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Outcomes of Direct Oral Anticoagulants in Patients With Mitral Stenosis

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ABSTRACT

BACKGROUND Patients with mitral stenosis and atrial fibrillation (AF) require anticoagulation for stroke prevention. Thus far, all studies on direct oral anticoagulants (DOACs) have excluded patients with moderate to severe mitral stenosis.

OBJECTIVES The aim of this study was to validate the efficacy of DOACs in patients with mitral stenosis.

METHODS The study population was enrolled from the Health Insurance Review and Assessment Service (HIRA) database in the Republic of Korea, and it included patients who were diagnosed with mitral stenosis and AF and either were prescribed DOACs for off-label use or received conventional treatment with warfarin. The primary efficacy endpoint was ischemic strokes or systemic embolisms, and the safety outcome was intracranial hemorrhage.

RESULTS A total of 2,230 patients (mean age 69.7 $\pm$ 10.5 years; 682 [30.6%] males) were included in the present study. Thromboembolic events occurred at a rate of 2.22%/year in the DOAC group, and 4.19%/year in the warfarin group (adjusted hazard ratio for DOAC: 0.28; 95% confidence interval: 0.18 to 0.45). Intracranial hemorrhage occurred in 0.49% of the DOAC group and 0.93% of the warfarin group (adjusted hazard ratio for DOAC: 0.53; 95% confidence interval: 0.22 to 1.26).

CONCLUSIONS In patients with AF accompanied with mitral stenosis, DOAC use is promising and hypothesis generating in preventing thromboembolism. Our results need to be replicated in a randomized trial.

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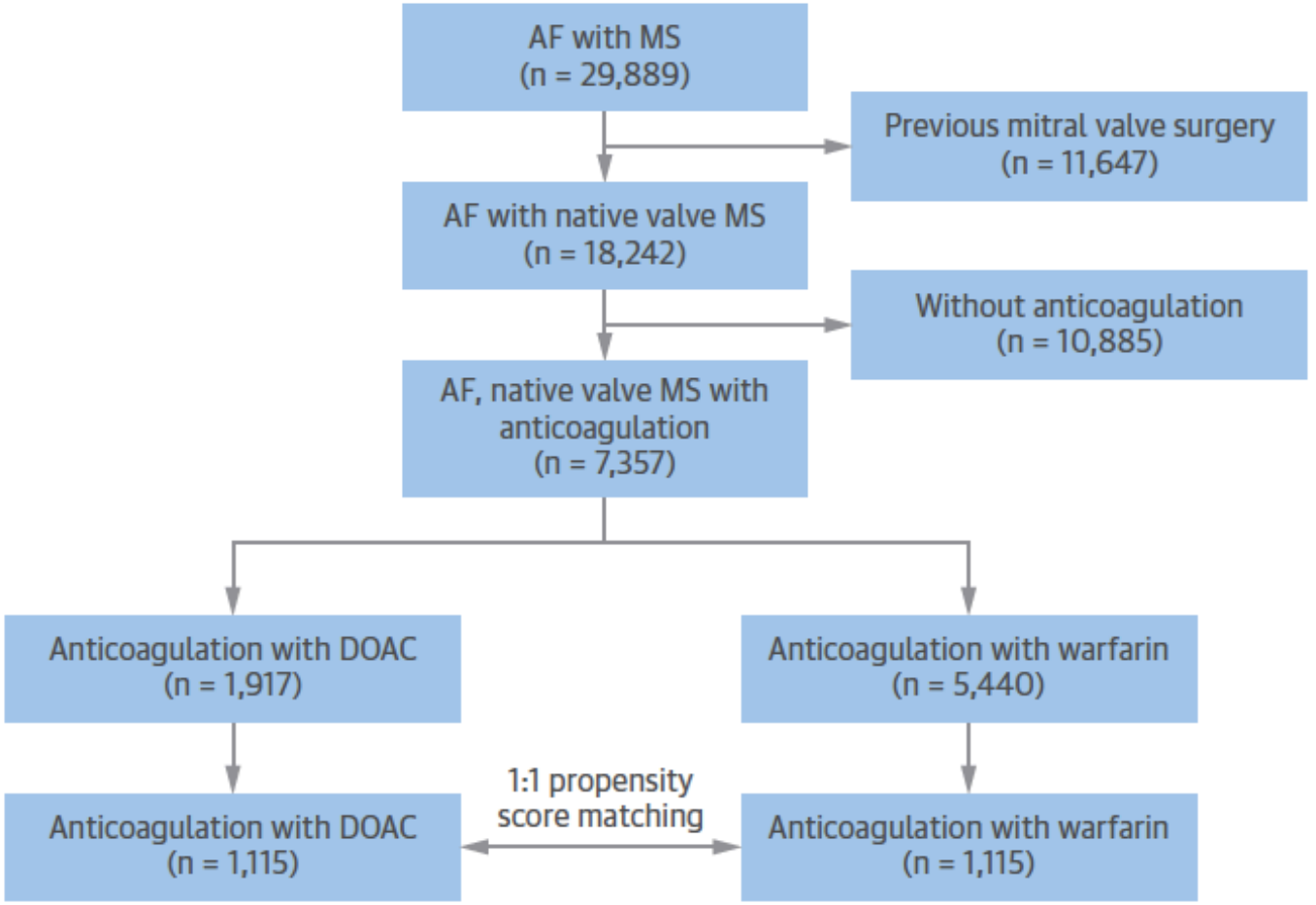
FIGURE 1 Flow Chart of Atrial Fibrillation With Mitral Stenosis Patients



