

SUPPLEMENTAL MATERIAL

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Table S1. Several causes of crossover.

	Number of Causes (n)
Early Rhythm Control to Usual Care	15
Follow-up loss	4
Infection (pneumonia, urinary tract infection)	5
Gastrointestinal bleeding	2
Chest pain (angina), coronary stent insertion	2
History of sick sinus syndrome	1
Interstitial lung disease	1

Table S2. Primary/secondary outcomes (per-protocol analysis: exclusion of 25 crossover patients)

	Early Rhythm Control (n=166)	Usual Care (n=85)	HR	95% CI	P-Value
Primary Outcome*					
Recurrent stroke in 3 months (n, %)	2 (1.2%)	4 (4.7%)	0.244	0.045~1.334	0.104
Recurrent stroke in 12 months (n, %)	3 (1.8%)	6 (7.1%)	0.236	0.059~0.943	0.041
Secondary Outcome#					
Composite outcome in 3 months (n, %)	16 (9.6%)	10 (11.8%)	0.794	0.360~1.749	0.566
Composite outcome in 12 months (n, %)	22 (13.3%)	16 (18.8%)	0.665	0.349~1.267	0.215
Arrhythmia-related events in 3 months (n, %)	2 (1.2%)	0 (0%)	NA	NA	NA
Arrhythmia-related events in 12 months (n, %)	4 (2.4%)	1 (1.2%)	1.919	0.214~17.176	0.560

*Primary; recurrent ischemic stroke (IS), recurrent IS in 3 and 12 months, respectively

#Secondary; a composite of death from any cause or hospitalization for any cause, recurrent stroke, arrhythmia-related events

Table S3. Primary/Secondary outcomes (on-treated analysis)

	Early Rhythm Control (n=176)	Usual Care (n=97)	HR	95% CI	P-value
Primary Outcome*					
Recurrent stroke in 3 months (n, %)	2 (1.1%)	4 (4.1%)	0.262	0.048~1.433	0.122
Recurrent stroke in 12 months (n, %)	3 (1.7%)	6 (6.2%)	0.253	0.063~1.013	0.052
Secondary Outcome#					
Composite outcome in 3 months (n, %)	16 (9.1%)	13 (13.4%)	0.653	0.314~1.357	0.254
Composite outcome in 12 months (n, %)	22 (12.5%)	19 (19.6%)	0.597	0.323~1.103	0.100
Arrhythmia-related events in 3 months (n, %)	2 (1.1%)	1 (1.0%)	1.066	0.097~11.76	0.958
Arrhythmia-related events in 12 months (n, %)	4 (2.3%)	2 (2.1%)	1.027	0.188~5.612	0.975

*Primary; recurrent ischemic stroke (IS), recurrent IS in 3 and 12 months, respectively

#Secondary; a composite of death from any cause or hospitalization for any cause, recurrent stroke, arrhythmia-related events

Table S4. Multivariate Cox regression analysis of secondary outcomes (12-month follow-up)

Composite Outcome Post-stroke 12 Months	Univariate			Multivariate		
	HR	95% CI	P-Value	HR	95% CI	P-Value
Age	1.082	1.031~1.135	0.001	1.062	1.012~1.114	0.014
Male	1.049	0.556~1.981	0.882			
Paroxysmal AF	0.764	0.414~1.412	0.391			
Body mass index	0.920	0.829~1.020	0.114			
The use of NOAC	0.302	0.147~0.617	0.001	0.361	0.174~0.748	0.006
Creatinine	0.922	0.545~1.558	0.761			
NIH stroke scale	1.102	1.057~1.149	<0.001	1.08	1.034~1.129	0.001
CHA ₂ DS ₂ VASc Score	1.296	1.045~1.607	0.018			
Congestive heart failure	1.456	0.518~4.090	0.476			
Hypertension	1.236	0.617~2.474	0.550			
Diabetes	1.112	0.581~2.129	0.749			
Vascular disease	2.141	0.839~5.465	0.111			
Early rhythm Control	0.808	0.431~1.513	0.505	0.855	0.448~1.632	0.635

AF; atrial fibrillation, NOAC; non-vitamin K antagonist, NIH; National Institute of Health

Table S5. The effect of early rhythm control on primary and secondary outcomes by AF type and sex

Outcome	Type of AF	HR	95% CI	P-value	P for interaction between intervention (early rhythm control vs. Usual control) and type of AF
Recurrent stroke in 12 months	Persistent AF	0.266	0.024~2.931	0.279	0.938
	Paroxysmal AF	0.235	0.043~1.287	0.095	
Composite outcome in 12 months	Persistent AF	0.971	0.407~2.315	0.948	0.545
	Paroxysmal AF	0.651	0.262~1.620	0.356	
Outcome	Sex	HR	95% CI	P-value	P for interaction between intervention (early rhythm control vs. Usual control) and sex
Recurrent stroke in 12 months	Female	0.474	0.030~7.578	0.598	0.624
	Male	0.208	0.040~1.073	0.061	
Composite outcome in 12 months	Female	0.994	0.340~2.908	0.991	0.631
	Male	0.722	0.332~1.572	0.412	

