Procedure- and Age-Specific Risk Stratification of Single Aortic Valve Replacement in Elderly Patients Based on Japan Adult Cardiovascular Surgery Database

Nobuhiro Handa, MD; Hiroaki Miyata, PhD; Noboru Motomura, MD; Takeshi Nishina, MD; Shinichi Takamoto, MD; The Japan Adult Cardiovascular Database Organization

Background: Successful introduction of trans-catheter aortic valve implantation for selected patients with critical aortic stenosis has raised the question of how to identify appropriate high-risk candidates.

Methods and Results: To assess the risk profile of patients undergoing single aortic valve replacement (sAVR), multiple logistic regression analysis was applied for open sAVR (n=7,883) registered in the Japan Cardiovascular Surgery Database to predict surgical mortality. Three subgroup analyses stratified by age, <70 years (young), 70–79 years (middle), and ≥80 years (elderly), were also performed. Preoperative patient characteristics indicated increased prevalence of several variables in the elderly subgroup including New York Heart Association (NYHA) class III/IV, 3-vessel coronary artery disease (3VCAD), respiratory insufficiency, and stroke. The following factors, however, were decreased in the elderly subgroup: dialysis, poor heart function, reoperation, renal dysfunction, and emergency surgery. Mortality was 3.0% in all sAVR patients and 5.2% in the elderly subgroup. Multivariate analysis in all patients produced 16 variables as operative risks ($P<0.05$) including respiratory insufficiency, dialysis, NYHA class III/IV, and reoperation. The analysis in the elderly subgroup produced 9 variables with more pronounced relative risk (RR), which included dialysis (RR=5.4), respiratory insufficiency (RR=3.3), preoperative arrhythmia (RR=3.0), 3VCAD (RR=3.6), and emergency surgery (RR=23.1).

Conclusions: sAVR has produced good surgical results in Japan. Procedure- and age-specific analyses have identified a risk profile that is unique to sAVR patients in the elderly population in Japan. (*Circ J* 2012; **76**: 356–364)

Key Words: Risk factor; Surgery; Valvular disease

Aortic stenosis (AS) is one of the most common valvular heart diseases in Japan¹ as well as in the Western world.² Because of an increase in the aging population, elderly patients with critical AS are more prevalent than before. Aortic valve replacement (AVR) is the definitive therapy for patients with severe AS who have symptoms or objective evidence of left ventricular dysfunction.^{3,4} Surgical results were satisfactory even in the elderly population when a surgical candidate was appropriately selected.^{5–8} Current guidelines from the American Heart Association/American College of Cardiology and European Society of Cardiology described that age, per se, is not a contraindication for AVR.^{3,4} There-

fore, it is widely indicated in octogenarians or even in nonagenarians.^{5–8} Symptoms and quality of life were improved, after surgery.⁵ Elderly patients, however, generally have a variety of comorbid conditions that increase surgical risks. As a result, approximately 30–40% of symptomatic patients having critical AS did not undergo open surgical AVR.^{2,9,10} Recent advances in trans-catheter aortic valve implantation (TAVI) have enabled this to be an alternative treatment modality, which is less invasive for patients who are ineligible for AVR or who carry extremely high risk for it.^{11,12} A prospective randomized trial, the Placement of AoRTic TraNscatheter (PARTNER) trial, recently reported the benefits and the

Received September 5, 2011; revised manuscript received October 1, 2011; accepted October 5, 2011; released online November 23, 2011
Time for primary review: 21 days

Department of Cardiovascular Surgery, National Hospital Organization, Nagara Medical Center, Gifu (N.H., T.N.); Departments of Healthcare Quality Assessment and Cardiac Surgery, Graduate School of Medicine, University of Tokyo, Tokyo (H.M., N.M.); and Mitsui Memorial Hospital, Tokyo (S.T.), Japan

Grant-in-Aid for Scientific Research, Japan Society for the Promotion of Science and Grant-in-Aid for Research Projects of the Ministry of Health, Labor, and Welfare in Japan.

Read at 63rd annual scientific meeting of the Japanese Association for Thoracic Surgery, October 24, 2010, Osaka, Japan.

