

항응고제를 복용하고 있는 심방세동환자의 치매 발병 위험도에서 스타틴 약물의 효과

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Statin Therapy Reduces Dementia Risk in Atrial Fibrillation Patients Receiving Oral Anticoagulants

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Abstract

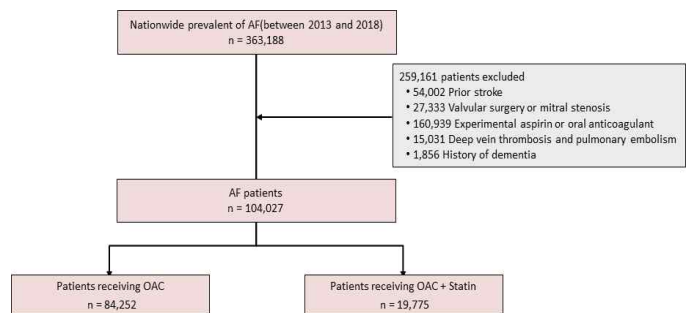
Background: Atrial fibrillation (AF) is generally regarded as a risk factor for dementia. The effect of oral anticoagulant (OAC) plus statin therapy on dementia risk has been unclear, particularly for dose-dependent statins. We sought to investigate the impact of statin therapy on dementia risk in AF patients receiving OAC. **Methods:** Using the Korean National Health Insurance Service database, we included 104,027 AF patients from January 2013 to December 2018. The clinical endpoint was the occurrence of dementia. We performed head to head comparisons of OAC(warfarin or non-vitamin K antagonist oral anticoagulant) and OAC+statin therapy. **Results:** OAC plus statin users had a significantly lower risk of dementia than OAC user in low (HR=0.84, 95%CI 0.69 - 0.98, p=0.041) and high-risk (HR=0.77, 95%CI 0.64 - 0.90, p=0.026) AF patients. Additionally, OAC plus dose dependent statin user was associated with a lower risk of dementia than OAC user in low and high-risk AF patients (P for trend=0.005 and P for trend<0.001, respectively) **Conclusions:** AF patients who take OAC plus statin therapy had lower risk of dementia than only OAC treated patients. Also, statin was associated with dose dependent reduction in the risk of dementia in OAC treated AF patients.

1. Introduction

Atrial fibrillation (AF) is generally regarded as a risk factor for dementia. The effect of oral anticoagulant (OAC) plus statin therapy on dementia risk has been unclear, particularly for dose-dependent statins. We sought to investigate the impact of statin therapy on dementia risk in AF patients receiving OAC.

2. Method

Using the Korean National Health Insurance Service database, we included 104,027 AF patients from January 2013 to December 2018. The clinical endpoint was the occurrence of dementia. We performed head to head comparisons of OAC(warfarin or non-vitamin K antagonist oral anticoagulant) and OAC+statin therapy.



[그림 1] Study Inflow

3. Result

Of the total, 84,252 patients (81.0%) were in the OAC therapy group and 19,775 patients (19.0%) were in the OAC plus statin therapy group. OAC plus statin users had a significantly lower risk of dementia than OAC user in low (HR=0.84, 95%CI 0.69 - 0.98, p=0.041) and high-risk (HR=0.77, 95%CI 0.64 - 0.90,

p=0.026) AF patients. Additionally, OAC plus dose dependent statin user was associated with a lower risk of dementia than OAC user in low and high-risk AF patients (P for trend=0.005 and P for trend<0.001, respectively)

[표 1] Baseline characteristics

	OAC [ⓐ] (n=84,252) [ⓐ]	OAC + Statin [ⓐ] (n=19,775) [ⓐ]	SMD [ⓐ]
Age, y (SD) [ⓐ]	67.5 ± 13.1 [ⓐ]	67.1 ± 13.0 [ⓐ]	0.013 [ⓐ]
Age, n (%) [ⓐ]			
< 65, n (%) [ⓐ]	26,539 (31.5) [ⓐ]	6,556 (33.2) [ⓐ]	
65-74, n (%) [ⓐ]	25,444 (30.2) [ⓐ]	6,662 (33.7) [ⓐ]	
≥ 75, n (%) [ⓐ]	32,269 (38.3) [ⓐ]	6,559 (33.2) [ⓐ]	
Female, n (%) [ⓐ]	40,104 (47.6) [ⓐ]	9,125 (46.1) [ⓐ]	0.199 [ⓐ]
Clinical history, n (%) [ⓐ]			
Hypertension [ⓐ]	53,753 (63.8) [ⓐ]	12,824 (64.8) [ⓐ]	0.154 [ⓐ]
Diabetes mellitus [ⓐ]	19,378 (23.0) [ⓐ]	4,685 (23.7) [ⓐ]	0.086 [ⓐ]
Heart failure [ⓐ]	27,382 (32.5) [ⓐ]	6,426 (32.5) [ⓐ]	0.009 [ⓐ]
Dyslipidemia [ⓐ]	29,067 (34.5) [ⓐ]	7,094 (35.9) [ⓐ]	0.196 [ⓐ]
Vascular disease [ⓐ]	16,176 (19.2) [ⓐ]	4,100 (20.7) [ⓐ]	0.203 [ⓐ]
Myocardial infarction [ⓐ]	2,780 (3.3) [ⓐ]	800 (4.0) [ⓐ]	0.114 [ⓐ]
PAD [ⓐ]	13,059 (15.5) [ⓐ]	3,145 (15.9) [ⓐ]	0.052 [ⓐ]
CHA2DS2-VASc score, (SD) [ⓐ]	3.9 ± 1.4 [ⓐ]	3.7 ± 1.4 [ⓐ]	0.088 [ⓐ]
CHA2DS2-VASc score, n (%) [ⓐ]			
0-1 [ⓐ]	14,491 (17.2) [ⓐ]	2,075 (10.5) [ⓐ]	
≥ 2 [ⓐ]	69,761 (82.8) [ⓐ]	17,700 (89.5) [ⓐ]	
Follow up, y (IQR) [ⓐ]	2.21 [1.59 - 2.83] [ⓐ]	2.22 [1.68 - 2.83] [ⓐ]	0.074 [ⓐ]

