Association of R_2-CHA_2DS_2-VASc Score and Clinical Outcomes after Bioprosthetic Valve Replacement: Subanalysis from BPV-AF Registry

Madoka Sano[1], Misa Takegami[2], Toshiaki Toyota[1], Tomohiko Taniguchi[1], Kitae Kim[1], Atsushi Kobori[1], Natsuhiko Ehara[1], Makoto Kinoshita[1], Kunihiro Nishimura[2], Makoto Miyake[3], Tadaaki Koyama[4], Tomoyuki Fujita[5], Takeshi Kitai[2], Chisato Izumi[2], Yutaka Furukawa[1], on the behalf of BPV-AF Registry Group

1) Kobe City Medical Center General Hospital. 2-1-1, Minatojima-minamimachi, Chuo-ku, Kobe, Japan.

2) National Cerebral and Cardiovascular Center 3) Tenri Hospital 4) Kansai Medical University 5) Tokyo Medical and Dental University

This study was supported by Daiichi Sankyo Co., Ltd
UMIN000034485

Background

- The incidences of valvular heart disease and atrial fibrillation (AF) are increasing in the aging society, and surgical valve replacement with bioprosthetic valve (BPV) is being widely performed.
- However, data about prognostic prediction focused on AF patients after BPV replacement are limited.

Purpose

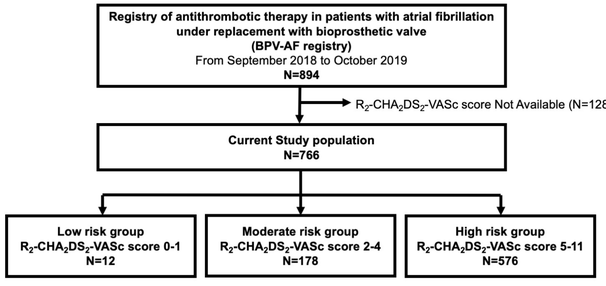
- We aimed to evaluate the predictive value of R_2-CHA_2DS_2-VASc score for future cardiovascular (CV) events in AF patients after BPV replacement.

R_2-CHA_2DS_2-VASc score		point
R_2	eGFR < 60 mL/min/1.73m^2	2
C	Congestive heart failure	1
H	Hypertension	1
A_2	Age > 75 years	2
D	Diabetes mellitus	1
S_2	Previous stroke or TIA	2
V	Vascular disease	1
A	Age 65–74	1
Sc	Sex category (female)	1

Methods

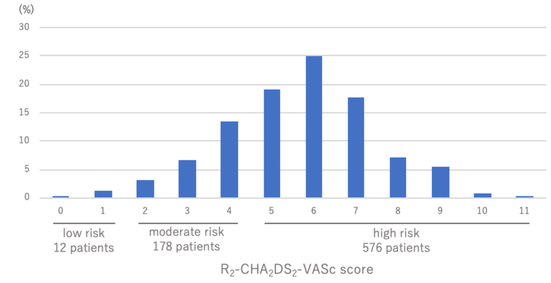
- BPV-AF is an observational, multicenter, prospective registry, and AF patients that underwent BPV replacement from September 2018 to October 2019 were enrolled.
- Patients were stratified into three risk groups according to their R_2-CHA_2DS_2-VASc score as follows; low (scores, 0–1), moderate (scores, 2–4), and high (scores, 5–11).
- **Primary outcome measure**: a composite of stroke, systemic embolism, CV events including heart failure hospitalization, and cardiac death.

Figure 1. Study population



Results

Figure 2. Distribution of the R_2-CHA_2DS_2-VASc score



The mean R_2-CHA2DS$_2$-VASc score was 5.7 ± 1.8.
More than half of the patients were classified into the high-risk group.