The study population was divided according to the type of oral anticoagulant. A total of 1,917 patients received DOAC therapy and 5,440 were treated with warfarin. After 1:1 propensity score matching, the data from a total of 2,230 patients were analyzed. AF = atrial fibrillation; DOAC = direct oral anticoagulant; MS = mitral stenosis.

TABLE 1 Baseline Characteristics According to the Type of Oral Anticoagulant

	DOAC (n = 1,115)	Warfarin (n = 1,115)	Standardized Difference	p Value
Age, yrs	69.2 ± 10.9	70.2 ± 10.2	0.0947	
<65	311 (27.9)	318 (28.5)	0.0192	0.90
65–74	401 (36.0)	404 (36.2)		
≥75	403 (36.1)	393 (35.3)		
Female	775 (69.5)	773 (69.3)	0.0039	0.93
Hypertension	1,076 (96.5)	1,080 (96.9)	0.0200	0.64
Diabetes mellitus	759 (68.1)	760 (68.2)	0.0019	0.96
Previous stroke	518 (46.5)	521 (46.7)	0.0054	0.90
Congestive heart failure	832 (74.6)	838 (75.2)	0.0124	0.77
Previous vascular disease	625 (56.1)	623 (55.9)	0.0036	0.93
Dyslipidemia	810 (72.7)	808 (72.5)	0.0040	0.92
COPD	265 (23.7)	267 (24.0)	0.0042	0.92
CKD	80 (3.59)	73 (6.55)	0.0248	0.56

Values are mean ± SD or n (%).

CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DOAC = direct oral anticoagulants.

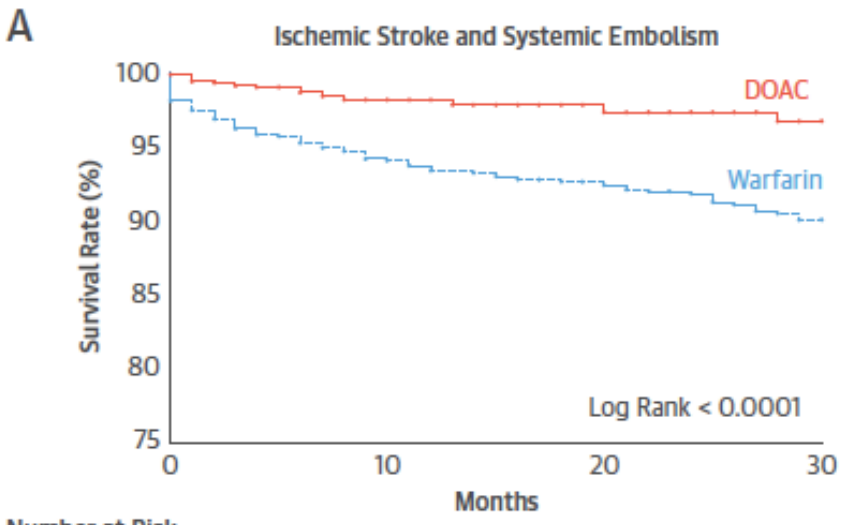
TABLE 2 Outcomes

		Ischemic Stroke or Systemic Embolism		Intracranial Hemorrhage	
	Patients	Events	Event Rate, %/yr	Events	Event rate, %/yr
DOAC	1,115	30	2.22	7	0.49
Warfarin	1,115	146	4.19	36	0.93

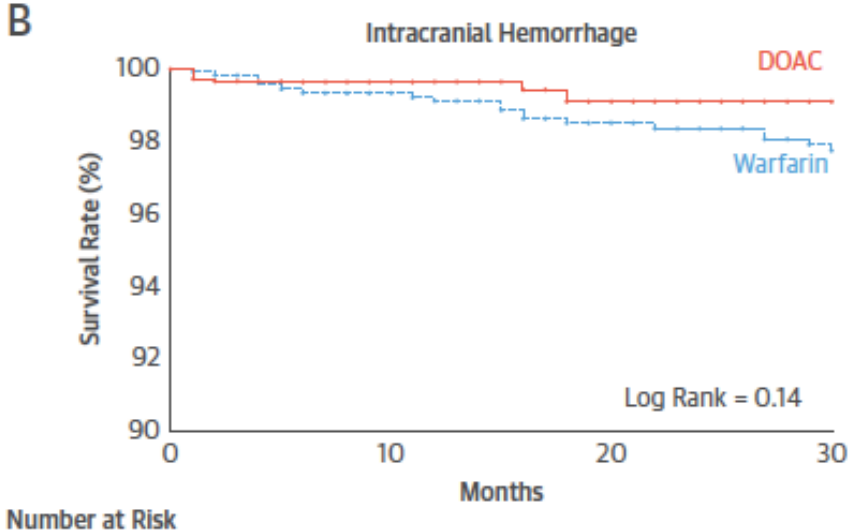
Values are n unless otherwise indicated.