Mailing address: Nobuhiro Handa, MD, Department of Cardiovascular Surgery, Nagara Medical Center, 1300-7 Nagara, Gifu 502-8558, Japan. E-mail: handa-kcgh@umin.ac.jp

ISSN-1346-9843 doi:10.1253/circj.CJ-11-0979

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advantages of TAVI over medical treatment mainly in the elderly and in high-risk patients,¹¹ which focused on the question of how to identify appropriate candidates for TAVI. Several risk models including the additive or logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE), Society of Thoracic Surgeons' (STS) risk score and their combinations were tested for risk prediction for single AVR (sAVR) for selecting a TAVI candidate.^{11,12} There was a criticism that the predictive ability of the risk calculator models was reduced in high-risk and in elderly patients.¹³ The risk models previously reported were established from heterogeneous surgical patients who were treated with various cardiac surgical procedures and whose age groups ranged widely.^{13–15} Because candidates for TAVI are generally very old patients with very poor clinical status, having severe coexisting conditions, their risk profile may be different from those identified from analyses of all open surgical patients or all valvular surgical patients that include the younger generation. In the present study, procedure-specific and additional age-stratified risk analyses were performed for patients who had AVR with or without coronary artery bypass grafting (CABG) using the Japan Adult Cardiovascular Surgery Database (JACVSD).

Methods

Subjects

The JACVSD was initiated in 2000 to estimate surgical outcomes after cardiovascular procedures in many centers throughout Japan. The JACVSD adult cardiovascular division currently captures clinical information from nearly two-thirds of all Japanese hospitals performing cardiovascular surgery. The data collection form has a total of 255 variables (definitions are available online at <http://www.jacvds.umin.jp>), and these are almost identical to those in the STS National Database (definitions are available online at <http://sts.org>). The JACVSD has developed software for the Web-based data collection system through which the data manager of each participating hospital submits their data electronically to the central office. Although participation in the JACVSD is voluntary, data completeness is a high priority. Accuracy of the submitted data is maintained by a data audit that is achieved by monthly visits by administrative office members to the participating hospital to check data against clinical records. Validity of data is further confirmed by an independent comparison of the volume of cardiac surgery at a particular hospital entered in the JACVSD vs. that reported to the Japanese Association for Thoracic Surgery annual survey.¹

We examined all surgical patients who had single AVR with or without CABG between 1 January 2005 and 31 December 2008. First, those JACVSD records that were obtained without patients' informed consent were excluded from this analysis. Records with missing age (or which were out of range), sex, or 30-day status were also excluded. After this data cleaning, the population for this risk model analysis consisted of 7,883 sAVR with or without CABG from 167 participating sites throughout Japan. Patients were divided into 3 subgroups by age: <70 years old (young subgroup, $n=3,387$); 70–79 years of age (middle subgroup, $n=3,482$); and ≥ 80 years old (elderly subgroup, $n=1,014$).

Endpoints

The primary outcome measure of the JACVSD was operative mortality, defined as either in-hospital or 30-day mortality, whichever was longer. It is equivalent to the 30-day operative mortality defined in the STS National Adult Database. The

secondary outcome measure of the present study was operative mortality and major morbidity. This includes any patient who died during the index hospitalization, regardless of the length of hospital stay, and any patient who died after being discharged from the hospital within 30 days of the operation. Using the definition from a previous study,^{16,17} major morbidity was defined as any of the following 5 postoperative in-hospital complications: stroke; reoperation for any reason; need for mechanical ventilation for >24 h after surgery; renal failure; or deep sternal wound infection.¹⁵

Statistical Analysis

We examined the differences among the 3 subgroups stratified by the 3 age subgroups, using bivariate tests of Pearson chi-square tests for categorical covariates, and 1-way ANOVA for continuous covariates. Intergroup comparison was conducted with Scheffe F test. $P<0.05$ was considered significant.

To develop risk models of sAVR with or without CABG and for the 3 subgroups, we conducted multivariate stepwise logistic regression analysis for each outcome for all sAVR patients and for the 3 subgroups. Stability of the model was checked every time a variable was eliminated. When all statistically non-significant variables ($P<0.1$) had been eliminated from the model, goodness of fit was evaluated, and the area under the receiver operating characteristic (ROC) curve was used to assess how well the model could discriminate between patients who lived and those who died.¹⁸ The Hosmer–Lemeshow test was used to examine to what extent the model-predicted mortality was similar to the observed mortality.¹⁸

Results

Patient Characteristics

Patient characteristics vs. subgroup as well as for the total group are summarized in **Tables 1,2**. Patients in the elderly subgroup comprised only 13% of all patients. Preoperative patient characteristics were significantly different between the 3 subgroups for 35 out of 42 preoperative variables. Men comprised 56% of patients who had sAVR with or without CABG and the mean age was 68 ± 12 years old. Male gender was prominent in the young subgroup (66.5%), whereas it was decreased in both the middle subgroup (50.6%) and in the elderly subgroup (36.4%).

