

Impatto del burden aterosclerotico sugli outcome vascolari nei pazienti con fibrillazione atriale

Risultati dello studio ATHENA

Background

- Atrial fibrillation-related ischemic strokes are associated with increased mortality, poorer functional outcomes, and increased recurrence rates and survivors are left more disabled and are more likely to suffer a recurrence compared to other non-AF-related stroke patients.
- AF frequently coexists with vascular diseases, such as coronary artery disease (CAD) and peripheral vascular disease (PAD).
- The CHA2DS2-VASc score, which includes vascular disease (V) as a criterion, is widely used to assess stroke risk

Background

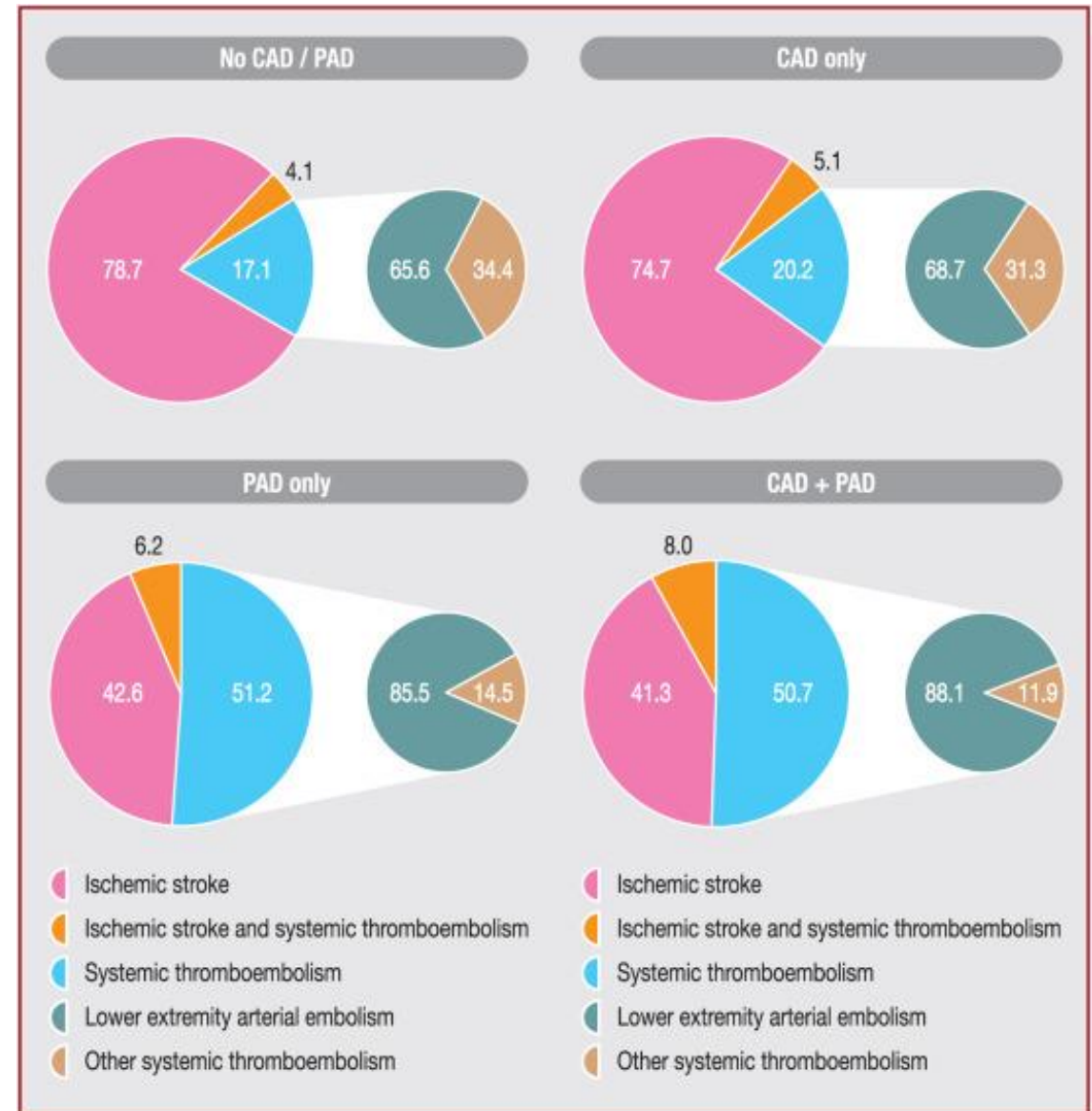
- It is crucial to recognize, however, that the CHA2DS2-VASc score, while comprehensive, does not account for the heightened risk that comes with the involvement of multiple vascular territories.
- Vascular disease in more than one arterial territory is a marker of advanced diffuse atherosclerosis and is associated with a worse prognosis than single-vessel disease.
- However, data regarding the impact of atherosclerotic burden as reflected by the involvement of multiple diseased vascular territories on vascular outcomes in stroke patients with AF are limited.

