

# Heart Valve Replacement for Patients with End-Stage Renal Disease in Japan

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There is some controversy regarding the choice of prosthetic valves in patients with heart disease and concomitant end-stage renal disease requiring chronic dialysis. Dialysis patients tend to have a short life expectancy. In Japan, the 1-year survival of the dialysis patients was 80% in the 1980s, but exceeds 85% in the 2000s. The 5-year survival has been 54%–60% for the past 20 years. In addition, the 10-year and 15-year survivals have been 35%–42% and 23%–31%, respectively. However, in the United States, the 5-year survival had only improved to 35% among patients who started dialysis between 1996 and 2000, and the life expectancies of chronic dialysis patients in their sixth, seventh and eighth decades is 5.3–6.2 years, 3.8–4.5 years, and 2.7–3.2 years, respectively. The life expectancy of dialysis patients in Japan is thus better than that of patients in the United States.

Some surgeons prefer to use bioprosthetic valves because of a high rate of hemorrhagic complications in dialysis patients. They are hesitant to use anticoagulation therapy in dialysis patients with mechanical valves. Others prefer mechanical valves because of the potential for early structural dysfunction of bioprosthetic valves implanted in the dialysis patients with abnormal calcium metabolism, which can cause calcium deposition on the bioprosthetic valves during the early postoperative period.

The life expectancy of dialysis patients in Japan is relatively high. The potential risk of early calcification of bioprosthetic valves should be taken into account when choosing prosthetic heart valves for these patients in Japan. (*Ann Thorac Cardiovasc Surg* 2010; 16: 4–8)

**Key words:** valve replacement, chronic dialysis, prosthetic heart valve

## Profiles of Patients with End-Stage Renal Disease

### a) Life expectancy

The Japanese Society for Dialysis Therapy has reported on the current situation of patients with end-stage renal disease requiring chronic dialysis in Japan.<sup>1)</sup> The number

of chronic dialysis patients was 36,397 in 1980 and increased to 275,119 in 2007 (Fig. 1). This represents more than a 4-fold increase over the last quarter of a century.

Although the introduction of dialysis in patients carries high risks such as aging, diabetes mellitus, and nephrosclerosis, the annual mortality of chronic dialysis patients has remained stable at 9.2%–9.7% since 1992 (Fig. 2). This suggests that dialysis is being managed adequately in Japan. The survival rate has also improved: The 1-year survival was 80% in the 1980s, but has exceeded 85% in the 2000s. The 5-year survival has been 54%–60% for the past 20 years. The 10-year and 15-year survivals are currently 35%–42% and 23%–31%, respectively.

In the United States, the 5-year survival had improved to 35% among patients who started dialysis between 1996 and 2000.<sup>2)</sup> The death rate of chronic dialysis patients

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Received May 29, 2009; accepted for publication July 21, 2009  
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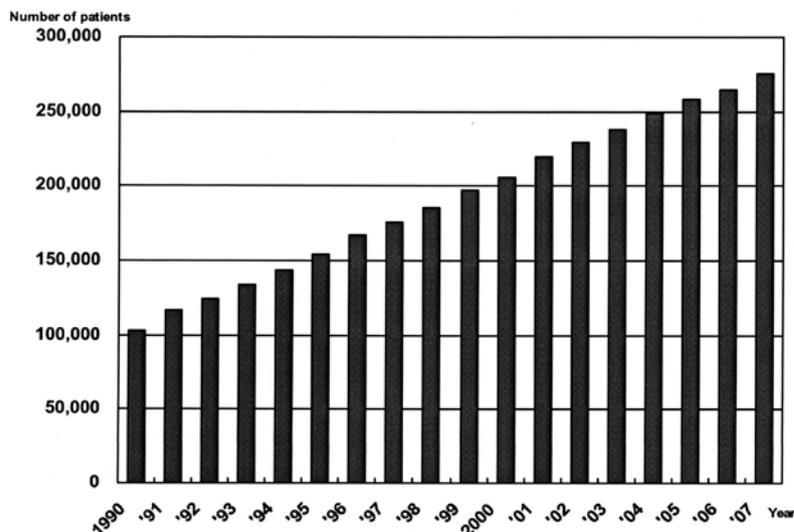


Fig. 1. Annual numbers of hemodialysis patients in Japan.

