Favorable Neurological outcome After Percutaneous LAAO

Jung-Sun Kim, MD, Ph D, FESC

Division of Cardiology, Severance Cardiovascular Hospital
Yonsei University College of Medicine

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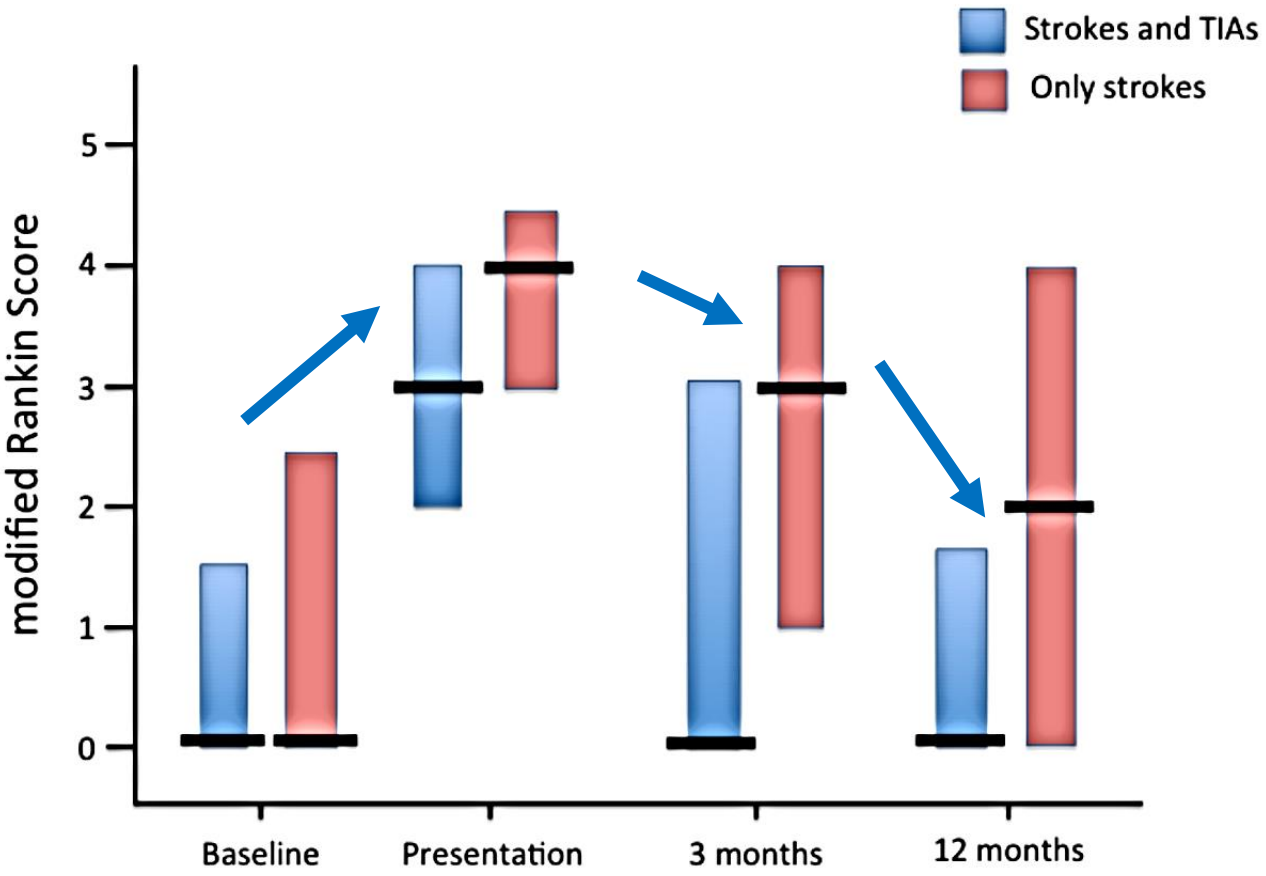
Disclosure