Thromboembolic events in atrial fibrillation: Different level of risk and pattern between peripheral artery disease and coronary artery disease

Patients with a new diagnosis of AF without anticoagulation

- 185,169 patients no CAD or PAD,
- 8113 patients with only PAD,
- 105,715 patients with only CAD,
- 7389 patients with CAD and PAD

After propensity score matching, the PAD-only group had significantly higher incidence of STE and IS/STE than the CAD-only group, across all levels of CHA2DS2-VASc score.



The Impact of Atherosclerotic Burden on Vascular Outcomes in Patients with Stroke and Atrial Fibrillation: The ATHENA study

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Methods

- Patients with IS and AF from the International RAF network included in a prospective 90-day follow-up.
- Atherosclerotic vascular disease was identified by at least one of the following:
 - symptomatic ischemic heart disease,
 - symptomatic peripheral artery disease,
 - internal carotid stenosis $\geq 50\%$,
 - plaques in the aorta.
- Primary outcome: composite of stroke, transient ischemic attack, systemic embolism, cerebral bleeding, and major extracranial bleeding within 90 days postacute stroke.

Aim of the study

- This study was aimed to assess the impact of AVD burden across affected vascular territories including coronary artery, carotid, aorta (ascending, arch, descending and abdominal, peripheral arteries) on the risk of vascular events among patients with recent stroke and AF within 90 days.
- Additionally, the authors explored the relationship between an increasing number of affected territories on the risk of vascular event.

Characteristics of the Patients

More than a third of the patients with AF had atherosclerotic disease

Patients in the AVD group were older and more likely to have risk factors

EPUB	Atherosclerosis* N = 744	No Atherosclerosis N = 1404	P Value
Age (mean)	77.51 ± 9.04	75.68 ± 10.10	<.001
NIHSS at admission (mean)	8.96 ± 6.78	8.10 ± 6.76	.005
Sex, male	407 (54.7%)	584 (41.6%)	<.0001
Diabetes	236 (31.7%)	244 (17.4%)	<.0001
Statins at admission	262 (35.2%)	322 (22.9%)	<.0001
Hypertension	652 (87.6%)	1029 (73.3%)	<.0001
Hyperlipidemia	342 (46.0%)	378 (26.9%)	<.0001
Paroxysmal AF	305 (41.0%)	621 (44.2%)	.169
History stroke/TIA	237 (31.5%)	328 (23.4%)	<.0001
Current smoker	79 (10.6%)	124 (8.8%)	.188
Alcoholism	56 (7.5%)	85 (6.0%)	.200
Pacemaker	70 (9.4%)	80 (5.7%)	.002
Congestive heart failure	193 (25.9%)	176 (12.5%)	<.0001
Leukoaraiosis	394 (52.9%)	695 (49.5%)	.145
Hemorrhagic transformation (24-72 h)	81 (10.9%)	157 (11.2%)	.885
Oral anticoagulant therapy after index event	570 (76.6%)	1190 (84.7%)	<.0001
DOAC therapy after index event	344 (46.2%)	869 (61.9%)	<.0001
Aspirin after index event	120 (16.1%)	120 (8.5%)	<.0001

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; AF, atrial fibrillation; TIA, transient ischemic attack.