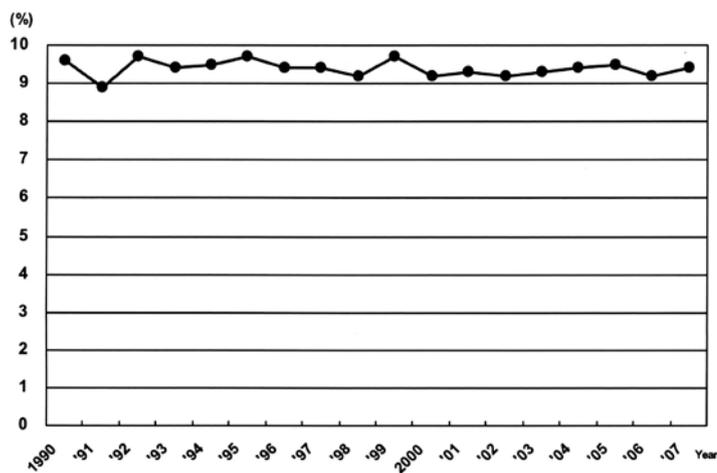


Fig. 2. Annual mortality of hemodialysis patients in Japan.

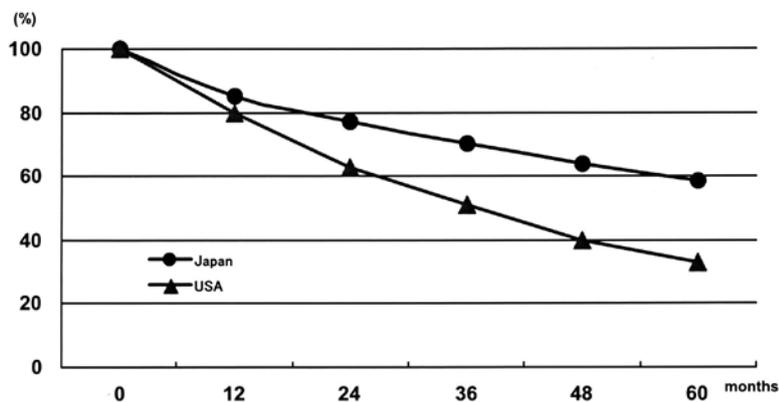
older than 65 years old is about 6 times that of the general population. In addition, the life expectancies of chronic dialysis patients in the United States during their sixth, seventh and eighth decades are 5.3–6.2 years, 3.8–4.5 years, and 2.7–3.2 years, respectively.

The statistical analyses of the data differ and it is therefore difficult to reach definite conclusions, but it is possible to identify outline differences in the prognostic profiles of end-stage renal disease patients between Japan and the United States. The prognoses for chronic dialysis patients are notably different between the two countries, with the life expectancy of dialysis patients in Japan being better than that of similar patients in the United

States (Fig. 3).

#### b) Complication rates of heart disease

Infections are the most common cause of death among chronic dialysis patients in Japan, with an incidence of 26%, followed by heart failure (23%), malignant tumors (10%), cerebrovascular disease (6%), and ischemic heart disease (3.2%). In the United States, the mortality due to cardiovascular diseases and infections are also high after the introduction of dialysis in patients with end-stage renal disease, and mortality due to cardiovascular diseases is high in the aging population and in Caucasians.



**Fig. 3.** Survival of hemodialysis patients in Japan and the United States of America. The survival of Japanese patients was made by referring to a table shown in the homepage of the Japanese Society for Dialysis Therapy,<sup>1)</sup> and that of USA was shown in the homepage of Department of Veterans Affairs.<sup>2)</sup>

## Heart Valve Surgery in Dialysis Patients

### a) Japan

Many chronic dialysis patients require surgery for heart diseases, and some studies have investigated dialysis patients undergoing heart valve surgery.

Ura and colleagues retrospectively reviewed the clinical results from 12 long-term renal dialysis patients undergoing valve replacement with mechanical prosthetic valves in Japan.<sup>3)</sup> The median follow-up period was 37.1 months. They showed that the hospital mortality was 8.3%, with non-cardiac late death in 2 patients (liver cirrhosis, gastric cancer), and non-fatal bleeding from digestive organs in one patient with end-stage liver cirrhosis. They concluded that their data supported the continuing use of mechanical valves in dialysis patients.