- **Relationships with commercial interests:**

- **Support/Consultant:** ***ACP and Amulet Proctor of Abbott***

- **Speaker's Bureau:** ***Abbott***

Cerebrovascular Events after LAAO Are Mostly Nondisabling

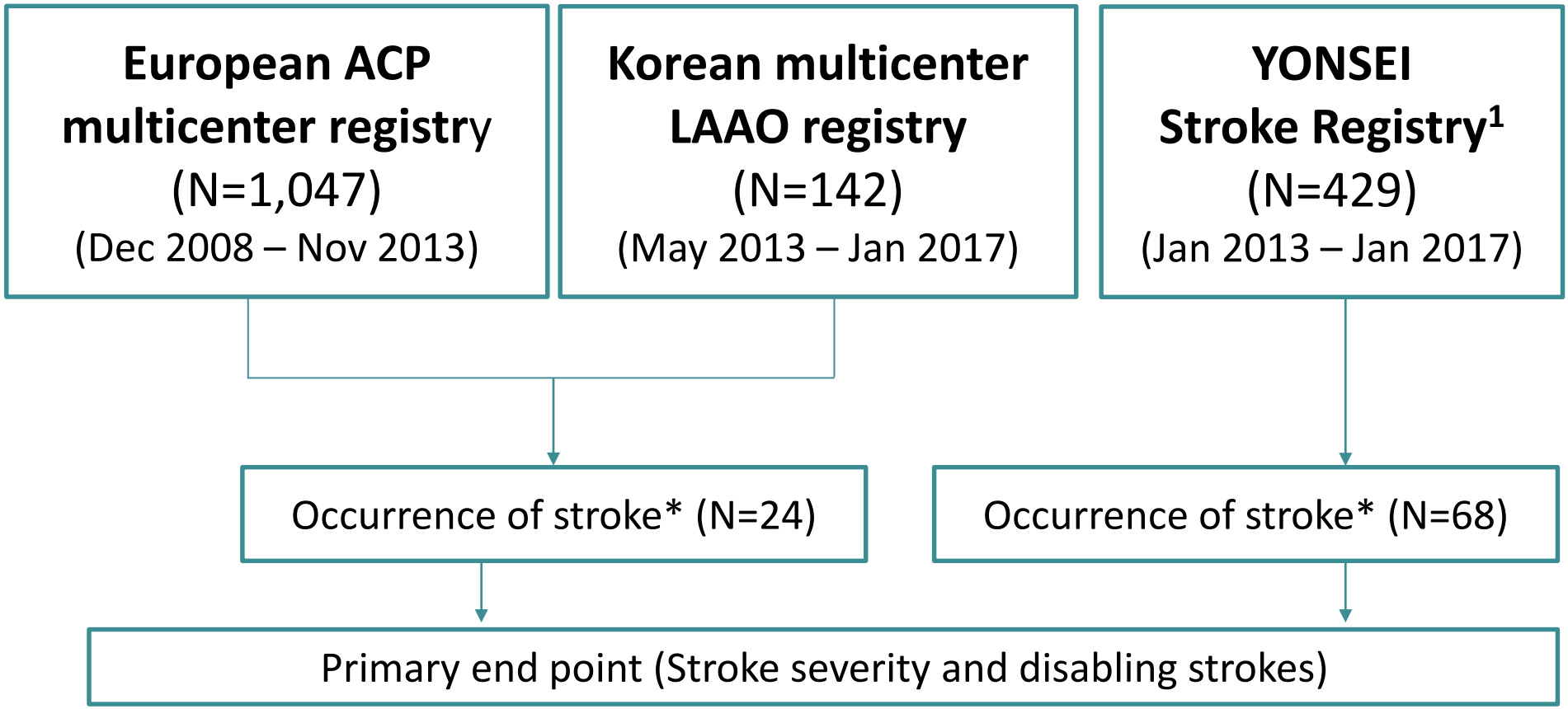


Non-disabling events were those with mRS of 0-2.

Frexia X, et al. Am J Cardiol 2016:118;1836-41

Q1. Are Neurological outcomes of Stroke After LAAO Better than those of Warfarin ?

Study at a Glance



*Ischemic stroke or transient ischemic attack (TIA)

1. Cerebrovasc Dis 2001;12:145-51

Definition

- **Stroke**[1,2]
  - **An acute episode of focal or global neurological dysfunction** caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction.
  - **Duration** of neurological dysfunction **> 24 hrs**.
  - Duration of neurological dysfunction < 24 hrs in case of **imaging – documented new hemorrhage or infarction.**
  - A neurological dysfunction resulting in death.
- **TIA**[1,2]
  - Any neurological dysfunction not satisfying the above criteria for stroke, specifically in lasting < 24hrs without imaging-documented acute brain infarction

- No other readily identifiable non-stroke cause
- All events were adjudicated by two cardiologists or neurologists

Definition

- Cerebrovascular events assessment focused on the ***modified Rankin Scale (mRS)***.[1]

Scale	Definition
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability. Requires some help, but able to walk unassisted
4	Moderately severe disability. Unable to attend to own bodily needs without assiatance, and unable to walk unassisted
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent
6	Dead

1. Hankey GJ, et al. Stroke 2010;41:1679-83

Baseline Characteristics

Variables	LAA Occlusion (n=24)	Warfarin (n=68)	P value
Age, years	73.4 ± 10.9	74.1 ± 9.5	0.76
Age ≥ 65 years	20 (83.3)	59 (86.8)	0.74
Male gender	13 (54.2)	41 (60.3)	0.60
Hypertension	23 (95.8)	58 (85.3)	0.28
Diabetes mellitus	15 (62.5)	24 (35.3)	**0.03**
Congestive heart failure	5 (20.8)	15 (22.1)	1.00
Previous stroke/TIA	12 (50.0)	28 (41.2)	0.45
$CHADS_2$ score	3.0 ± 1.3	2.7 ± 1.4	0.42
CHA_2DS_2-VASc score	4.7 ± 1.6	4.4 ± 1.8	0.49
HAS-BLED score	3.3 ± 1.0	4.2 ± 0.9	**<0.01**

Lee OH, Kim JS, et al. Catheter Cardiovasc Interv 2018

Procedural Characteristics

Variables	LAA Occlusion (n=24)
Device	
Watchman	3 (12.5)
ACP	21 (87.5)
Device thrombosis	1 (4.2)
Significant peri-device leakage[a]	1 (4.2)

Data are presented as the number (%)
Abbreviation: ACP = Amplatzer cardiac plug, LAA = left atrial appendage.

[a]Significant peri-device leakage was defined as ≥ 3 and 5 mm ACP and Watchman, respectively.