Multivariate Analysis on the Associations of Baseline Characteristics With Atherosclerosis

Patients with increased atherosclerotic territory involvement tended to have higher CHA2DS2-VASc scores

EPUB	Atherosclerosis N = 744	OR (95%CI) Lower Limit-Upper Limit	P Value
Age (mean)	77.51 ± 9.04	1.02 (1.01-1.03)	<.001
Sex, male	407 (54.7%)	1.86 (1.52-2.29)	<.001
NIHSS at admission (mean)	8.96 ± 6.78	1.02 (1.01-1.03)	.001
Diabetes	236 (31.7%)	1.83 (1.46-2.30)	<.001
Hypertension	652 (87.6%)	1.95 (1.48-2.57)	<.001
Hyperlipidemia	342 (46.0%)	1.84 (1.50-2.26)	<.001
Paroxysmal AF	305 (41.0%)	1.15 (0.94-1.41)	.172
History stroke/TIA	237 (31.5%)	1.20 (0.97-1.50)	.086
Current smoker	79 (10.6%)	1.56 (1.10-2.21)	.013
Alcoholism	56 (7.5%)	1.04 (0.70-1.55)	.820
Pacemaker	70 (9.4%)	1.39 (0.95-2.01)	.082
Congestive heart failure	193 (25.9%)	2.14 (1.66-2.75)	<.001

Characteristics of Atherosclerotic Territories

EPUB

Atherosclerosis	Ischemic Heart Disease	Peripheral Artery Disease	Aorta Sclerosis	Carotid Stenosis
1 Territory	167	65	71	240
2 Territories	84	71	57	87
3 Territories	37	39	32	30
4 Territories	6	6	6	6

Outcomes of Patients With and Without Atherosclerosis

	Atherosclerosis N = 744	No Atherosclerosis N = 1404 EPUB	Odds Ratio (95%CI)	P Value
Combined outcome	77 (10.3%)	97 (6.9%)	Unadjusted 1.56 (1.14-2.13) Adjusted 1.22 (0.87-1.92)	.006 .2
Ischemic outcome ^a	46 (6.2%)	55 (3.9%)	Unadjusted 1.62 (1.08-2.42) Adjusted 1.24 (0.80-1.92)	.018 .3
Hemorrhagic outcome ^b	31 (4.1%)	42 (3.0%)	Unadjusted 1.41 (0.88-2.26) Adjusted 1.22 (0.74-2.03)	.135 .4

^aIschemic outcomes (ischemic stroke and systemic embolism including MI).