It was noted that coexisting conditions such as respiratory insufficiency, history of stroke and concomitant 3-vessel coronary artery disease (3VCAD) were more prevalent in the elderly subgroup in comparison with the other 2 subgroups. Preoperative heart condition, such as congestive heart failure and New York Heart Association functional class (NYHA) III or IV was very prominent in the elderly subgroup. Concomitant mitral regurgitation ($\geq$ grade II) was recognized but was not treated so that sAVR was conducted more frequently in the elderly subgroup. Conversely, the following factors were less prevalent in the elderly subgroup: male gender, obesity, dialysis, poor heart function, reoperation, and renal dysfunction. Preoperative creatinine level was significantly better in the elderly subgroup.

Early Mortality and Morbidity

Mortality and morbidity in all sAVR patients and vs. subgroup are detailed in **Table 3**. Observed operative mortality in all sAVR patients was 3.0%. Operative mortality according to subgroup was 2.1% in the young subgroup, 3.2% in the middle subgroup, and 5.2% in the elderly subgroup, respectively. The endpoint of operative mortality and major morbidity

Table 1. Patient Characteristics

Variables (years)	All patients (n=7,883)	Young (<70 years) (n=3,387)	Middle (70–79 years) (n=3,482)	Elderly (≥80 years) (n=1,014)	P value
Sex (male)	4,384 (55.6)	2,252 (66.5)	1,763 (50.6)	369 (36.4)	<0.001
Smoker	2,637 (33.5)	1,320 (39.0)	1,092 (31.4)	225 (22.2)	<0.001
Current smoker	817 (10.4)	496 (14.6)	260 (7.5)	61 (6.0)	<0.001
Diabetes	1,548 (19.6)	570 (16.8)	799 (22.9)	179 (17.7)	<0.001
Renal failure	954 (12.1)	456 (13.5)	391 (11.2)	107 (10.6)	0.005
Dialysis	585 (7.4)	329 (9.7)	219 (6.3)	37 (3.6)	<0.001
Hyperlipidemia	2,524 (32)	952 (28.1)	1,232 (35.4)	340 (33.5)	<0.001
Hypertension	4,908 (62.3)	1,817 (53.6)	2,379 (68.3)	712 (70.2)	<0.001
Stroke/TIA	719 (9.1)	277 (8.2)	338 (9.7)	104 (10.3)	0.036
Active infective endocarditis	261 (3.3)	180 (5.3)	66 (1.9)	15 (1.5)	<0.001
Respiratory insufficiency	192 (2.4)	53 (1.6)	97 (2.8)	42 (4.1)	<0.001
Extracardiac arteriopathy	649 (8.2)	254 (7.5)	315 (9.0)	80 (7.9)	0.060
Peripheral vascular disease	461 (5.8)	155 (4.6)	239 (6.9)	67 (6.6)	<0.001
Aortic disease	239 (3.0)	123 (3.6)	95 (2.7)	21 (2.1)	0.015
Neurological deficit	166 (2.1)	73 (2.2)	73 (2.1)	20 (2.0)	0.937
History of coronary intervention	467 (5.9)	126 (3.7)	264 (7.6)	77 (7.6)	<0.001
History of myocardial infarction	293 (3.7)	96 (2.8)	147 (4.2)	50 (4.9)	0.001
Preoperative CHF	2,376 (30.1)	952 (28.1)	1,020 (29.3)	404 (39.8)	<0.001
Angina symptom	1,401 (17.8)	404 (11.9)	749 (21.5)	248 (24.5)	<0.001
Unstable angina	202 (2.6)	55 (1.6)	104 (3.0)	43 (4.2)	<0.001
Preoperative shock	128 (1.6)	59 (1.7)	53 (1.5)	16 (1.6)	0.765
Arrhythmia	1,065 (13.5)	389 (11.5)	498 (14.3)	178 (17.8)	<0.001
Preoperative inotrope support	171 (2.2)	66 (1.9)	84 (2.4)	21 (2.1)	0.408
Aortic valve etiology (stenosis)	5,291 (67.1)	1,814 (53.6)	2,582 (74.2)	895 (88.3)	<0.001
Aortic regurgitation (grade ≥II)	4,501 (57.1)	2,242 (66.2)	1,795 (51.6)	464 (45.8)	<0.001
MR (grade ≥II)	1,538 (19.5)	540 (15.9)	710 (20.4)	288 (28.4)	<0.001
TR (grade ≥II)	875 (11.1)	273 (8.1)	417 (12.0)	185 (18.2)	<0.001
Concomitant mitral stenosis	176 (2.2)	63 (1.9)	71 (2.0)	42 (4.1)	<0.001
Reoperation	345 (4.4)	188 (5.6)	128 (3.7)	29 (2.9)	<0.001
Urgent surgery	253 (3.2)	130 (3.8)	85 (2.4)	38 (3.7)	0.003
Emergency surgery	111 (1.4)	67 (2.0)	35 (1.0)	9 (0.9)	0.001
Unexpected CABG	52 (0.7)	19 (0.6)	22 (0.6)	11 (1.1)	0.188
BMI >26	1,393 (17.7)	645 (19.0)	616 (17.7)	132 (13.0)	<0.001
BMI >30	271 (3.4)	128 (3.8)	128 (3.7)	15 (1.5)	0.001
NYHA class III or IV	1,731 (22.0)	594 (17.5)	781 (22.4)	356 (35.1)	<0.001
3-vessel CAD	498 (6.3)	145 (4.3)	266 (7.6)	87 (8.6)	<0.001
Left main disease	298 (3.8)	91 (2.7)	148 (4.3)	59 (5.8)	<0.001
Poor LV function	262 (3.3)	140 (4.1)	96 (2.8)	26 (2.6)	0.002
Concomitant CABG	1,504 (19.1)	412 (12.2)	823 (23.6)	269 (26.5)	<0.001