Table 1. Baseline patients characteristics

	All (n=766)	low risk (n=12)	moderate risk (n=178)	high risk (n=576)	p-value
Female	419 (54.7%)	0 (0.0%)	67.0 (37.6%)	352 (61.1%)	<0.001
Age (years), mean ± SD	80.3 ± 6.8	66.4 ± 5.8	76.4 ± 6.7	81.8 ± 5.9	<0.001
BMI (kg/m^2), mean ± SD	22.2 ± 3.7	22.7 ± 3.4	21.9 ± 3.1	22.3 ± 3.9	0.531
HAS-BLED score, mean ± SD	2.4 ± 1.0	1.1 ± 0.7	2.0 ± 0.8	2.6 ± 1.0	<0.001
eGFR (mL/min/1.73m^2)	47.1 ± 17.5	68.9 ± 5.6	61.5 ± 17.6	42.1 ± 14.7	<0.001
CCr (mL/min)	40.9±18.2	76.0±13.6	55.2±18.5	36.0±14.9	<0.001
Type of AF					0.277
Paroxysmal	288 (37.6%)	4 (33.3%)	65 (36.5%)	219 (38.0%)	
Persistent	254 (33.2%)	6 (50.0%)	68 (38.2%)	180 (31.3%)	
Permanent	224 (29.2%)	2 (16.7%)	45 (25.3%)	177 (30.7%)	
Left atrial plication, LAA occlusion/excision	86 (11.2%)	1 (8.3%)	22 (12.4%)	63 (11.0%)	0.831
Previous history of CVD					
Ischemic stroke	108 (14.1%)	0 (0.0%)	4 (2.3%)	104 (18.1%)	<0.001
Hemorrhagic stroke	19 (2.5%)	0 (0.0%)	2 (1.1%)	17 (3.0%)	0.463
Intracranial hemorrhage	26 (3.4%)	0 (0.0%)	6 (3.4%)	20 (3.5%)	0.806
Systemic embolism	11 (1.4%)	0 (0.0%)	1 (0.6%)	10 (1.7%)	0.558
Major bleeding	45 (5.9%)	1 (8.3%)	11 (6.2%)	33 (5.7%)	0.913
Comorbidities					
Hypertension	575 (75.1%)	4 (33.3%)	104 (58.4%)	467 (81.1%)	<0.001
Heart failure	434 (56.7%)	5 (41.7%)	71 (39.9%)	358 (62.2%)	<0.001
Dyslipidemia	384 (50.1%)	2 (16.7%)	70 (39.3%)	312 (54.2%)	<0.001
Diabetes mellitus	160 (20.9%)	0 (0.0%)	22 (12.4%)	138 (24.0%)	<0.001
Renal dysfunction	70 (9.1%)	0 (0.0%)	6 (3.4%)	64 (11.1%)	0.004
Chronic respiratory disease	65 (8.5%)	0 (0.0%)	16 (9.0%)	49 (8.5%)	0.557
Malignant tumour	61 (8.0%)	1 (8.3%)	9 (5.1%)	51 (8.9%)	0.262
Myocardial infarction	39 (5.1%)	0 (0.0%)	5 (2.8%)	34 (5.9%)	0.188
Peripheral arterial disease	28 (3.7%)	0 (0.0%)	1 (0.6%)	27 (4.7%)	0.030
Thrombosis and embolism	24 (3.1%)	0 (0.0%)	1 (0.6%)	23 (4.0%)	0.059
Liver dysfunction	21 (2.7%)	1 (8.3%)	5 (2.8%)	15 (2.6%)	0.371
Dementia	37 (4.8%)	0 (0.0%)	3 (1.7%)	34 (5.9%)	0.053
Left ventricular ejection fraction					0.272
< 40%	51 (7.1%)	1 (8.3%)	7 (4.2%)	43 (8.0%)	
40% to 49%	67 (9.4%)	1 (8.3%)	20 (12.0%)	46 (8.6%)	
≥ 50%	598 (83.5%)	10 (83.3%)	140 (83.8%)	448 (83.4%)	

BMI=body mass index; eGFR=estimated glomerular filtration rate; CCr=creatinine clearance; LAA=left atrial appendage

The median follow-up period was 491 (IQR 393–561) days .