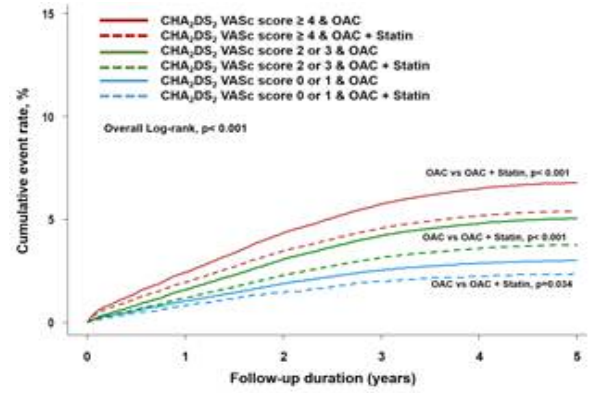
Values are n (%), mean ± SD (standard deviation) or median IQR (interquartile range). OAC, oral anticoagulant (warfarin or non-vitamin K antagonist oral anticoagulant); PAD, peripheral artery disease; SMD, standard mean difference.[ⓐ]

[표 2] Risk of dementia in AF patients according to treatment

OAC vs. OAC + Statin [ⓐ]	No. of Events [ⓐ]	Annual IR [ⓐ] (95% CI) [ⓐ]	HR [ⓐ] (95% CI) [ⓐ]	p-value [ⓐ]	[ⓐ] p [ⓐ]
CHA2DS2-VASc score 0-1[ⓐ]					
OAC [ⓐ]	320/10,934 [ⓐ]	4.59 (4.33 - 4.86) [ⓐ]	Reference [ⓐ]		
OAC + Statin [ⓐ]	58/2,075 [ⓐ]	4.36 (3.79 - 4.94) [ⓐ]	0.84 (0.69 - 0.98) [ⓐ]	0.041 [ⓐ]	
OAC [ⓐ]			Reference [ⓐ]	0.013 [ⓐ]	
OAC + Statin [ⓐ]					
Low intensity [ⓐ]	25/676 [ⓐ]	4.50 (4.41 - 4.59) [ⓐ]	0.92 (0.80 - 1.06) [ⓐ]	0.357 [ⓐ]	0.005 [ⓐ]
Moderate intensity [ⓐ]	18/643 [ⓐ]	4.29 (4.19 - 4.39) [ⓐ]	0.84 (0.71 - 0.96) [ⓐ]	0.043 [ⓐ]	
High intensity [ⓐ]	15/756 [ⓐ]	4.09 (3.99 - 4.20) [ⓐ]	0.74 (0.61 - 0.87) [ⓐ]	0.009 [ⓐ]	
CHA2DS2-VASc score ≥ 2[ⓐ]					
OAC [ⓐ]	3,876/73,318 [ⓐ]	6.02 (5.92 - 6.11) [ⓐ]	Reference [ⓐ]		
OAC + Statin [ⓐ]	870/17,700 [ⓐ]	5.08 (4.90 - 5.25) [ⓐ]	0.77 (0.64 - 0.90) [ⓐ]	0.026 [ⓐ]	
OAC [ⓐ]			Reference [ⓐ]	0.002 [ⓐ]	
OAC + Statin [ⓐ]					
Low intensity [ⓐ]	295/5,772 [ⓐ]	5.22 (5.19 - 5.25) [ⓐ]	0.81 (0.69 - 0.94) [ⓐ]	0.034 [ⓐ]	<0.001 [ⓐ]
Moderate intensity [ⓐ]	277/5,492 [ⓐ]	5.04 (5.01 - 5.07) [ⓐ]	0.74 (0.61 - 0.88) [ⓐ]	0.010 [ⓐ]	
High intensity [ⓐ]	298/6,436 [ⓐ]	4.74 (4.71 - 4.77) [ⓐ]	0.67 (0.55 - 0.80) [ⓐ]	<0.001 [ⓐ]	

CI, confidence intervals; HR, hazard ratio; IR, incidence rate (events divided by 100 person-years, %/y); OAC, oral anticoagulant. [ⓐ]p for trend.[ⓐ]

[그림 2] Kaplan-Meier curve according to treatment



AF patients who take OAC plus statin therapy had lower risk of dementia than only OAC treated patients. Also, statin was associated with dose dependent reduction in the risk of dementia in OAC treated AF patients.

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4. Conclusion

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