Data given as n (%).

TIA, transient ischemic attack; CHF, congestive heart failure; MR, mitral regurgitation; TR, tricuspid regurgitation; CABG, coronary artery bypass grafting; BMI, body mass index; NYHA, New York Heart Association; CAD, coronary artery disease; LV, left ventricular.

Table 2. Continuous Variables

Variables (years)	All patients (n=7,883)	Young (<70 years) (n=3,387)	Middle (70–79 years) (n=3,482)	Elderly (≥80 years) (n=1,014)	P value
Body surface area	1.56±0.19	1.63±0.19	1.52±0.17	1.44±0.16	<0.001†
BMI	23.0±18.0	23.4±26.5	22.9±4.5	22.1±3.4	0.065
Preoperative creatinine	1.40±0.24	1.56±3.08	1.30±1.70	1.15±0.134	<0.0001†

Data given as mean ± SD. †Young <Middle <Elderly (Scheffe F test); †young >middle or elderly (Scheffe F test).

BMI, body mass index.

Table 3. Mortality and Morbidity

Variables (years)	All patients (n=7,883)	Young (<70 years) (n=3,387)	Middle (70–79 years) (n=3,482)	Elderly (≥80 years) (n=1,014)	P value
Operative mortality	233 (3.0)	70 (2.1)	110 (3.2)	53 (5.2)	<0.001
Operative mortality and major morbidity	1,119 (14.2)	385 (11.4)	545 (15.7)	189 (18.6)	<0.001
Reoperation	479 (5.5)	186 (6.4)	222 (6.4)	71 (7.0)	0.129
Stroke	140 (1.8)	41 (1.2)	72 (2.1)	27 (2.7)	0.002
Dialysis	189 (2.4)	69 (2.0)	88 (2.5)	32 (3.2)	0.099
Infection	114 (1.4)	42 (1.2)	57 (1.6)	15 (1.5)	0.385
Paraparesis	28 (0.4)	13 (0.4)	10 (0.3)	5 (0.5)	0.583
Prolonged ventilation (>24 h)	468 (5.9)	140 (4.1)	238 (6.8)	90 (8.9)	<0.001
Re-exploration for bleeding	306 (3.9)	113 (3.3)	147 (4.2)	46 (4.5)	0.084
TIA	130 (1.6)	41 (1.2)	71 (2.0)	18 (1.8)	0.025
Coma	55 (0.7)	17 (0.5)	31 (0.9)	7 (0.7)	0.154
Renal failure	394 (5.0)	124 (3.7)	195 (5.6)	75 (7.4)	<0.001
Heart block	164 (2.1)	70 (2.1)	70 (2.0)	24 (2.4)	0.781
Cardiac arrest	98 (1.2)	38 (1.1)	42 (1.2)	18 (1.8)	0.249
Anticoagulant-related bleeding	43 (0.5)	13 (0.4)	22 (0.6)	8 (0.8)	0.200
Tamponade	158 (2.0)	57 (1.7)	77 (2.2)	24 (2.4)	0.200