Lee OH, Kim JS, et al. Catheter Cardiovasc Interv 2018

Duration and Incidence of Stroke

- **Mean time of stroke or TIA**
  - **LAA occlusion group : 15.5** ±11.0 months
  - **Warfarin group : 63.2** ± 38.6 months, P < 0.01
- **24/1189 (2.0%) patients in LAA closure group**
  - **13 ischemic strokes and 11 TIAs**
  - **Medication at clinical presentation**
    - **SAPT : 18 patients (75%)**
    - **DAPT : 5 patients (20.8%)**
    - **Warfarin : 1 patient (AF with HCM)**

Lee OH, Kim JS, et al. Catheter Cardiovasc Interv 2018

Stroke Burden Before Adjustment

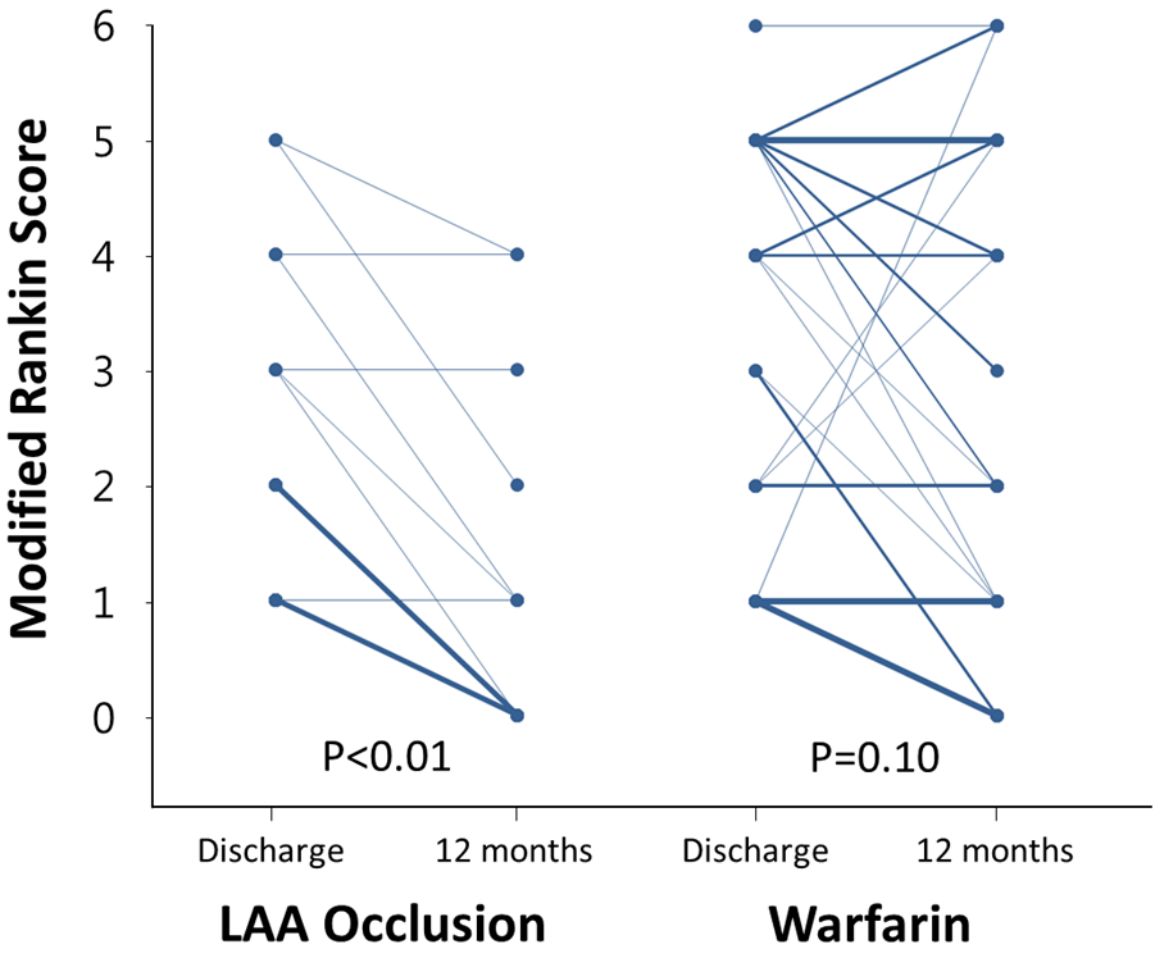
Variables	LAA Occlusion (n=24)	Warfarin (n=68)	P value
mRS before the event	0.4 ± 1.1	0.4 ± 1.0	0.98
mRS at discharge	2.5 ± 1.4	3.2 ± 1.7	**0.04**
Disabling strokes at discharge	9 (37.5)	40 (58.8)	0.07
mRS at 3 months	1.0 ± 1.5	2.6 ± 1.9	**<0.01**
Disabling strokes at 3 months	5 (20.8)	29 (42.6)	0.08
mRS at 12 months	0.7 ± 1.3	2.7 ± 2.1	**<0.01**
Disabling strokes at 12 months	3 (12.5)	27 (39.7)	**0.02**
Recovery to nondisabling strokes, 12 mo.	4 (44.4)	10 (25.0)	0.75

Data are presented as mean ± standard deviation or number (%).

Abbreviation: LAA = left atrial appendage; MRS = modified Rankin scale, TIA = transient ischemic attack.

