Pros. RCT	310	55-70	- Coronary artery disease.	- Aortic	- Biologic valve.	- The same survival rate was observed for both groups after 13 years.	- 41 died in biologic valve and 45 died in prosthetic valve.
				- Previous myocardial infarction.		- Mechanical prosthetic valve.	- Valve failure was more in biologic valve group.	- Other complications include Thromboembolism and bleeding endocarditis.
<b>Risteski et al.</b> <sup>(14)</sup>	Pros. RCT	40	> 75	Aortic stenosis	- Aortic	Biologic valve (stentless and stented)	Hemodynamic performance of the valves did not differ significantly between groups.	- After 5 years follow-up there was 25% death in stentless group and 30% death in stented group. - Other complications include recurrent endocarditis.
<b>Oxenham et al.</b> <sup>(15)</sup>	Pros. RCT	533	53.9±10.6	Ischemic heart disease	- Aortic - Mitral - Both	- Bjork-Shiley mechanical prosthesis. - porcine bioprosthesis	No significant differences in survival rate.	After 20 years follow-up there was 202 death for each group separately.
<b>Doss et al.</b> <sup>(16)</sup>	Pros. RCT	120	55-75	Aortic valve stenosis	- Aortic	- Pulmonary autograft valve.	Pulmonary valve group had significantly lower gradient	Complications include stroke and gastrointestinal bleeding.

Reference of article	Study design	Sample size	Age of patients	Indication of surgery (congestive heart failure, pulmonary edema)	Name of valve	Type of valve	Outcomes of surgery	Complications
					(aortic, pulmonary)	(prosthetic, native)	(Success rate)	(early death, late death, rapture, relapse)
						- Mechanical prosthesis.	than mechanical prosthesis valve.	
<b>Cheatham et al.</b> <sup>(17)</sup>	Pros. RCT	171	19	Ventricular track obstruction or regurgitation	Pulmonary	Melody valve	- After 7 years follow-up 113 patients were alive. - NYHA classification was class I or II.	- 57 died after 7 years follow-up. - 1 patient had mild pulmonary regurgitation.
<b>Kim et al.</b> <sup>(20)</sup>	CT	569	51.1±10.2	Atrial fibrillation.	Tricuspid valve	Mechanical valve prosthesis with Maze procedure	Improvement of left ventricle function	Replacement with Mechanical valve plus Maze procedure reduce the prevalence of thromboembolic complications
<b>Akhyari et al.</b> <sup>(21)</sup>	Pros. CT	223	> 60	Re-replacement of aortic valve prosthesis	Aortic valve	- Mechanical valve prosthesis - Biological valve.	Survival rate was comparable (73.9%±3.6% and 70.5%±6.3% for mechanical and biological groups, respectively).	Endocarditis as early mortality complication (8.4% and 12.5% for mechanical and biological groups, respectively).
<b>Dandekar et al.</b> <sup>(22)</sup>	Pros. CT	46	Aug-78	Congestive heart failure.	- Aortic	Silzone valve	Incidence of thromboembolic complications was modest.	Early mortality rate was 6.5%, 6 death occurred by non-cardiac cause, and 1 death occurred by cardiac cause not related to the valve.
				- Atrial fibrillation.	- Mitral			
					- Both			

## DISCUSSION

The main objectives of the cardiac surgery for infective endocarditis are: a) debriding and removing the all infected or necrotic tissues and b) restoring the anatomical morphology of the hart as well as restoring the function. These objectives, however, are depending greatly on status of the endocardium infection and thus may include the replacing one or more valves. Replacement of the whole entire heart (heart transplantation) can be performed but in certain cases where extremely endocarditis is exist with a history of multiple unsuccessful surgeries. The first replacement of the valve is dated back to 50 years ago and was performed by Dr. Young WG. at Duke University Medical Center.

It has been considered the standard for most endocarditis cases treated surgically. However, no consensus has been reached for the best choice of valve when surgically treating the infective endocarditis. Some surgeons emphasize that the debridement of the infected area and determining the risk factos of possibly recurrent IE is more important. Although the most common affected valve is tricuspid valve accounting for 50% of the reported cases followed by aortic and mitral valve with less than 20% of the reported cases <sup>(23, 24)</sup>, the most affected valve reported in the current review was the aortic valve followed by mitral valve while, only one study reported replacement of the tricuspid valve. This might related to the type of the studies included in this review.

Some death rates reported in the included studies were related to valve-related causes but only few studies reported the pathology of the source of infection. Staphylococcus aureus is still the main cause for infective endocarditis resulting in more hospitalization time and higher death rates <sup>(25, 26)</sup>. Despite the use of similar types of valves for the treatment of the infective endocarditis, the outcome differed considerably among the studies. Mechanical valves are made of biocompatible materials. This type of valves requires the patient to continue taking using drugs such as anticoagulant for the rest of his life to prevent blood clotting. However, biological valves such as porcine bioprosthetic valves are biological valves made from human or animal tissue. This type, similar to mechanical valves, can last through the patient's life. Moreover, patients with biological valves might not need to continue using medications for the reminder of their lives <sup>(6, 11)</sup>. The surgery results of infective endocarditis have been

reported as difficult conditions with considerable risk of morbidity and mortality. This risk increases with infection with staphylococcus aureus and with the presence of prosthetic valves <sup>(25)</sup>. The difference in the follow-up system of the in the included studies revealed difference in the complications and outcomes.

However, comparison between prosthetic and biologic valves in most of studies revealed no considerable difference with regard to the early and late mortality. This may indicate that the outcomes and complications of infective endocarditis through these variable follow-up systems and as well as variable periods of conducting the studies remains the same with no clear improvement despite of the advancement of technology in both surgical and medicinal fields. This alarming the need for improvement of the surgical techniques and/or the materials of the replacing valves. Further randomized trials studies are also needed with more follow-up system and among different people and areas.

## CONCLUSION

From the findings of this review it can be concluded that the infective endocarditis is still a life-threatening disease requires more efforts for prevention and management. Surgical treatment of infective endocarditis with prosthetic or biologic valves does not differ significantly in outcomes or complications with a little bit higher in complications when using biologic valves.

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