GI complication	145 (1.8)	45 (1.3)	73 (2.1)	27 (2.7)	0.007
Multiple organ failure	104 (1.3)	31 (0.9)	52 (1.5)	21 (2.1)	0.009
Atrial fibrillation	1,676 (21.3)	583 (17.2)	829 (23.8)	264 (26.0)	<0.001
Septicemia	106 (1.3)	36 (1.1)	56 (1.6)	14 (1.4)	0.145
Urinary tract infection	58 (0.7)	12 (0.4)	32 (0.9)	14 (1.4)	0.001
Pneumonia	183 (2.3)	60 (1.8)	91 (2.6)	32 (3.2)	0.011
ICU stay (>7-days)	485 (6.2)	152 (4.5)	235 (6.7)	98 (9.7)	<0.001

Data given as n (%).

GI, gastrointestinal; ICU, intensive care unit.

Table 4. Comparison of Risk Models

Age groups	All patients (n=7,883)	Young (<70 years) (n=3,387)	Middle (70–79 years) (n=3,482)	Elderly (≥80 years) (n=1,014)
Age at surgery	1.03 (1.02–1.05)*	–	–	–
Dialysis	4.18 (2.98–5.86)*	3.92 (2.18–7.02)*	4.97 (3.06–8.06)*	5.42 (2.15–13.69)*
3-vessel CAD	1.87 (1.20–2.93)**	–	2.22 (1.23–4.02)**	3.61 (1.64–7.96)*
Respiratory insufficiency	2.35 (1.30–4.25)**	3.78 (1.12–12.76)†	3.34 (1.22–9.17)†	–
Emergency surgery	2.96 (1.51–5.81)**	3.39 (1.44–8.01)**	–	23.1 (5.31–100.9)*
Urgent surgery	1.87 (1.12–3.15)†	–	–	3.21 (1.19–8.68)†
Preoperative arrhythmia	1.53 (1.09–2.14)†	–	–	2.98 (1.56–5.72)*
Unexpected CABG	2.85 (1.06–7.66)†	–	–	8.41 (1.86–37.9)**
Peripheral vascular disease	1.65 (1.09–2.50)†	–	1.96 (1.12–3.42)†	–
Preoperative shock	2.16 (1.10–3.94)†	–	3.76 (1.72–8.25)*	–
Reoperation	2.21 (1.35–3.61)**	–	–	–
Concomitant MR (grade ≥II)	1.42 (1.04–1.93)†	–	1.63 (1.06–2.51)†	–
Infective endocarditis	2.21 (1.20–3.98)**	–	4.85 (2.16–10.91)*	–
NYHA class III or IV	1.99 (1.46–2.71)*	2.51 (1.31–4.81)**	2.1 (1.38–3.19)*	–
LV dysfunction	1.63 (1.65–4.22)**	3.82 (1.90–7.68)*	–	–
Concomitant CABG	1.63 (1.14–2.33)**	2.90 (1.62–5.19)*	–	–
Concomitant TR (grade ≥III)	–	4.33 (1.63–11.5)**	–	2.00 (1.03–3.88)†
Current smoker	–	–	2.31 (1.29–4.13)**	2.90 (1.13–7.48)†

Data given as relative risk (95% confidence interval).

Abbreviations see in Table 1.

†P<0.05; **P<0.01; *P<0.001.