Figure S1. Type of anti-arrhythmic drug use according to the assigned groups

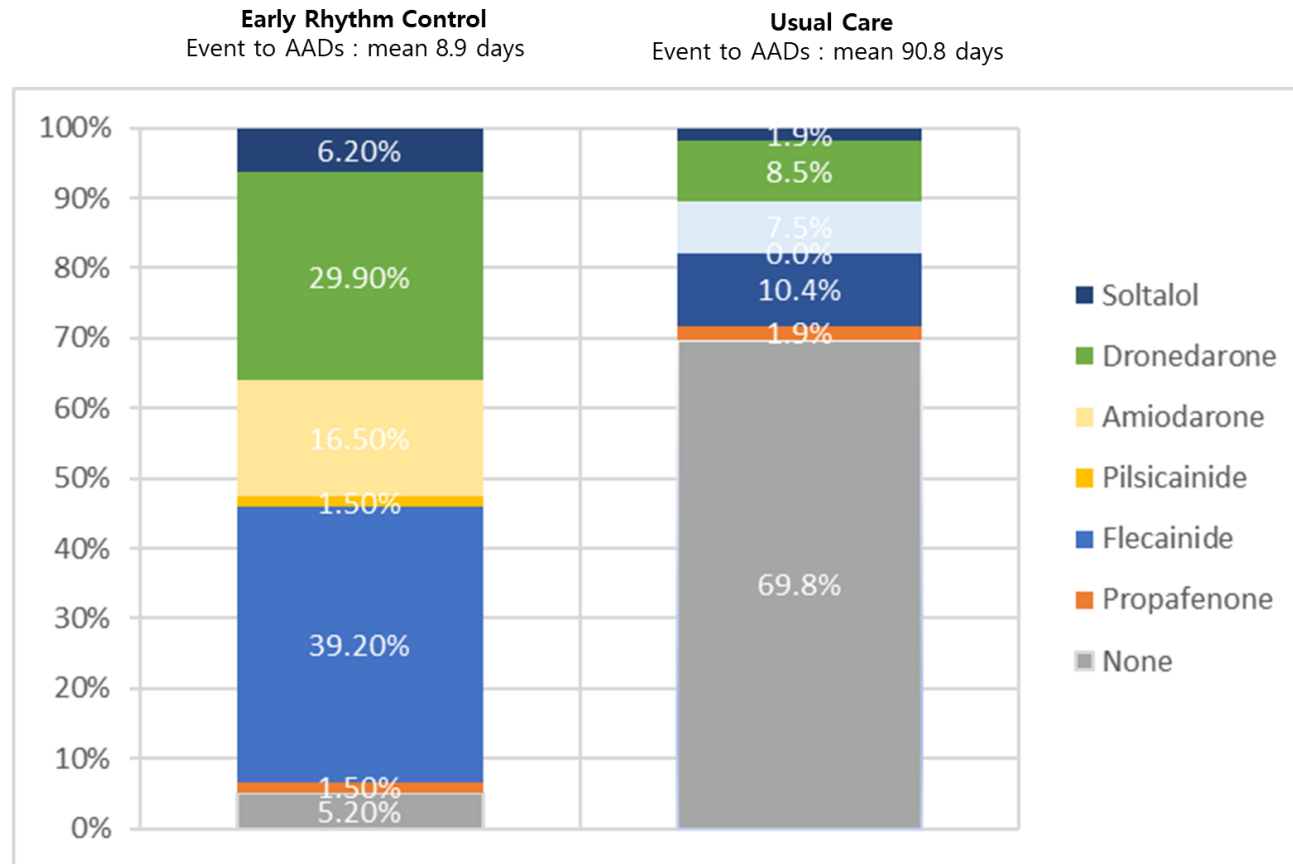


Figure S2. (A) Subgroup analysis of the primary endpoint (recurrent IS within 12 months)