Lee OH, Kim JS, et al. Catheter Cardiovasc Interv 2018

mRS at Discharge and 12 months



Stroke Burden after Adjustments

Variables	LAA Occlusion (n=24)	Warfarin (n=68)	P value
Model 1[a]			
mRS at discharge	2.4 ± 0.3	3.3 ± 0.2	0.03
mRS at 3 months	0.9 ± 0.4	2.6 ± 0.2	<0.01
mRS at 12 months	0.7 ± 0.4	2.8 ± 0.2	<0.01
Model 2[b]			
mRS at discharge	2.6 ± 0.4	3.2 ± 0.2	0.23
mRS at 3 months	1.2 ± 0.4	2.5 ± 0.2	0.01
mRS at 12 months	0.6 ± 0.5	2.8 ± 0.3	<0.01
Model 3[c]			
mRS at discharge	2.3 ± 0.4	3.2 ± 0.2	0.09
mRS at 3 months	0.9 ± 0.5	2.6 ± 0.2	<0.01
mRS at 12 months	0.3 ± 0.6	2.9 ± 0.3	<0.01

Data are presented as mean ± standard deviation. Abbreviation: MRS = modified Rankin scale.

[a]Model 1: adjusted by CHA_2DS_2-VASc score.

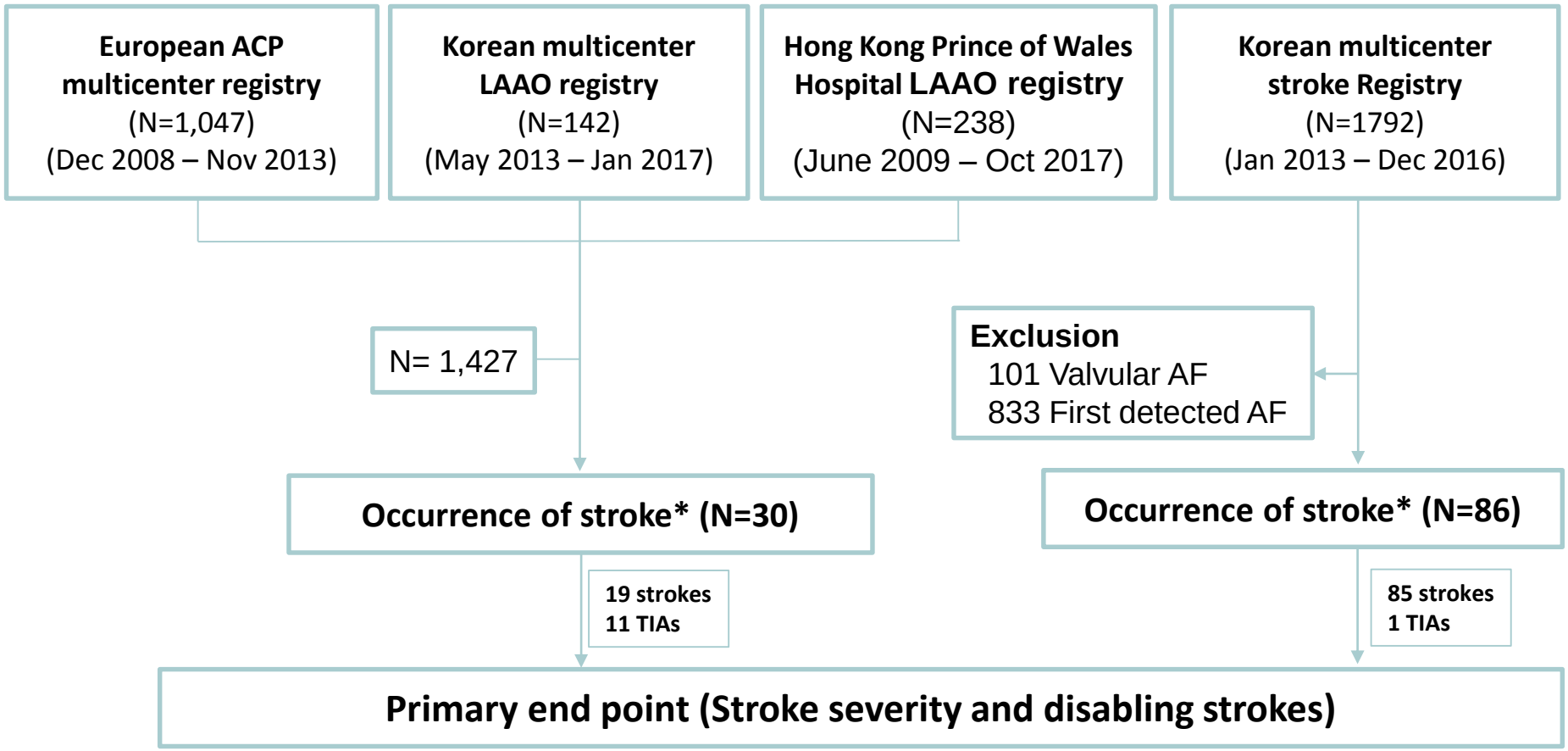
Model 2: Similar to Model 1, with the additional inclusion of HAS-BLED score.

Model 3: Similar to Model 2, with the additional inclusion of age, gender, and cardiovascular risk factors.

Q2. Are Neurological outcomes of Stroke After LAAO Even Better than those of NOAC ?