Miura and colleagues also reported on 41 valve replacement cases.<sup>4)</sup> They implanted 44 mechanical valves and 7 bioprosthetic ones. The overall hospital mortality was 22% (9 cases) and the cumulative 5-year survival was 49%. Although the follow-up period was less than 1 year, no structural valve deterioration was detected in the bioprosthetic group. The causes of late death included infections in 6 and hemorrhagic disease in 6 cases. Other nonfatal hemorrhagic complications, such as intestinal bleeding, were also recognized in 14 cases. Anticoagulation therapy in the patients with bioprosthetic valves was limited to within 3 months after operation. In the mechanical valve group, the international normalized ratio (INR) was maintained at around 2.0 for the aortic position and around 2.5 for the mitral position.

They concluded that bioprosthetic valves should be considered as an option when dialysis patients require valve replacement.

Aoki and colleagues reported mid-term results of 9 bioprosthetic valve cases and 36 mechanical valve ones.<sup>5)</sup> Mitral valve plasty was performed as a concomitant procedure in 6 cases. The hospital mortality in all patients was 7%, and the cumulative 5-year survival was 47%. Hemorrhagic complications and thromboembolism were recognized in 3 cases in the mechanical valve group. Structural deterioration was detected in the valves in the bioprosthetic valve group, requiring re-operation at 19, 24, and 50 months after their initial operation. In this study, INR was maintained between 1.5 and 2.0 for post-operative anticoagulation therapy when mechanical valves were implanted. They concluded that mechanical prosthetic valves were preferable for dialysis patients.

Kato and colleagues retrospectively analyzed 27 dialysis patients who underwent isolated valve replacement from 1993 to 2002.<sup>6)</sup> The overall survival was 85.2% at 3 years and 72.9% at 5 years, and the survival of 23 patients with mechanical valves was 82.6% at 3 years and 76.7% at 5 years. One patient with a bioprosthesis developed structural deterioration after 3 years.

Umezu and colleagues recently reported the clinical results from 63 consecutive dialysis patients who underwent valvular surgery.<sup>7)</sup> The patient profiles differed slightly between patients receiving mechanical and bioprosthetic valves. Combined aortic and mitral valve replacement were performed more frequently in the former, while aortic valve replacement was more common in the latter.

They concluded that the choice of prosthesis did not influence the surgical outcome, except in terms of early mortality. Unfortunately, their mean follow-up period was only 49 months. Longer follow-up studies are required to confirm the suitability of mechanical or bio-prosthetic valves for dialysis patients in Japan.

In addition to potential complications arising from heart valve surgery, the outcomes of heart diseases in dialysis patients are also poor in comparison with non-dialysis patient. Kawahito and colleagues examined 87 dialysis patients undergoing concomitant coronary artery bypass grafting.<sup>8)</sup> The hospital mortality was 14.9%, and the authors concluded that combined valve surgery and age over 70 years were risk factors for hospital death. Boku and colleagues compared the results of 37 elective and 17 urgent/emergency cardiovascular operations in patients with chronic dialysis, and showed that the midterm clinical results after elective cardiovascular surgery were acceptable, whereas the results after urgent/emergency surgery were poor.<sup>9)</sup>

#### **b) The US**

There have been many studies on prosthetic valve selection in chronic dialysis patients in the United States. Lucke and colleagues retrospectively compared 9 patients with bioprosthetic valves with 10 with mechanical ones.<sup>10)</sup> Patients in both groups were similar ages (56.5 versus 56.6 years). The estimated survival of all patients at 5 years was  $42 \pm 14\%$ . Mechanical valve patients had a significantly higher rate of cerebrovascular accidents and bleeding complications. No subsequent re-operations were required for biological valve failure at a mean follow-up of  $32 \pm 53$  months. Thus, they concluded that preference should be given to biological valve prostheses, instead of mechanical ones, in patients undergoing chronic renal dialysis.