Figure 1. Receiver operating characteristic curves and areas under the curve for all single aortic valve replacement patients and according to age subgroup (SG): young, <70 years; middle, 70–79 years; elderly, ≥80 years.

also increased with the advancing age (young, 11.4%; middle, 15.7%; and elderly, 18.6%, respectively). Observed operative mortality for isolated AVR and AVR+CABG was 2.4% and 5.4%, respectively. Operative mortality for isolated AVR and AVR+CABG according to subgroup was 1.6% and 5.6% in the young, 2.6% and 5.0% in the middle, and 4.6% and 7.1% in the elderly, respectively. Postoperative complications of stroke, transient ischemic attack, prolonged ventilation (>24 h), postoperative renal failure, gastrointestinal complication, mul-

tle organ failure, urinary tract infection, atrial fibrillation, and pneumonia were increased as well from the young subgroup, middle subgroup, to elderly subgroup. As a result, prolonged intensive care unit stay (>7 days) was 6.2% for all sAVR patients and was increased from 4.5% in the young subgroup, to 6.7% in the middle subgroup, to 9.7% in the elderly subgroup.

Figure 2. Evaluation of goodness of fit using Hosmer–Lemeshow test of risk model calibrations for all for all single aortic valve replacement patients and according to age subgroup (SG): young, <70 years; middle, 70–79 years; elderly, ≥80 years.

Risk Models

The results of multiple logistic regression analyses for all patients and vs. subgroup are listed in [Table 4](#). Multiple regression analyses for all sAVR patients identified 16 preoperative risks affecting operative mortality ([Table 4](#)). Eight out of 16 risk factors had relative risk (RR) >2.0. Preoperative comorbid conditions such as respiratory insufficiency, history of previous surgery, and concomitant CAD significantly increased the surgical risks. Mode of surgery such as emergency surgery and preoperative shock state did as well. An 8 additional factors were identified as operative risks in all sAVR patients, whose RR was between 1.0 and 2.0. Risk profiles of the 3 subgroups are expressed as RR with 95% confidence interval in [Table 4](#). The factor of “dialysis” was the only common risk in all 3 subgroups. Risk profile was very different among the 3 subgroups. In the elderly subgroup, 9 variables were identified as significant risks, which were more pronounced RR such

as “dialysis” (RR=5.4), “respiratory insufficiency” (RR=3.3), “preoperative arrhythmia” (RR=3.0), 3VCAD (RR=3.6), and “emergency mode of surgery” (RR=23.1). ROC curves were used to evaluate model performance ([Figure 1](#)). The area under the curve for all sAVR patients was 0.818 ($P<0.001$). Although sample size was very small, particularly in the elderly subgroup, risk model calibration was conducted using the Hosmer–Lemeshow test to compare the predicted mortality with the observed mortality ([Figure 2](#)).

Discussion

The present study addresses several aspects of clinical medicine regarding the surgical management of aortic valve disease in Japan. First, the operative mortality of sAVR with or without CABG in all sAVR patients was 3.0%, which is very good because the subject group included 19% of patients who

Table 5. Relative Risk: Elderly Subgroup vs. All Patients

	sAVR		All valve patients ¹⁵ (n=6,562) ^{††}
	≥80 years (n=1,014)	All patients (n=7,883)	
Urgent surgery	3.21	1.87	2.01
Emergency surgery	23.1	2.96	4.12
Preoperative arrhythmia	2.98	1.53	—
3-vessel CAD	3.61	2.35	—
Respiratory insufficiency	3.34	2.35	1.59
TR	2.00	—	1.79
Dialysis	5.42	4.18	—
Unexpected CABG	8.41	2.85	—
Current smoker	2.90	—	—

sAVR, single aortic valve replacement with/without CABG. Other abbreviations see in Table 1.

^{††}sAVR with CABG, n=446; sAVR without CABG, n=3,301.¹⁵

had AVR and CABG. One possible criticism is that AVR and AVR+CABG were not analyzed separately, as was done in the STS database.^{19,20} The primary goal of the present study, however, was to assess the risk stratification for potential TAVI candidates, who consist mainly of the elderly population and who have a substantial rate of concomitant CAD. Accordingly, we decided to analyze 1 risk model rather than 2 separate risk models for AVR with and without CAD. Therefore, in the present analysis, CAD and CABG were considered as important risk factors. Observed operative mortality of isolated AVR and AVR+CABG was 2.4% and 5.4%, respectively. In the literature, operative mortality of isolated AVR and AVR+CABG was reported as 2–5% and 5–7%, respectively, from Europe and North America.^{2,19–21} The present results are equivalent to these results. In the present study, operative mortality in sAVR patients was increased from 2.1% in the young subgroup to 5.2% in the elderly subgroup, as age increased. It is also noted that operative mortality and major morbidity rate rose from 11.4% in the young subgroup to 18.6% in the elderly subgroup. Major morbidity often restricts quality of life after surgery for a substantial period of time, which potentially reduces the benefit of surgical treatment itself.