Table 2. Operative characteristics

	All (n=766)	low risk (n=12)	moderate risk (n=178)	high risk (n=576)	p-value
Prosthesis position					<0.001
Aortic valve	491 (64.1%)	8 (66.7%)	86 (48.3%)	397 (68.9%)	
Mitral valve	176 (23.0%)	3 (25.0%)	61 (34.3%)	112 (19.4%)	
Both valves	99 (12.9%)	1 (8.3%)	31 (17.4%)	67 (11.6%)	
Aortic valve	(n=491)	(n=8)	(n=86)	(n=397)	
Subtype of valvular heart disease					<0.001
Stenosis	364 (74.1%)	3 (37.5%)	50 (58.1%)	311 (78.3%)	
Regurgitation	101 (20.6%)	3 (37.5%)	32 (37.2%)	66 (16.6%)	
Others	9 (1.8%)	1 (12.5%)	2 (2.3%)	6 (1.5%)	
Operation type					<0.001
Surgery	291 (59.3%)	8 (100.0%)	71 (82.6%)	212 (53.4%)	
TAVI	200 (40.7%)	0 (0.0%)	15 (17.4%)	185 (46.6%)	
History of replacement					0.147
First replacement	465 (94.7%)	6 (75.0%)	83 (96.5%)	376 (94.7%)	
Re-replacement	24 (4.9%)	2 (25.0%)	3 (3.5%)	19 (4.8%)	
Mitral valve	(n=176)	(n=3)	(n=61)	(n=112)	
Subtype of valvular heart disease					0.040
Stenosis	72 (40.9%)	0 (0.0%)	29 (47.5%)	43 (38.4%)	
Regurgitation	88 (50.0%)	2 (66.7%)	24 (39.3%)	62 (55.4%)	
Others	9 (5.1%)	1 (33.3%)	3 (4.9%)	5 (4.5%)	
History of replacement					0.311
First replacement	155 (88.1%)	2 (66.7%)	53 (86.9%)	100 (89.3%)	
Re-replacement	21 (11.9%)	1 (33.3%)	8 (13.1%)	12 (10.7%)	

TAVI= transcatheter aortic valve implantation

Aortic stenosis, as the primary heart valve disease, and the TAVI procedure were more frequent in the high-risk group.

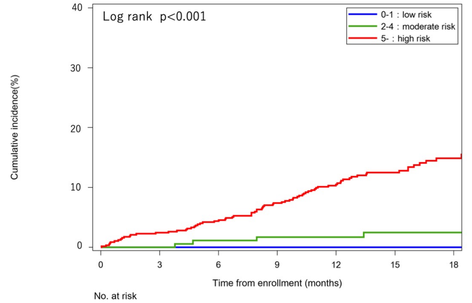
Table 3. Administration status of antithrombotic agents

