Estimating the Prognosis of Patients With Aortic Stenosis in the Current Japanese Population

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The importance of estimating the prognosis of patients with aortic stenosis (AS) can not be emphasized too much. Today, aortic valve replacement (AVR) has been established as the standard therapy for symptomatic AS, but alternative therapies such as transcatheter aortic valve replacement (TAVR) are available for high-risk patients who are not eligible for open surgery. However, for the severest patients with a life expectancy <1 year or the chance of “survival with benefit” <25% at 2 years,¹ TAVR is also not recommended. Recently, to overcome this clinical discrepancy, the balloon aortic valvuloplasty has been recovered its importance as a bridge therapy to the advanced therapy such as AVR or

TAVR. Overall, the strategies for AS treatment have become more complex than ever, so the estimation of the prognosis of AS patients is quite important in the current clinical era.

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To estimate the prognosis of AS in the current era, it is also essential to realize that the average age of AS patients has been getting higher as expected lifespan has been prolonged. A recent prospective population-based study demonstrated that the prevalence of AS in 50–59, 60–69, 70–79 and 80–89 year olds was 0.2, 1.3, 3.9 and 9.8%, respectively.² Also, age-related

Table. Survival Rate of Patients With AS

Author	Launch year	No. of participants	Inclusion criteria	Survival rate (%)					
				1 year	2 years	3 years	4 years	5 years	Afterward
Frank et al ⁶	1954	15	AVPG ≥50 mmHg or AVA ≤0.7 cm ² /m ²	–	85	64	–	48	10 (10 years)
Chizner et al ⁷	1966	42	AS patients (32 symptomatic, 23 moderate or severe)	74	52	43	–	–	–
Pellikka et al ⁸	1984	622	Asymptomatic AS, APF ≥4.0 m/s	80	63	–	–	25	–
Otto et al ⁹	1989	123	Asymptomatic AS, APF ≥2.5 m/s	93	–	62	–	26	–
Bouma et al ¹⁰	1991	205	AVPG ≥50 mmHg or AVA ≤1.0 cm ²	–	–	49	–	–	–
Rosenhek et al ¹¹	1994	126	Asymptomatic AS, APF ≥4.0 m/s	67	56	–	33	–	–
Rosenhek et al ¹²	1995	116	Asymptomatic AS, APF ≥5.0 m/s	64	36	25	12	–	3 (6 years)
Perera et al ⁴	2005	25	Asymptomatic AS, AVA ≤1.0 cm ² of APF ≥4.0 m/s or AVPG >40 mmHg	–	–	64	–	–	–
		41	Symptomatic AS, AVA ≤1.0 cm ² or APF ≥4.0 m/s or AVPG >40 mmHg	–	–	27	–	–	–
Barasch et al ¹³	2003	241	AVA <0.6 cm ² /m ² and LVEF >50%	71	–	–	–	28	12 (9.5 years)
Sato et al ³	2006	412	AVPG ≥30 mmHg	–	–	82	–	–	–
		154	NYHA class I (asymptomatic)	–	–	90	–	–	–
		208	NYHA class II	–	–	83	–	–	–
		47	NYHA class III/IV	–	–	50	–	–	–
		255	NYHA class II/III/IV (symptomatic)	–	–	79	–	–	–

Indicated are the survival rates at indicated time points in each study. APF, aortic peak flow; AS, aortic stenosis; AVA, aortic valve area; AVPG, aortic valve peak pressure gradient; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

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comorbidities are increasing and having a significant effect on the prognosis of AS patients. Thus, in the advanced aging society that we are facing in Japan today, the natural history of AS patients will differ from previous reports in other countries.

In this issue of the Journal, Sato et al³ report the prognosis of Japanese AS patients as well as proposing an original risk score to estimate the prognosis of AS patients. The authors enrolled 412 patients with AS, which was defined as aortic valve peak pressure gradient (AVPG) >30 mmHg, from their CHART-2 study. After their follow-up for 3-years, the overall mortality rate was 17.7% (73 events). Crude 3-year mortality was 9.5%, 16.5% and 49.7% for patients with NYHA class I, II, and III/IV, respectively. Furthermore, from their stepwise Cox regression analysis, the authors identified 7 factors and proposed a novel risk score to estimate the prognosis by summing up the weighted score of each factor: NYHA class III/IV (score 6), male sex (3), serum albumin level ≤ 4 g/dl (2), aortic peak flow (APF) ≥ 4.5 m/s (2), age ≥ 75 years, chronic kidney disease (2) and anemia (1). Each case was assigned to a low- (sum of the scores 0–6), intermediate- (7–10) or high-risk (11–18) group. Compared with the low-risk group, the hazard ratios of the intermediate- and high-risk groups were significantly higher for all-cause mortality (HR 4.49, 95% confidence interval (CI) 2.23–8.43, $P < 0.01$; HR 18.34, 95% CI 9.18–36.63, $P < 0.01$, respectively) and it was also the case for cardiovascular death and non-cardiovascular death.

One of the most important facts provided here is the natural history of AS in the current Japanese population. The prognosis of AS demonstrated in previous papers has varied widely (Table). Even the study designs were different, the prognosis of AS tends to be better in the recent studies. The 2-year event-free survival in asymptomatic patients was 63% and 56% in the studies conducted in 1984 and 1994, respectively, but lower than 3-year event-free survival in 2005 (64%). This was mainly achieved by advancements in medical care through the decades. Also, it should be taken into account that the mortality of AS patients will vary among the cohorts. In Table, the 3-year survival of symptomatic AS shown by Sato et al is as high as 79%,³ whereas that by Perera et al is 27%⁴ (note that the majority of the patients become symptomatic when the disease becomes severe eg, APF ≥ 4.0 m/s). It indicates that mortality of AS patients might be higher in Japan compared with previous reports.

Another feature of the present study is the original risk stratification score using comorbidities. In an aged society, the comorbidities of patients directly affect the outcome. Indeed, Martinez-Selles et al recently reported that the average Charlson comorbidity index was 3.0 ± 1.7 in patients with severe AS aged over 80 and that 16.3% of them showed high comorbidity (index ≥ 5).⁵ They also described the Charlson index as an independent predictor of prognosis. Additionally, the planned medical intervention was not associated with prognosis in patients with high comorbidity, which is clearly indicating that the estimation of prognosis is never accurate without consideration of the comorbidities in AS patients. In the present paper, Sato et al successfully identify 7 comorbidities and weight them to generate their original risk score.

The present report may have a substantial effect on the care of AS patients. In daily practice, the prognosis of each AS

patient could be estimated from his/her individual clinical data, which may strongly support objective decision making by patients, especially whether or not to undergo invasive interventions.

Then, what comes next to improve more? As the participants of the present study were recruited from the CHART-2 study, the available comorbidity data were limited. The major life-limiting comorbidities, such as cancer, stroke, respiratory disorders etc., might have been missed. In addition, information about congenital abnormalities (uni- and bicuspid valve) and possible risks for progression of AS such as diabetes or a history of smoking may have a potential contributory effect on the accuracy of the risk score. Finally, just as the present study revealed, the natural course of AS does change according to the population, era and sociomedical factors. Continuous updates of objective study and appropriate application to clinical decision-making in the real world are the keys to best practice for AS.

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