Kaplon and colleagues reported on 17 patients with mechanical valves and 25 with bioprosthetic ones, and demonstrated postoperative survival rates at 3 and 5 years of 50% and 33%, respectively, for mechanical valve replacement, and 36% and 27%, respectively, after bioprosthetic valve replacement.<sup>11)</sup> Although the difference between these two groups was not significant, Kaplon and colleagues showed that one case in the mechanical valve group and three in the bioprosthetic group required re-operation for prosthetic endocarditis, and that one case in the bioprosthetic group required re-operation because of structural dysfunction 10 months after the initial operation. The author concluded that prosthetic valve endocarditis

tended to occur in chronic dialysis patients and that bio-prosthetic valves could be used despite the possibility of early prosthetic valve dysfunction, because of the poor life expectancy of dialysis patients.

Brinkman and colleagues reported on a 15-year experience of heart valve replacement in patients with end-stage renal disease.<sup>12)</sup> The subjects consisted of 55 aortic valve, 30 mitral valve, and 3 tricuspid valve cases, as well as others. The author analyzed 46 patients who survived for > 30 days. Seventeen patients out of 34 with mechanical valves had bleeding or stroke, compared with one of 12 with bioprosthetic valves. The 1-, 3-, and 6-year survival rates of all patients were 60.5%, 28.5%, 15.9%, respectively. The author concluded that bioprosthetic valves were the preferred valve substitute in patients on chronic dialysis, because of their poor prognosis and the higher incidence of late bleeding or stroke associated with mechanical valves. However, 2 cases in this study also required re-operation because of structural dysfunction, at 15.2 months and 54.6 months after the initial operation, respectively.

In 2002, Herzog and colleagues discussed the validity of prosthetic valve selection, based on the long-term clinical results of chronic dialysis patients in the United States.<sup>13)</sup> The hospital mortality of 5,858 patients between 1978 and 1998 was 20.7%. Aortic valve replacement was performed in 3,415, mitral valve replacement in 1,848, and both aortic and mitral valve replacement in 562 patients. The study showed that the 1-, 3-, and 5-year survivals were 54.7%, 27.2%, and 13.8%, respectively, and that the survival rates were similar for patients with mechanical and bioprosthetic valves. Thus, they concluded that the initial practice guidelines proscribing bioprosthetic heart valves in hemodialysis patients in the United States, published in 1998, should be rescinded. However, they also reported that one patient required re-operation for bioprosthetic valve structural dysfunction at 10 months after the initial operation.

In 2006, Chan and colleagues compared 47 bioprostheses and 22 mechanical prostheses.<sup>14)</sup> A survival advantage was observed in favor of the mechanical prostheses. Five-year freedom from all valve-related complications was  $82.8 \pm 8.1\%$  for the bioprostheses and  $76.4 \pm 12.7\%$  for mechanical ones, including one case of structural bioprosthetic valve deterioration at 95 months after surgery.

#### **Prosthetic Valve Selection in Japan**

It is inappropriate to apply the revised guidelines of the American College of Cardiology and American Heart

Association to Japan, because of the huge difference in prognoses between American and Japanese dialysis patients. The revised guidelines withdraw the recommendation for valve replacement with mechanical prostheses for patients with renal failure or on hemodialysis.<sup>15)</sup> However, as mentioned above, life expectancy differs dramatically between Japan and the United States. A bioprosthetic valve implanted in a chronic dialysis patient has a potential risk of early calcification, causing structural dysfunction due to abnormal calcium metabolism. This potential risk must be taken into consideration in Japan, where the life expectancy exceeds that in the United States.

Chronic dialysis patients tend to have more hemorrhagic complications. Therefore, dialysis patients undergoing anticoagulation therapy may be at increased risk of these complications. The target value for anticoagulation therapy is generally lower in Japan than in Europe and the United States: INR is 1.5–2.5 in the case of dialysis patients in Japan. This level is lower than that recommended by the guidelines for the management of patients with valvular heart disease revised by the American College of Cardiology and American Heart Association. However, the fatal hemorrhagic complication rate in dialysis patients with mechanical valves is regarded as acceptable.

## Conclusions

The life expectancy of chronic dialysis patients in Japan is longer than that in the United States. Bioprosthetic valves implanted in such patients are associated with the potential risk of early calcification, leading to prosthetic valve deterioration. And, the postoperative management for patients with prosthetic valves is minute in Japan. Thus, the risk of calcification must be taken into account when choosing between bioprosthetic and mechanical valve prostheses for dialysis patients in Japan.

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