

# Clinical Application of Bioprosthesis in China: Current Status and Future\*

Yin WANG<sup>1†</sup>, Wei-wei JIANG<sup>2†</sup>, Nian-guo DONG<sup>1#</sup>

<sup>1</sup>Department of Cardiovascular Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China

<sup>2</sup>Department of Gastroenterology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China

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**Summary:** China is one of the countries which have a high incidence of heart valvular disease, but the use of biological valve is limited in China before because the majority of patients are young patients suffering from rheumatic heart disease. The biological valve has a good application prospect in China. On the one hand, the new generation of biological valves have been significantly improved in the aspects of anti-calcification treatment, anti-metabolism, material quality control, valve frame mechanics design, and leaflet sewing technology, and the application effect is improved; on the other hand, surgeons should adapt to the new concept changes, and correctly understand and rationally apply biological valves, master valve repair, atrial fibrillation ablation and other techniques, combined with interventional, minimally invasive techniques, etc., according to the specific conditions of the disease and choose the surgery type to ensure the patients' long-term life quality.

**Key words:** biological valve; valve surgery; clinical application; China

## 1 Current Status of Bioprosthesis in China and Characteristics of Valve Surgery

Statistically, there are about 400 000 valve replacements per year in the world, of which biological valves account for about 75%, and increase at a rate of 10% per year. During the “Twelfth Five-Year Plan” period, our department analyzed the application of artificial valve in 10 heart centers in China. The results showed the bioprosthesis accounted for 14.1% of all kinds of valve substitutes, and the rate of bioprosthesis application was 12.7%, 14.9%, 50.8% and 22.2% during the replacement of the mitral valve, aortic valve, tricuspid valve and pulmonary valve, respectively. There are large differences in different units. The use rate of biological valves in China has increased year by year, and remained at 15%–20% for the past 5 years. The average age of patients was 61.9 years, and the operative mortality was 2.8%. The 10-year survival rate was >82%, and the reoperation rate was >86%.

The number of cardiac surgeries in China has now exceeded 200 000 cases/year, and valve surgery

accounts for 20%–25%. At present, China's valve surgery has the following characteristics: (1) although the disease is still mainly rheumatic valvular disease, the proportion of degenerative and ischemic valvular diseases is higher than before; (2) the average age of patients with valvular disease is significantly higher than before; (3) the incidence of atrial fibrillation is higher, and the surgical methods and effects of valvular surgery for atrial fibrillation are gradually recognized. (4) valve repair technology has been developed rapidly in recent years, and there is still a gap between China and developed countries; (5) although the proportion of valve repair increases, valve replacement is still the mainstream surgery.

## 2 Reflections on Application of Biological Valves

### 2.1 Reasonable Grasp of Indications

According to the European and American guidelines, the age-related factors are excluded, and the current biological valve selection criteria (Class I recommendation) are as follows: (1) the patient's own requirements; (2) the quality of anticoagulant therapy cannot be guaranteed (coagulation contraindications, high risk, poor compliance, lifestyle and occupational limitations); (3) patients who have undergone secondary surgery for thrombosis after mechanical valve replacement have been confirmed to have poor

Yin WANG, E-mail: [wangyin0817@hotmail.com](mailto:wangyin0817@hotmail.com); Wei-wei JIANG, E-mail: [jiangwwuh@163.com](mailto:jiangwwuh@163.com)

<sup>†</sup>The authors contributed equally to this study.

<sup>#</sup>Corresponding author, E-mail: [dongnianguo63@gmail.com](mailto:dongnianguo63@gmail.com)

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anticoagulant effect; (4) patients have a low risk of secondary surgery<sup>[1-3]</sup>. Age is one of the most important factors affecting the choice of prosthetic valves<sup>[6]</sup>. The selection of biological flaps for elderly patients over 65 years of age has good durability and long-term effects have been confirmed by a large number of studies<sup>[4, 5]</sup>. The 2017 AHA/ACC Management of Valvular Diseases proposes an expanded age range for bioprosthetic applications. It is recommended that biovalvular indications can be reduced from 60–70 years to 50–70 years in patients undergoing aortic or mitral valve replacement (Class II). However, how to grasp the bioprosthetic indication for patients aged 50–70 is an urgent problem to be solved<sup>[6]</sup>. Our department analyzed the clinical data of aortic valve replacement under the age of 60 years from 2004 to 2016. The results showed that the hospital mortality, 5-year and 10-year survival rate were similar between the mechanical valve group and bioprosthesis group. Moreover, there were no statistically significant differences in valve-related reoperation rates, thrombosis, and bleeding events<sup>[7, 8]</sup>. Glaser *et al* performed a propensity-matched study on 2198 patients of aged 50–69 years undergoing aortic valve replacement and reported that 15-year survival rate was significantly improved in patients with a mechanical prosthesis. An important subgroup analysis according to age showed that the benefit of a mechanical over a bioprosthetic valve was only evident in patients aged 50–59 but not in those aged 60–69<sup>[9]</sup>. Kaneko *et al* reported 768 consecutive patients aged <65 years and propensity score matching yielded a cohort of 125 pairs of patients with similar etiology mixes undergoing mitral mechanical and bioprosthetic valve replacement. The operative mortality was also similar between the two groups. However, Kaplan-Meier analysis showed the MVRb group had a greater reoperation rate and shorter estimated survival<sup>[10]</sup>. Therefore, for younger patients, the choice of artificial valve should be specifically analyzed, considering age, occupation, mental condition, life expectancy, valve replacement site, presence or absence of pregnancy, long-term anticoagulation, combined diseases, thromboembolic risk, economy conditions and other factors.