Study at a Glance

***Multi-National Cohort Study**



***Ischemic stroke or transient ischemic attack**

- **Exclusion** : 11 patients who underwent LAA closure due to ICH or periprocedural strokes.
  - 2 intracranial hemorrhage from Hong Kong registry
    9 peri-procedural strokes from European ACP registry

Baseline Characteristics

Variables	LAA Occlusion (n=30)	NOAC (n=86)	P value
Age, years	73.0 ± 10.1	73.5 ± 9.1	0.78
Age ≥ 65 years	25 (83.3)	68 (79.1)	0.79
Male gender	14 (46.7)	40 (46.5)	0.99
Hypertension	28 (93.3)	76 (88.4)	0.73
Diabetes mellitus	17 (56.7)	31 (36.3)	**0.048**
Congestive heart failure	7 (23.3)	7 (8.1)	**0.03**
Previous stroke/TIA	14 (46.7)	53 (61.6)	0.15
$CHADS_2$ score	3.0±1.2	3.1±1.2	0.75
CHA_2DS_2-VASc score	4.7±1.5	4.8±1.6	0.79
HAS-BLED score	3.0±1.0	3.2±1.2	0.56
mRS before the event			
mRS 0-1	27 (90.0)	74 (86.0)	0.76
mRS 0-2	28 (93.3)	78 (90.7)	1.00
mRS 0-3	29 (96.7)	81 (94.2)	1.00
mRS 0-4	30 (100)	86 (100)	-

Data are presented as mean ± standard deviation or number (%)

Baseline Characteristics

Variables	LAA Occlusion (n=30)	NOAC (n=86)	P value
Type of NOAC			
Dabigatran		34 (39.5)	
Rivaroxaban		20 (23.3)	
Apixaban		28 (32.6)	
Edoxaban		4 (4.7)	
Dose			
Full dose		35 (40.7)	
Reduced dose		51 (59.3)	

Data are presented as mean ± standard deviation or number (%)
Abbreviation: LAAO, left atrial appendage occlusion; TIA, transient ischemic attack; NOAC, novel oral anticoagulants; mRS, modified rankin scale

Procedural Characteristics

Variables	LAA Occlusion (n=30)
Device	
Watchman	6 (20.0)
ACP	24 (80.0)
Device thrombosis	4 (13.3)
Significant peri-device leakage[a]	3 (10.0)

Data are presented as the number (%)
Abbreviation: ACP = Amplatzer cardiac plug, LAA = left atrial appendage.

[a]Significant peri-device leakage was defined as ≥ 3 and 5 mm ACP and Watchman, respectively.

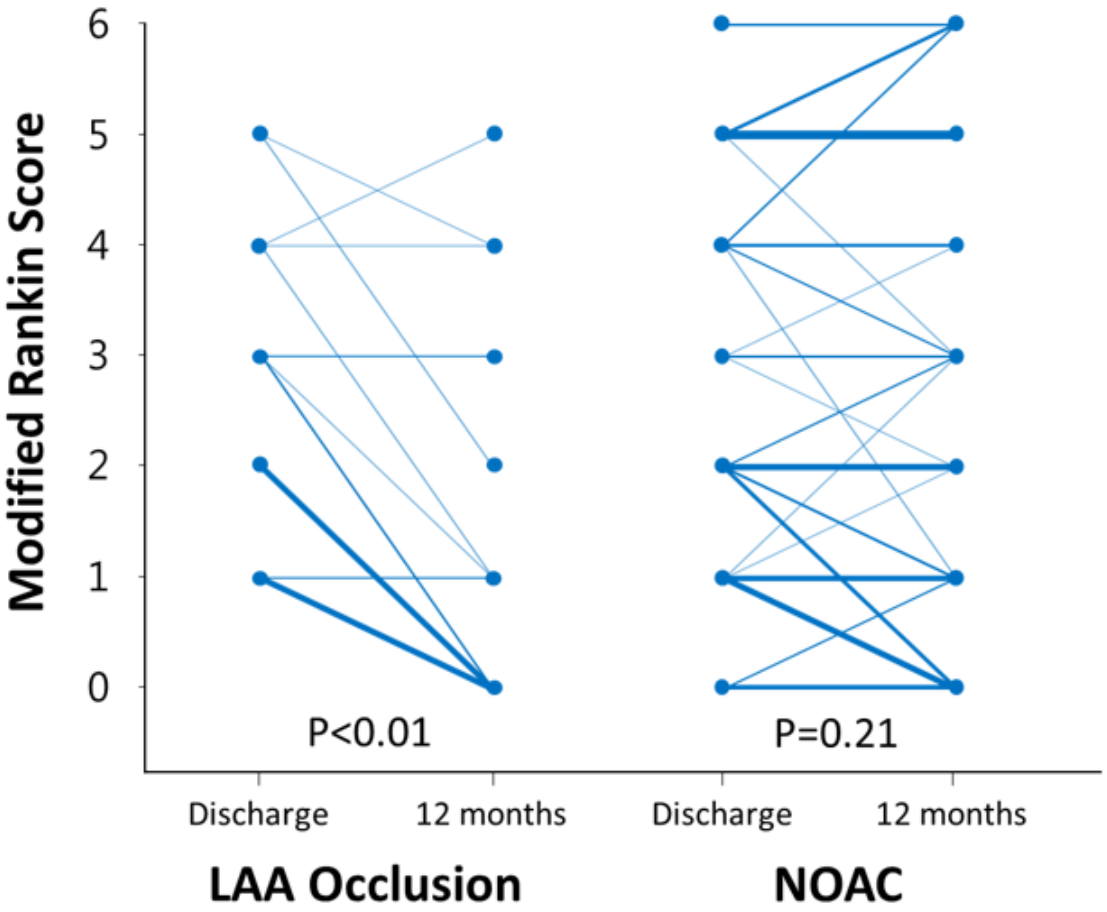
Duration and Incidence of Stroke

- **Mean time of stroke or TIA**
  - **LAA occlusion group : 20.1** ± 20.2 months.
  - **NOAC group : 9.9** ± 9.8 months
- **30/1427 (1.5%) patients in LAA closure group**
  - **19 ischemic strokes and 11 TIAs**
  - **Medication at clinical presentation**
    - **SAPT : 23/30 patients (76.7%)**
    - **DAPT : 5/30 patients (16.7%)**
    - **Anticoagulation ; 2/30 (6.7%)**
      - ✓ **Warfarin : 1/30 (3.3%), AF with HCM**
      - ✓ **Ribaroxaban : 1/30 (3.3%), Device thrombosis**