Second, according to the patient characteristics, the prevalence of many factors were significantly different among the 3 age groups. The prevalence of several comorbid conditions including hypertension, history of stroke, respiratory insufficiency, history of myocardial infarction, concomitant mitral regurgitation, and 3VCAD, was increased in order of the young subgroup, the middle subgroup, to the elderly subgroup. Heart conditions such as congestive heart failure and NYHA class III/IV were increased in the elderly subgroup as well, which may be associated with the timing of surgical referral. In contrast, the prevalence of several comorbid conditions such as renal failure, dialysis, and history of open-heart surgery was decreased in the elderly subgroup. These results are assumed to reflect referral bias, surgical selection bias, or possibly patient preference.

Third, procedure-specific risk stratification identified a risk profile that is unique to sAVR patients in the Japanese population. **Table 5** summarizes the present results; the reference data are taken from Motomura et al, and they describe the risk models of Japanese valve surgery using the entire patient population of cardiac valve procedures in a different dataset from JACVSD.¹⁵ From a statistical standpoint, it is impossible to compare the present study with a different dataset from

previous reports. Also in **Table 5**, procedure-specific analysis identified risk excluding concomitant tricuspid regurgitation, and the age-specific risk analysis indicated higher RR in elderly patients.

Fourth, age is an extremely important factor affecting the results of sAVR. Early mortality rate in the elderly subgroup was increased to 5.2%, which is the baseline sAVR operative mortality in Japanese octogenarians and nonagenarians. The elderly population is vulnerable to any kind of risk factor compared with the younger generation.²² Age-specific risk stratification produced only a limited number of risk profiles, but the higher RR are thought to reflect this vulnerability of the elderly population. Surprisingly, only the factor “dialysis” was common among the 3 age subgroups. Risk profiles identified in the present study were very different and specific to each generation.

Finally, the areas under the ROC curves allowed reasonable discrimination between patients who were alive and those who died. But, because the present sample sizes were limited, particularly in the elderly subgroup, the interpretation of model calibration by Hosmer–Lemeshow test must be cautious. It is also inappropriate to do a validation study by dividing those small sample sizes into a construction group and a validation group. A validation study is required in the future.

Several risk models for valvular heart surgery have been utilized for risk prediction, which include the STS National Adult Database,²³ EuroSCORE,²⁴ and, in particular, the Japan SCORE for Japanese population.¹⁵ The primary goal of the surgical database and the risk model is to assess the surgical results and to enhance the quality control of surgical services.²⁵ Strictly speaking, the risk calculator model is not recommended to be used as a substitute for clinical decision-making.²⁵ With the introduction, however, of less invasive technology such as TAVI into clinical medicine, physicians often try to estimate surgical mortality with risk calculator models to identify appropriate candidates who are expected to have a high procedural risk of open AVR.

The recent report on the prospective randomized trial, the PARTNER trial, comparing TAVI with best medical treatment, demonstrated the benefits and the advantages of TAVI over medical treatment.²⁶ The study reported a 5% procedural 30-day mortality and survival advantage of TAVI over medical treatment during 2 years. It was noted that patients who were treated with TAVI were a mean age of 83 years old, and 46% of patients were ≥85 years old.²⁶ It is obvious that current candidates for TAVI are very old and very high-risk patients

having severe comorbid conditions. TAVI, however, still has several unsolved issues such as vascular complication associated with a trans-femoral approach, the relatively high incidence of stroke, and atrio-ventricular block.²⁷ Residual aortic regurgitation (AR) is frequent, although mild to moderate AR may not alter the short-term clinical consequences.^{27,28} A German study of a TAVI registry showed that residual AR, defined as $\geq$ grade II, occurred in 17% of the patients and that it was an independent predictor of early mortality.²⁸ Current guidelines for management of valvular heart disease note that AVR is a standard treatment for symptomatic aortic valve disease and that age, per se, is not a contraindication for surgical AVR.^{3,4} Therefore, it is extremely important to identify very high-risk patients who are to be excluded for open AVR in the elderly population. The combination of the EuroSCORE and STS risk score has frequently been used for risk prediction of sAVR patients and for selecting TAVI candidate in many clinical reports.^{12,14} There is a criticism, however, that the predictive ability of EuroSCORE and STS score is significantly reduced for high-risk and elderly patients, who are the target population for TAVI.^{29,30} A study from Mayo Clinic demonstrated that the predicted mortality calculated by EuroSCORE was 23.6% for high-risk sAVR patients, whereas the real observed mortality was only 5.7%.³⁰