Our department retrospectively analyzed the clinical data of tricuspid valve replacement in 1999–2014. It was confirmed that for patients with tricuspid valve replacement alone, the long-term survival rate of mechanical valve application is higher, and the short-term survival rate is equivalent. For the cases of Ebstein malformation, there is no significant difference in the long-term survival rate between the biological valve and the mechanical valve. The former has a higher survival rate in the near future. For pulmonary valve replacement, studies have also shown no significant difference in the rate of reoperation without mechanical

surgery after 5 years of mechanical valve replacement.

## 2.2 Selection of Biological Valve and Valve Repair

In recent years, accompanied with the maturity of valvular repair technology, the proportion of biological valve application has reduced to a certain extent. Most clinical studies have shown that the mortality of mitral valvuloplasty is significantly lower than that of mitral valve replacement. Meanwhile, mitral valvuloplasty can preserve better left ventricular function, avoid thromboembolism, anticoagulation hemorrhage, structural decline and other problems caused by artificial valve replacement<sup>[11]</sup>. Mitral valvuloplasty in elderly patients has achieved good long-term results, but for mitral valve disease caused by non-degenerative lesions, the advantages of valvuloplasty compared with replacement surgery are not obvious<sup>[12]</sup>. A recent report showed that the aortic valve formation in the young patients with severe aortic regurgitation was comparable to the bioprosthetic replacement at this site, and the early postoperative outcome was comparable. There was no significant difference in the perioperative complication rate. Although the rate of reoperation was lower in the repair group than the replacement group, the proportion of reflux was higher in the repair group. Therefore, aortic repair may be an option for patients with aortic valve disease, but it is not superior to bioprosthetic valve replacement.

## 2.3 Selection of Biological Valve and Interventional Valve

In recent years, transcatheter aortic valve replacement (TAVI), Mitraclip and other interventional valve surgery have become the choice of some patients. PARTNER clinical trials show that TAVI has a good effect on high-risk patients with severe aortic regurgitation. The all-cause mortality rate is lower in TAVI than that of traditional valve surgery at 1st year after surgery, but the decay rate is about 50% after 8 years. Can it be further in the future? To improve the long-term effect, a large sample control study<sup>[13]</sup> is still needed. For patients with high-risk severe mitral regurgitation, Mitraclip technology can achieve a similar edge-to-edge diporation effect, which can help alleviate mitral regurgitation, but this technique does not have obvious advantages compared with valve replacement. Therefore, it is currently believed that the clinical indications for Mitraclip should be more stringent.

## 2.4 Effect of Atrial Fibrillation on Application of Biological Valve

Atrial fibrillation is the most common arrhythmia associated with valvular disease in China. Anticoagulant drugs such as warfarin must be taken to prevent the occurrence of stroke and thromboembolism. The use of bioprosthetic replacement for simultaneous surgical atrial fibrillation is one of the most highly regarded procedures. For the case of a previous history of clear

embolization, left atrial diameter >80 mm, and poor long-term effects after atrial fibrillation ablation, it is recommended to choose a mechanical valve to promote anti-coagulation therapy.

## 2.5 Leaflet Replacement and Bioprosthetic Replacement

Considering that the artificial valve replacement is difficult to apply in children with valvular disease, for a specific child patient, the surgeon may cut the diseased leaflet into a suitable shape with a self-pericardial or bovine pericardium, suture it at the annulus position, and perform leaflet replacement. This procedure does not require anticoagulation and retains some of the healthy leaflets and annulus functions. Therefore, it has certain advantages for children who cannot implant biological flaps. However, calcification of biomaterials is still a difficult problem. Studies have shown that adult patients (mean age 30 years) use bovine pericardium to replace aortic valve leaflets, and the 10-year and 16-year exemption rate is 78% and 55% respectively. Its durability is worse than that of biological valves. The reason may be that the anti-calcification treatment process of autologous pericardium or bovine pericardium has not reached the level of bioprosthetic production. Therefore, valve leaf replacement should strictly grasp the indications in adult patients with valvular disease.

## 2.6 Future Prosthetic Valve Development Direction—Tissue Engineered Valve

Tissue engineered heart valve is a special kind of biological valve. The biggest difference from the existing commercial biological valve is that it is constructed according to the principle of tissue engineering, with autologous living cells and extracellular matrix, so that it has self-renewal and transformation ability. Because of excellent biomechanical and hemodynamic performance, good durability, and no need for anticoagulation, tissue engineered heart valve is expected to overcome the shortcomings of existing prosthetic valves and become an ideal valve replacement<sup>[14, 15]</sup>.

### Conflict of Interest Statement

All authors declare that they have no competing financial interests.

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