Stroke Burden Before Adjustment

Variables	LAA Occlusion (n=30)	NOAC (n=86)	P value
mRS before the event	0.4 ± 1.1	0.4 ± 1.0	0.98
mRS at discharge	2.5 ± 1.4	3.2 ± 1.7	0.04
mRS at 3 months	1.0 ± 1.5	2.6 ± 1.9	<0.01
mRS at 12 months	0.7 ± 1.3	2.7 ± 2.1	<0.01

mRS at Discharge and 12 months

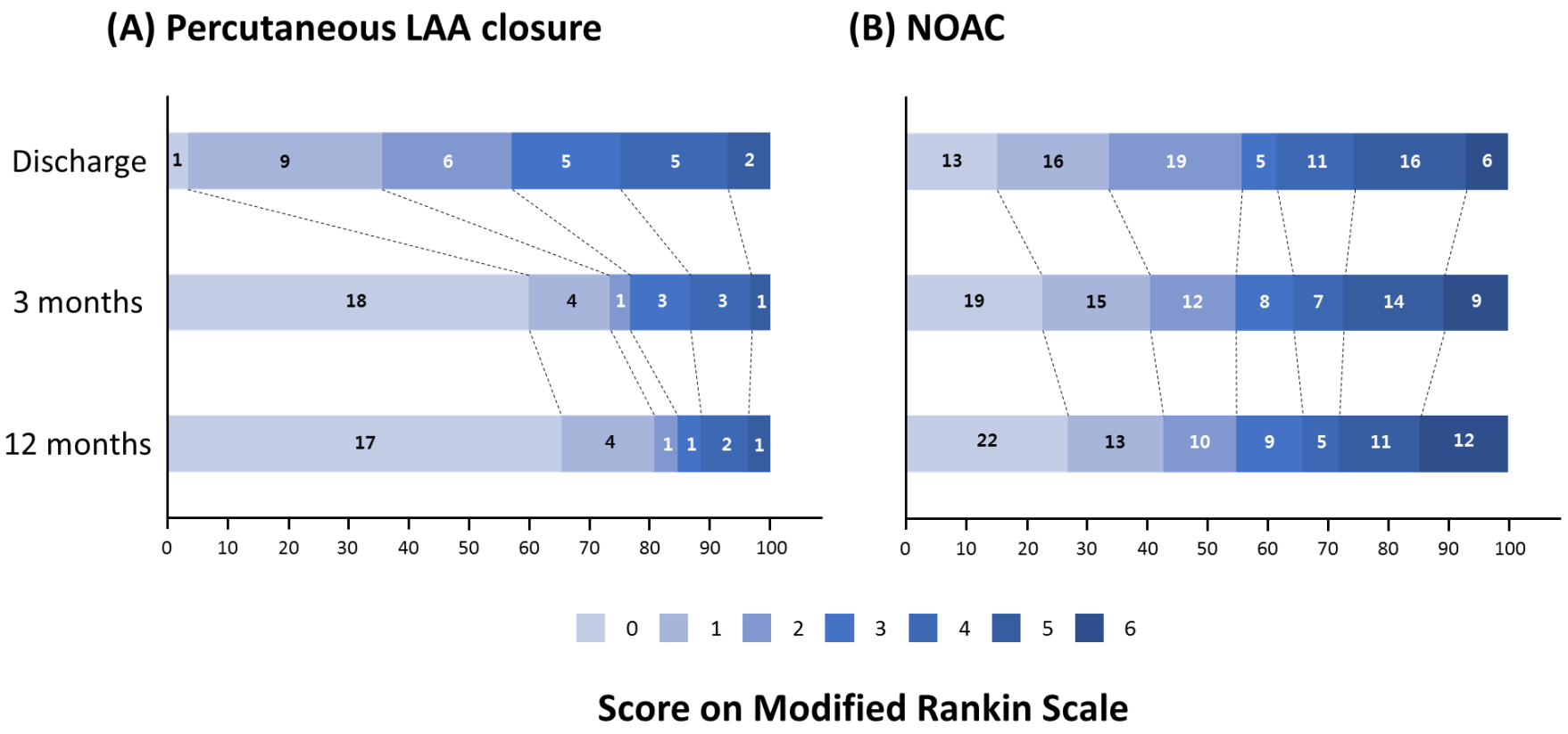


Stroke Burden After Adjustment

Variables	LAA Occlusion (n=30)	NOAC (n=86)	P value
Model 1[a]			
mRS at discharge	2.4±0.3	2.7±0.2	0.47
mRS at 3 months	1.1±0.4	2.6±0.2	<0.01
mRS at 12 months	0.9±0.4	2.5±0.2	<0.01
Model 2[a]			
mRS at discharge	2.4±0.3	2.7±0.2	0.51
mRS at 3 months	1.1±0.4	2.6±0.2	<0.01
mRS at 12 months	0.9±0.4	2.5±0.2	<0.01
Model 3[a]			
mRS at discharge	2.5±0.4	2.6±0.2	0.68
mRS at 3 months	1.2±0.4	2.5±0.2	<0.01
mRS at 12 months	1.1±0.4	2.4±0.2	<0.01