DOAC = direct oral anticoagulant.

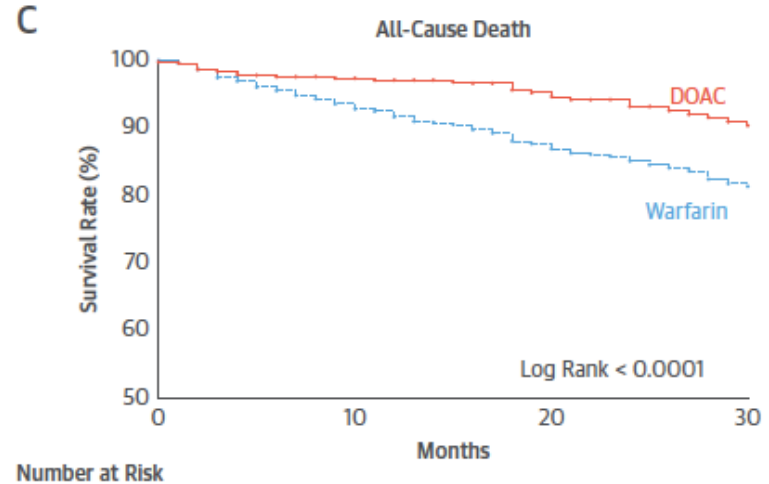
FIGURE 2 Kaplan-Meier Curves of the Primary Efficacy and Safety Outcomes (Warfarin vs. DOAC)



Number at Risk				
DOAC	1,115	703	192	140
Warfarin	1,115	853	701	560



Number at Risk				
DOAC	1,115	718	199	150
Warfarin	1,115	905	759	620

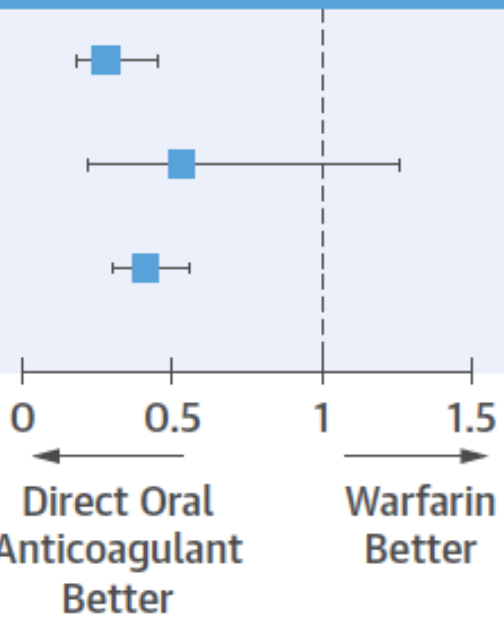


Number at Risk				
DOAC	1,115	710	198	147
Warfarin	1,115	879	724	578

The efficacy outcome **(A)** was freedom from ischemic strokes or systemic embolisms (adjusted hazard ratio [HR]: 0.28; 95% confidential interval [CI]: 0.18 to 0.45). The safety outcome was freedom from **(B)** intracranial hemorrhage (adjusted HR: 0.53; 95% CI: 0.22 to 1.26), and **(C)** all-cause death (adjusted HR: 0.41; 95% CI: 0.30 to 0.56). DOAC = direct oral anticoagulant.

CENTRAL ILLUSTRATION **Mitral Stenosis and Atrial Fibrillation for Direct Oral Anticoagulant Versus Warfarin: Hazard Ratios**

Direct Oral Anticoagulant Versus Warfarin	HR (95% CI)
Ischemic Stroke and Systemic Embolism	0.28 (0.18-0.45)
Intracranial Hemorrhage	0.53 (0.22-1.26)
All-Cause Death	0.41 (0.30-0.56)



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Strokes or systemic embolisms and all-cause death rates were significantly lower in the direct oral anticoagulant group compared with the warfarin group. There was a nonsignificant difference in the rate of the incidence of intracranial hemorrhages between the direct oral anticoagulant group and the warfarin group. CI = confidence interval; HR = hazard ratio.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Observational data suggest that DOACs may be effective for prevention of thromboembolism in patients with mitral stenosis and atrial fibrillation.

TRANSLATIONAL OUTLOOK: Randomized trials are needed to confirm the safety and efficacy of DOACs relative to vitamin K antagonists in patients with mitral stenosis and atrial fibrillation.