	All (n=766)	low risk (n=12)	moderate risk (n=178)	high risk (n=576)	p-value
No antithrombotic drug	38 (5.0%)	2 (16.7%)	12 (6.7%)	24 (4.2%)	
Warfarin-based therapy	419 (54.7%)	5 (41.7%)	107 (60.1%)	307 (53.3%)	
No antiplatelet drug	306 (73.0%)	5 (100.0%)	80 (74.8%)	221 (72.0%)	0.420
With antiplatelet drug	113 (27.0%)	0 (0.0%)	27 (25.2%)	86 (28.0%)	
With aspirin (monotherapy)	97 (23.2%)	0 (0.0%)	26 (24.3%)	71 (23.1%)	0.682
With P2Y12 (monotherapy)	11 (2.6%)	0 (0.0%)	0 (0.0%)	11 (3.6%)	0.156
With DAPT	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
With others	5 (1.2%)	0 (0.0%)	1 (0.9%)	4 (1.3%)	1.000
Warfarin monitoring					
Time in therapeutic range, % Median (IQR)	85.2 (45.6 - 100.0)	86.1 (36.1 - 100.0)	99.1 (64.3 - 100.0)	81.3 (39.2 - 100.0)	0.056
DOAC-based therapy	241 (31.5%)	3 (25.0%)	37 (20.8%)	201 (34.9%)	
No antiplatelet drug	173 (71.8%)	2 (66.7%)	25 (67.6%)	146 (72.6%)	0.691
With antiplatelet drug	68 (28.2%)	1 (33.3%)	12 (32.4%)	55 (27.4%)	
With aspirin (monotherapy)	50 (20.8%)	1 (33.3%)	10 (27.0%)	39 (19.4%)	0.312
With P2Y12 (monotherapy)	15 (6.2%)	0 (0.0%)	1 (2.7%)	14 (7.0%)	0.570
With DAPT	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
With others	3 (1.2%)	0 (0.0%)	1 (2.7%)	2 (1.0%)	0.421
Antiplatelet therapy (without warfarin/DOAC)	68 (8.9%)	2 (16.7%)	22 (12.4%)	44 (7.6%)	
Aspirin (monotherapy)	54 (79.4%)	2 (100.0%)	19 (86.4%)	33 (75.0%)	0.594
P2Y12 (monotherapy)	9 (13.2%)	0 (0.0%)	3 (13.6%)	6 (13.6%)	1.000
DAPT	3 (4.4%)	0 (0.0%)	0 (0.0%)	3 (6.8%)	0.585
With others	2 (2.9%)	0 (0.0%)	0 (0.0%)	2 (4.6%)	0.575

DOAC=direct oral anticoagulant; DAPT=dual antiplatelet therapy

Administration status of antithrombotic agents was not significantly different among the three groups.

Figure 3. Cumulative incidence of composite CV events



The incidence of the composite CV events was higher in the high-risk group.

Table 4. Cox proportional hazards regression models

Variable	R_2-CHA_2DS_2-VASc score	
	Univariate model	
	Hazard ratio (95% confidence interval)	P value
Composite outcome	1.33 (1.18 - 1.51)	<0.001
Stroke/systemic embolism	1.48 (1.13 - 1.94)	0.005
Major bleeding	1.16 (0.88 - 1.54)	0.282
†Cardiovascular events	1.43 (1.10 - 1.86)	0.008
Heart failure requiring hospitalization	1.24 (1.07 - 1.44)	0.004
Cardiovascular death	1.73 (1.19 - 2.53)	0.005
All-cause death	1.14 (0.95 - 1.36)	0.156
Reoperation of the BPV	0.79 (0.52 - 1.22)	0.290
	*Multivariate model	
Composite outcome	1.36 (1.18 - 1.55)	<0.001
Stroke/systemic embolism	1.53 (1.12 - 2.08)	0.007
Major bleeding	1.16 (0.84 - 1.58)	0.368
†Cardiovascular events	1.47 (1.10 - 1.98)	0.010
Heart failure requiring hospitalization	1.29 (1.10 - 1.52)	0.002
Cardiovascular death	1.67 (1.10 - 2.53)	0.016
All-cause death	1.07 (0.88 - 1.30)	0.484
Reoperation of the BPV	0.78 (0.49 - 1.25)	0.302

*Adjusted for antiplatelet use, type of AF, transcatheter aortic valve implantation, malignancy, and valve position (mitral, aortic, or both).
†Myocardial infarction, stroke, systemic embolism, and death from bleeding.

The R_2-CHA_2DS_2-VASc score as a continuous variable was an independent predictor of the composite CV events by the multivariate analysis.

Conclusions

- The R_2-CHA_2DS_2-VASc score is useful for CV risk stratification in AF patients after BPV replacement.