Data are presented as the mean ± SD.
Abbreviation: MRS, modified Rankin scale; SD, standard deviation.
[a]Model 1: adjusted by CHA_2DS_2-VASc score.
Model 2: Similar to Model 1, with the additional inclusion of HAS-BLED score.
Model 3: Similar to Model 2, with the additional inclusion of age, gender, and cardiovascular risk factors.

mRS Distribution



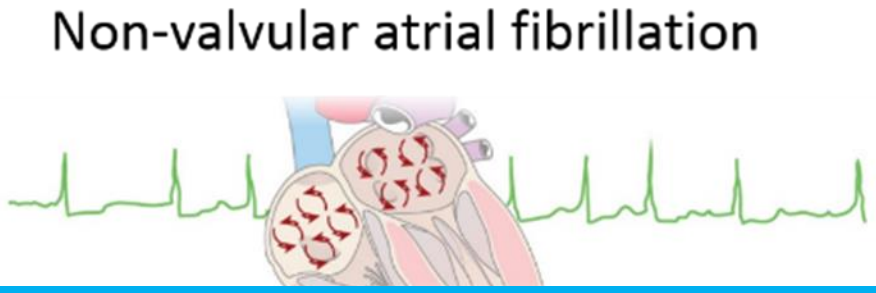
Possible Explanation

- LAA occlusion could **reduce a thrombus burden in LA with the effective closure of LAA**, because most strokes in NVAF patients are caused by cardioembolic thrombi that originated from the LAA.

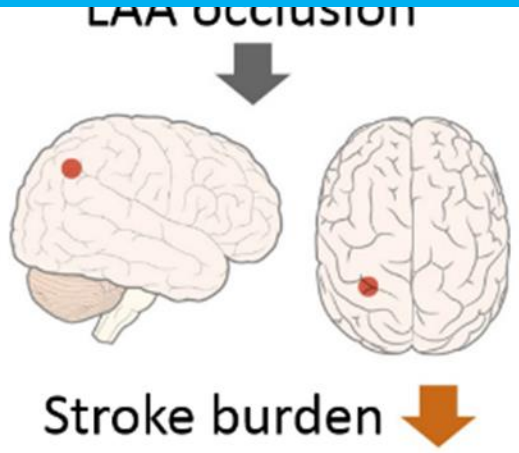
- Although oral anticoagulation therapy can prevent the formation of intracardiac thrombi, **its efficacy may be insufficient** with higher CHA_2DS_2-VASc scores or previous history of stroke.

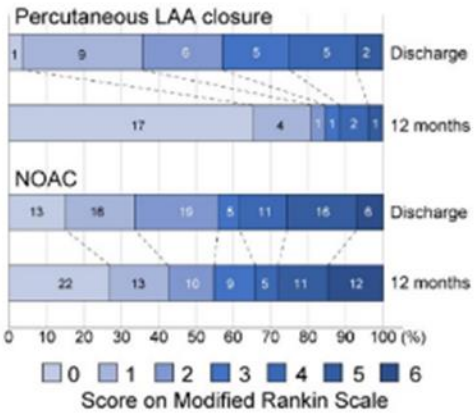
- **Poor adherence to NOACs** is also barrier to effective stroke prevention.

