

中文題目：比較亞洲雙葉型主動脈瓣與三葉型主動脈瓣之患者在中重度以上主動脈逆流之不同

英文題目：Comparison between Bicuspid and Tricuspid Aortic Regurgitation in Asian population: Presentation, Survival and Aorta Complications

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## **Background:**

Bicuspid aortic valve(BAV) is the most frequently seen congenital heart defect and represents an increasing etiology of hemodynamically significant aortic regurgitation(AR), which is the third most common valvular heart disease. As compared to tricuspid aortic valve(TAV), BAV-AR patients are distinctly different: they are more than one decade younger, had more mixed mechanisms of AR including cusp prolapse and root dilatation, had larger aortic annulus and exhibited better survival. Despite these inherent differences, publications comparing BAV versus TAV in hemodynamically significant AR are scarce and Asian data is especially lacking. Our study is to examine whether there are differences between Asian BAV-AR and TAV-AR in those with hemodynamically significant AR, including aorta complications.

## **Methods:**

Between 2008-2020, all consecutive patients  $\geq 18$  years-old with  $\geq$ moderate-severe chronic AR by transthoracic echocardiogram(TTE) were retrospectively identified from electronic echo database in a Taiwan tertiary medical center. All cases were manually reviewed to determine eligibility. Exclusion criteria included: mitral stenosis/regurgitation and aortic stenosis of more than mild, prior mitral/aortic surgery, complex cyanotic congenital heart disease, and acute AR(dissection, trauma, active endocarditis).

Primary endpoint were all-cause mortality during total follow-up(observation stopped at death or last follow-up), under medical surveillance(observation stopped at aortic valve surgery[AVS], death or last follow-up) and post-AVS.

Secondary endpoint included, 1) Cumulative incidence of AVS (i.e. AV repair or replacement), 2) surgical indications(symptoms, left ventricular ejection fraction[LVEF] $< 50\%$ , aorta surgery, LV end-systolic dimension(LVESD) $> 50\text{mm}$ , LVESD index(LVESDi) $> 25\text{mm}/\text{m}^2$ , and LV end-diastolic dimension[LVEDD] $> 65\text{mm}$ ) based on guidelines, 3) LV recovery defined as LV reverse remodeling between pre-surgical and post-AVS TTE (within 6-18 months

post-AVS), and 4) incidence of aortic dissection(AD).

### **Results:**

There were 149 BAV-AR(age  $48\pm 16$  years) and 562 TAV-AR(age  $68\pm 15$  years,  $P<0.0001$ ) patients; baseline indexed LV, indexed sinus of Valsalva(SOV), and indexed ascending aorta size were larger in TAV-AR. Total follow-up was 4.8(IQR: 2.0-8.4) years, 185 patients died (28 died post-AVS), including 170(30%) TAV and 15(10%) BAV patients. BAV-AR had significantly better 10-year survival both for the total follow-up ( $86\pm 4\%$  versus  $57\pm 3\%$ ,  $p<0.0001$ ) and follow-up under medical surveillance ( $85\pm 4\%$  versus  $47\pm 4\%$ ,  $p<0.0001$ ), but became insignificant after age adjustment( $P=0.33$ ). As compared with age- and sex-matched population, TAV-AR(Hazard ratio[HR], 3.1) had survival penalty( $P<0.0001$ ). Post-AVS 10-year survival was  $93\pm 5\%$  in BAV-AR and  $78\pm 5\%$  in TAV-AR, respectively( $P=0.08$ ).

In total, 252(35%) patients underwent AVS, including 51 BAV and 201 TAV patients. The 10-year AVS incidence in TAV vs. BAV was  $51\pm 4\%$  vs.  $40\pm 5\%$  ( $P=0.09$ ), respectively; TAV-patients had 2.84-fold risk of having AVS after adjustment for age, sex, Charlson comorbidity index score, LVEF, and New York Heart Association functional classification (HR, 2.85; 95% CI, 1.98-4.10;  $P<0.0001$ ). Regarding surgical-indications, BAV-AR patients were less operated on for symptoms, but more so for LVEDD(i)  $>50\text{mm}$  ( $25\text{mm}/\text{m}^2$ ), LVEDD $>65\text{mm}$  and early surgery, as compared to TAV-AR patients. Of 252 patients undergoing AVS, 133(53%) had a follow-up TTE between 6 to 18 months post-AVS (median time, 12[IQR: 9.5-14.5] months). Post-AVS LVEDD, LVEDS, and LVEDSi decreased significantly as compared to pre-AVS TTE in both groups(all  $P<0.0001$ ).

Aortic dissection(AD) occurred in 18 patients (type A in 17 and type B in 1; average age,  $63\pm 15$  years; average BSA,  $1.76\pm 0.24$  m<sup>2</sup>; 4[22%] female), including 1 BAV (type A dissection) and 17 TAV patients. The overall cumulative AD-incidence was  $3.7\pm 1.0\%$  at 10-year (incidence rate, 48.6 [95% CI, 29.7- 75.4]) per 10,000 person-year). The 10-year cumulative incidence of AD was higher in TAV-AR( $4.8\pm 1.5\%$ ) than in BAV-AR( $0.9\pm 0.9\%$ ), and was determined by aorta greater than 45mm( $P\leq 0.015$ ).

### **Conclusion:**

In this large contemporary Asian cohort, we compared differences between TAV and BAV patients with hemodynamically-significant AR for the first time. Our findings suggested that Asian TAV-AR patients were at later stage of AR course, had survival penalty, and had high AD-rate as opposed to BAV-AR. The cumulative incidence of AD, which was reported for the first time in significant AR-cohort, was

higher in TAV and seemed to be related to aorta size  $\geq 45$ mm. The important clinical implications are: first, clinicians can reassure BAV patients with AR about low AD risks during observation in the absence of other risk factors (i.e. family history), similar life expectancy to general population, good post-AVS survival, and good LV recovery, which again emphasized that age and not valve-anatomy determined AR-survival. Second, for patients with AR, regular TTE surveillance and clear reporting for AR-progression and most importantly, aorta-progression both before AVS and post-AVS is paramount because fatal AD may be prevented through early intervention once the aorta size was  $\geq 45$ mm. Third, in the face of culture-related surgery-hesitancy, good post-AVS survival in both BAV-AR and TAV-AR patients should reassure the patient for prompt intervention. The overall survival penalty of TAV-AR patients alerts clinicians in Asia to be more vigilant about significant AR and to refer patients earlier for timely intervention; educating the patients may improve their acceptance for AVS and subsequently restore the life expectancy.