Potential reasons for the low predictive capacity of the EuroSCORE for the elderly patients having sAVR are as follows: (1) EuroSCORE was established from a multicenter database of 19,030 open surgical patients from 10 European countries in 1995; (2) EuroSCORE was based on the analyses from a heterogeneous surgical database consisting mainly of coronary bypass procedure, and some aortic surgery, as well as of a variety of valve procedures (patients who had AVR comprised only 17% of the database); and (3) the mean age of the subjects was 62.5 ± 10.7 years. It is obvious that EuroSCORE was not specifically designed for predicting surgical risk of sAVR in the elderly population.³¹ Multiple studies have unanimously reported that EuroSCORE overestimates the surgical risk.^{14,30,32} STS score seems to be better, but underestimates the risk for sAVR patients.¹⁴ No single risk calculator accurately predicts surgical mortality and selects a TAVI candidate at present.

Several inherent shortcomings of the risk models need to be acknowledged and must be taken into account when using them. Patients with critical AS who have never been referred for AVR may limit the accuracy of risk assessment. It is difficult to define inoperable patients using the analyses of patients who underwent open AVR even if they carry a variety of risk factors. Patients who were not referred to surgeons need to be investigated.³³ One study from Euro Heart survey reported that approximately one-third of the patients with critical aortic valve stenosis >75 years of age refused AVR.^{2,9} Multivariate analysis showed that those patients carried risk factors of older age, poor left ventricular function, and preoperative neurological dysfunction, as well as the important factor of patient refusal.³⁴ Simple refusal for open AVR according to patient preference should not be regarded as an indication for a less invasive procedure.

Another issue with the currently available risk models is that a number of demographic variables that potentially affect operative mortality could not be studied, because the required number of cases could not be reached due to the less frequent prevalence of the condition. Such demographic variables include mediastinal irradiation, porcelain aorta, liver cirrhosis, and so on.¹⁴ Whether these factors affect surgical risk estimation and the decision to choose a less invasive procedure is not

fully determined.

In addition to perioperative mortality, estimation of postoperative morbidity and long-term outcomes are also required for surgical decision making. A postoperative debilitating condition often limits the quality of life and reduces the benefits of surgical AVR. TAVI may reduce the risk of morbidity by avoiding median sternotomy, cardiopulmonary bypass, and cardioplegic arrest of the heart. Because life expectancy is limited in the elderly population, the goal in treatment of critical AS is rather to improve the quality of life than to extend a reduced life expectancy.

Accordingly, it is suggested that the objective assessment of multiple risk calculations should be used in combination with subjective assessment by an experienced surgeon in a multidisciplinary team approach.¹⁴ This approach allows the team to take into account risk factors that are not covered in risk scores and other factors not often seen in practice. It is obviously ideal that a single risk model cover any type of disease, treatment, and age group for the quality control of medical practice. A single risk model is also preferable in order to develop and to improve continually the predictive ability of a risk calculator specific for the disease, target age, and treatment modality.

In conclusion, the present study has demonstrated the good surgical outcome of sAVR including concomitant CABG in Japan. A variety of coexisting conditions, however, increased the operative mortality in the elderly population. In the process of developing a risk scoring system for TAVI candidates, the present study has provided valuable information and better risk stratification that is more specific for the procedure and for the target age group.

Acknowledgments

These studies were partly supported by a Grant-in-Aid for Scientific Research, Japan Society for the Promotion of Science and a Grant-in-Aid for Research Projects of the Ministry of Health, Labor, and Welfare in Japan.

Disclosures

Conflict of interest: none declared.

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Supplemental Files

Supplemental File 1

Data S1. Appendix: Definition of Preoperative Variables

Please find supplemental file(s);

<http://dx.doi.org/10.1253/circj.CJ-11-0979>