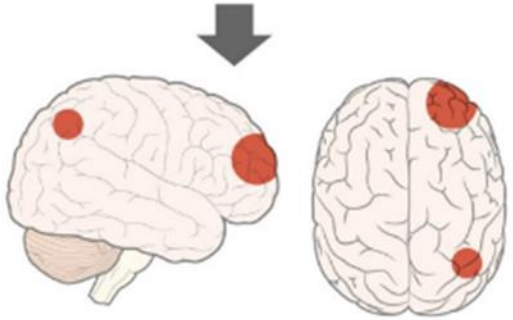
Summary

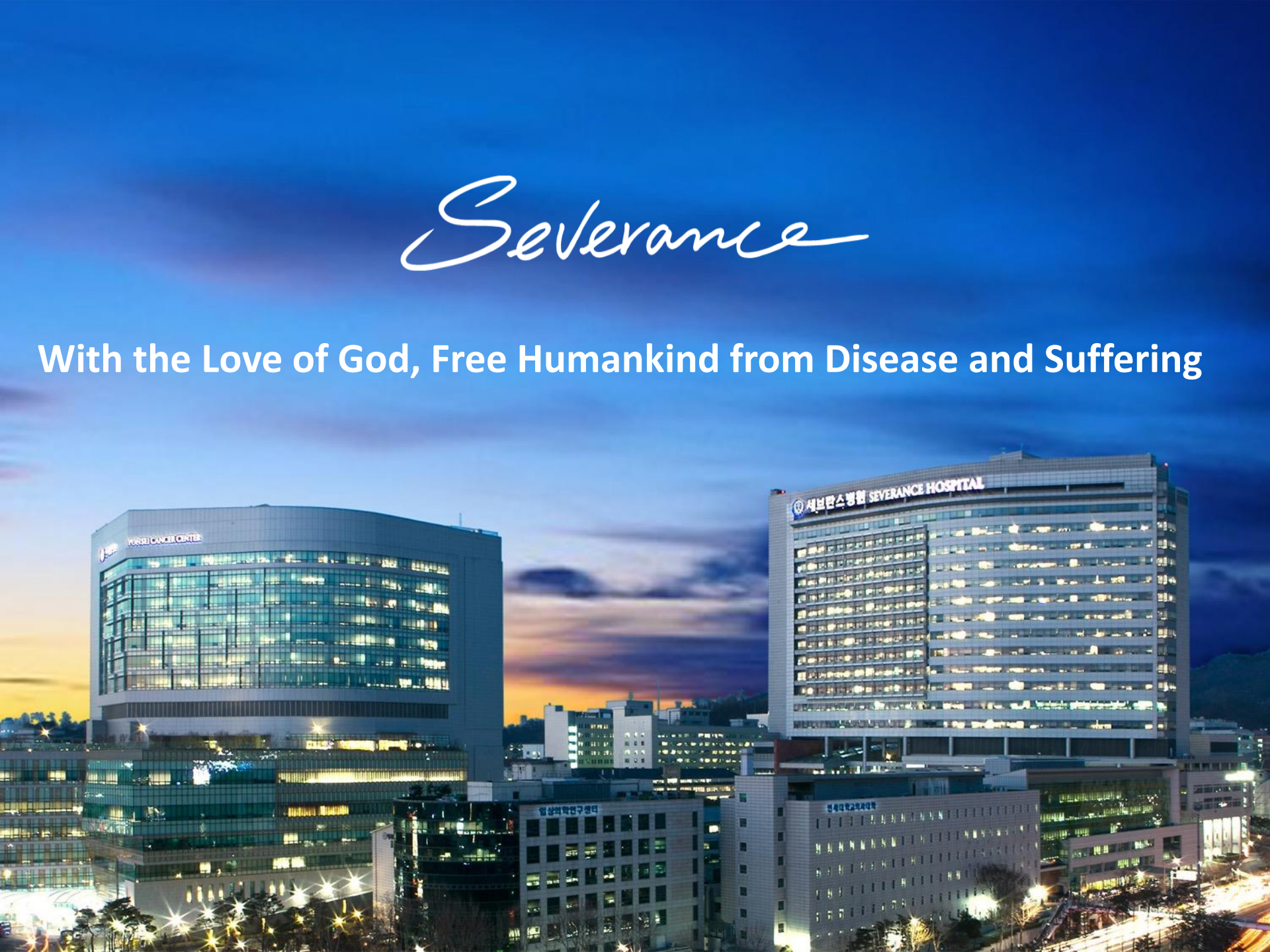


LAA occlusion can be an option to reduce the thrombus burden in the left atrium to prevent stroke and even improve prognosis after stroke.





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Stroke Burden after Adjustments

After exclusion of patients
who had previous functional disability (mRS ≥ 3) before index event

Variables	LAA Occlusion (n=28)	NOAC (n=78)	P value
MRS before the event	0.1±0.4	0.3±0.6	0.052
MRS at discharge	2.3±1.4	2.5±1.9	0.56
Disabling strokes at discharge	10 (35.7)	30 (38.5)	0.80
MRS at 3 months	0.9±1.5	2.4±2.1	<0.01
Disabling strokes at 3 months	5 (17.9)	30 (39.5)	0.06
MRS at 12 months	0.6±1.3	2.3 ±2.2	<0.01
Disabling strokes at 12 months	2 (8.3)	29 (38.7)	<0.01
Recovery to nondisabling strokes, 12 mo.	6 (60.0)	2 (6.9)	<0.01

Data are presented as mean ± standard deviation or number (%).
Abbreviation: LAA, left atrial appendage; MRS, modified Rankin scale; NOAC, novel oral anticoagulants

Stroke Burden Before Adjustment

After exclusion of patients
who had previous functional disability (mRS ≥ 3) before index event

Variables	LAA Occlusion (n=22)	Warfarin (n=67)	P value
mRS before the event	0.1 ± 0.4	0.3 ± 0.8	0.13
mRS at discharge	2.4 ± 1.4	3.2 ± 1.7	**0.03**
Disabling strokes at discharge	7 (31.8)	39 (58.2)	**0.03**
mRS at 3 months	0.7 ± 1.3	2.5 ± 1.9	**<0.01**
Disabling strokes at 3 months	3 (13.6)	28 (41.8)	**0.02**
mRS at 12 months	0.5 ± 1.0	2.7 ± 2.1	**<0.01**
Disabling strokes at 12 months	1 (5.0)	26 (44.1)	**0.02**
Recovery to nondisabling strokes, 12 mo.	4 (57.1)	10 (25.6)	0.74

Data are presented as mean ± standard deviation or number (%).
Abbreviation: LAA = left atrial appendage; MRS = modified Rankin scale, TIA = transient ischemic attack.

Study participants

- **LAAO Group**
  - From May 2013 to January 2017, LAA occlusions were performed in facilities within a **Korean multicenter registry**.
    - Yonsei University Severance Cardiovascular Hospital, Anam Hospital, Sejong General Hospital, Gachon University Hospital, Ulsan University Hospital
  - **Hong Kong Prince of Wales Hospital LAA occlusion registry**
  - **European Amplatzer Cardiac Plug Multi-center Registry**
  - **Exclusion** : 11 patients who underwent LAA closure due to intracranial hemorrhages and periprocedural strokes.
    - 2 intracranial hemorrhage from Hong Kong registry
      9 peri-procedural strokes from European ACP registry

Study participants

- **NOAC group**
  - An 1,691 consecutive patients with NVAF who had an acute IS or TIA within 7 days from stroke onset and were admitted to the Department of Neurology of **six hospitals** in Korea between January 2013 and December 2016.
    - Severance Stroke Center, Gangnam Severance Stroke Center, Kyung Hee University Hospital Stroke Center, Changwon Fatima Hospital, Inje Paik Hospital, and Pusan National University Hospital