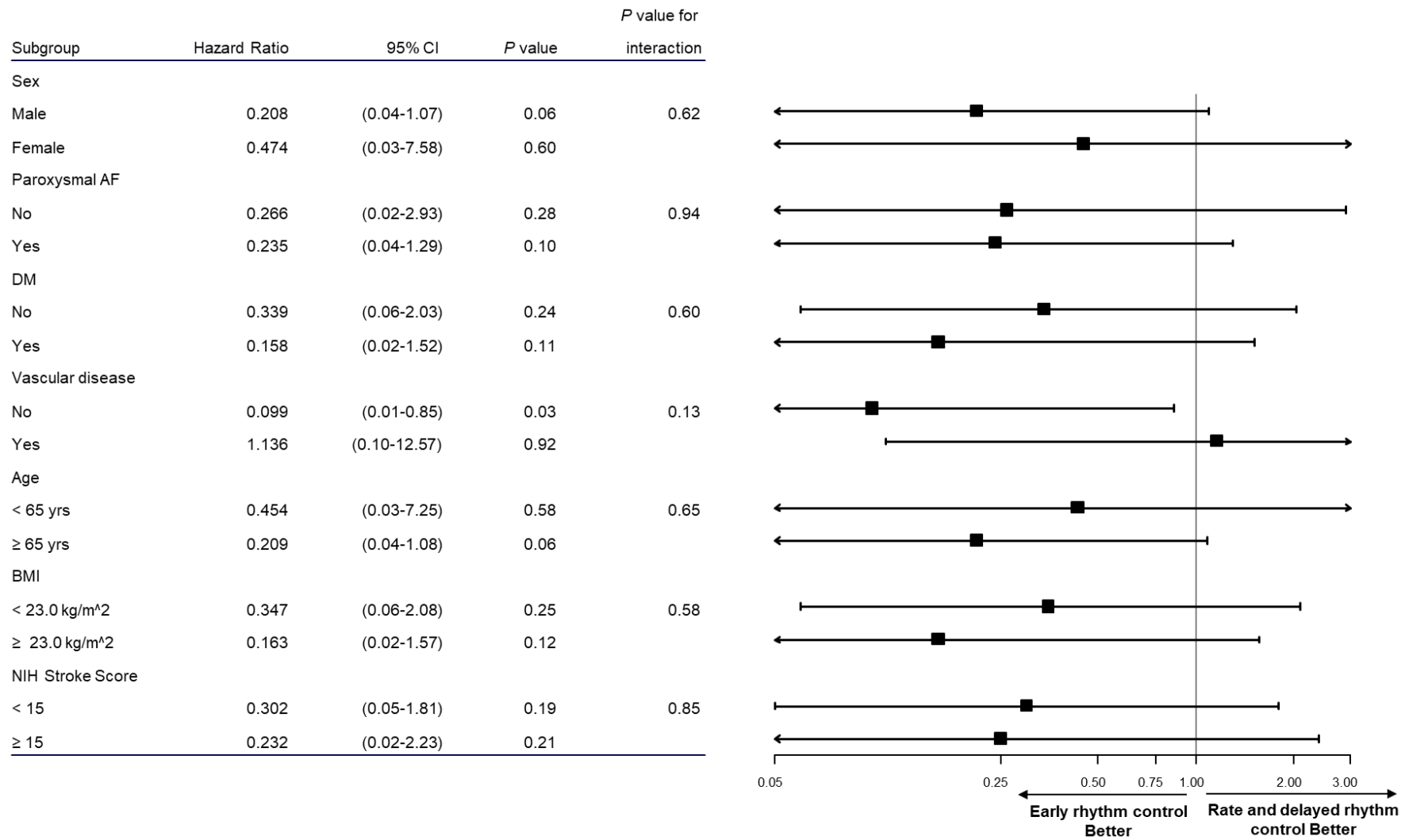


Figure S2 (continued) (B) Subgroup analysis of the secondary endpoints (within 12 months)

Subgroup	Hazard Ratio	95% CI	P value	P value for interaction
Sex				
Male	0.722	(0.33-1.57)	0.41	0.63
Female	0.994	(0.34-2.91)	0.99	
Paroxysmal AF				
No	0.971	(0.41-2.32)	0.95	0.54
Yes	0.651	(0.26-1.62)	0.36	
NOAC				
No	0.709	(0.20-2.52)	0.60	0.90
Yes	0.783	(0.38-1.63)	0.51	
HTN				
No	1.712	(0.37-7.93)	0.49	0.34
Yes	0.727	(0.35-1.51)	0.39	
DM				
No	1.196	(0.52-2.75)	0.67	0.18
Yes	0.474	(0.17-1.35)	0.16	
Vascular disease				
No	0.762	(0.39-1.50)	0.43	0.34
Yes	2.303	(0.26-20.63)	0.46	
Age				
< 65 yrs	1.165	(0.23-6.00)	0.86	0.64
≥ 65 yrs	0.768	(0.39-1.52)	0.45	
BMI				
< 23.0 kg/m ²	0.699	(0.28-1.77)	0.45	0.67
≥ 23.0 kg/m ²	0.929	(0.39-2.19)	0.87	
eGFR				
≥ 60 ml/min/1.73m ²	1.075	(0.49-2.36)	0.86	0.29
< 60 ml/min/1.73m ²	0.490	(0.15-1.61)	0.24	
NIH Stroke Score				
< 15	1.088	(0.42-2.83)	0.86	0.53
≥ 15	0.724	(0.30-1.74)	0.47	