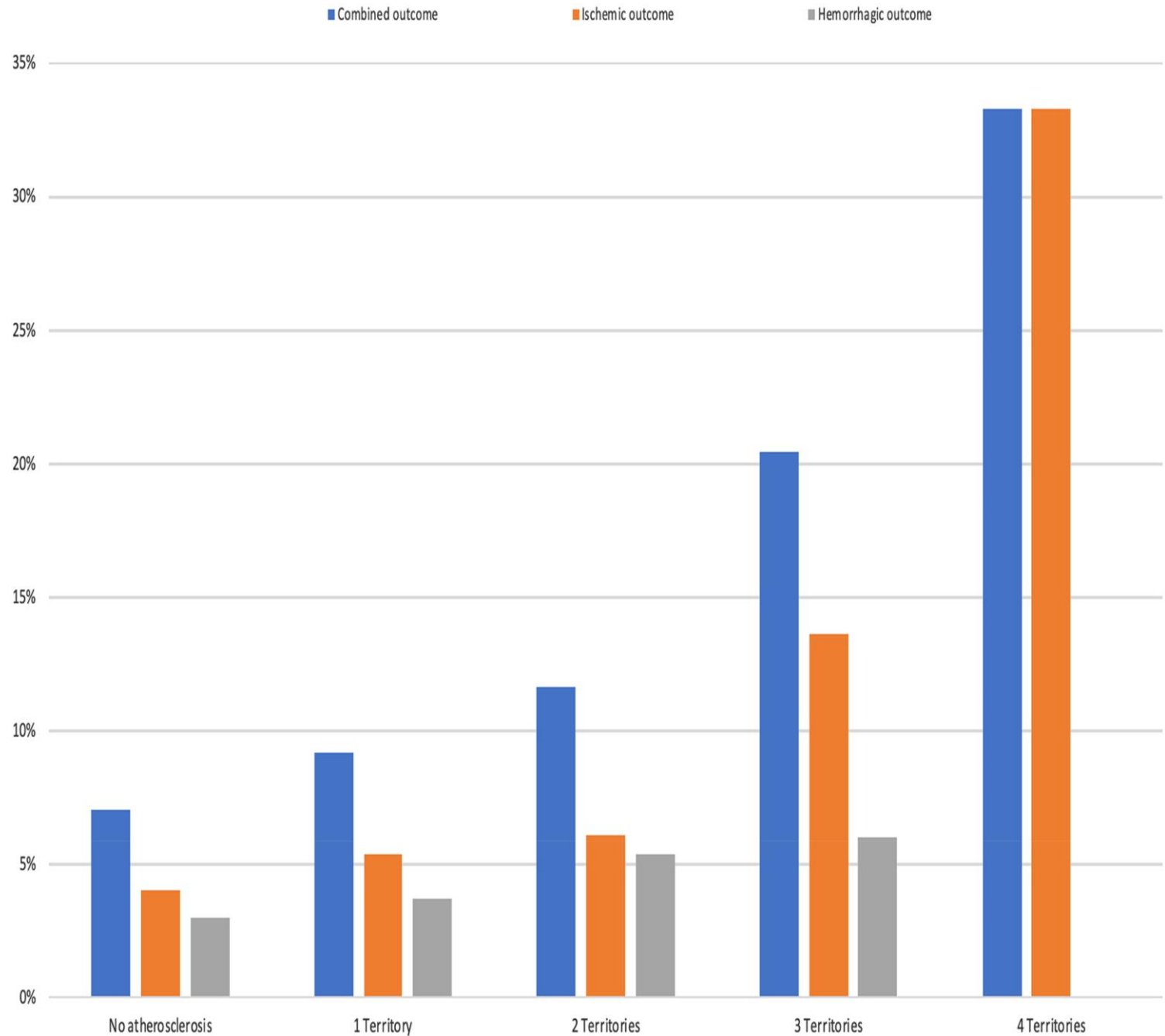
^bHemorrhagic outcomes (intracranial hemorrhage and severe extracranial bleeding).

Adjusted OR for Outcomes in Patients With Atherosclerosis According to the Number of Vascular Territories Involved

The higher the burden of atherosclerosis with more vascular territories involved, the higher the risk of stroke events

	Adjusted OR (95%CI)	P value
<i>Combined outcome</i>		
No atherosclerosis	1 (Reference)	
Atherosclerosis		
1. Territory	1.08 (0.74-1.58)	.6
2. Territories	1.39 (0.77-2.49)	.2
3. Territories	2.80 (1.20-6.52)	.01
4. Territories	6.81 (1.02-36.24)	.04
<i>Ischemic outcome</i>		
No atherosclerosis	1 (Reference)	
Atherosclerosis		
1. Territory	1.14 (0.70-1.85)	.5
2. Territories	1.17 (0.54-2.52)	.6
3. Territories	2.88 (1.04-7.95)	.04
4. Territories	7.76 (1.22-49.23)	.03
<i>Hemorrhagic outcome</i>		
No atherosclerosis	1 (Reference)	
Atherosclerosis		
1. Territory	1.08 (0.62-1.89)	.7
2. Territories	1.72 (0.75-3.93)	.2
3. Territories	2.16 (0.56-8.26)	.2
4. Territories	NA	

Outcomes in patients with atherosclerosis according to the number of atherosclerotic vascular territories involved



Therapy

- Patients with AVD were taking less oral anticoagulant therapy and more statins on admission.
- Despite having higher cardiovascular risk, they tended to be undertreated and to have more severe strokes at admission.

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Therapy

- Add-on treatment with aspirin does not reduce the recurrence risk but increases only the hemorrhagic risk.
- A possible strategy in these patients would be an optimal control of vascular risk factors, which is part of the current holistic or integrated care approach to AF management recommended in guidelines.

Limitations

- As a post hoc analysis of observational, nonrandomized studies, there is potential for selection bias despite the use of adjusted statistical models to control for confounders.
- The relatively low number of outcome events may reduce the statistical power of the analyses.
- Outcomes were not centrally adjudicated but instead assessed by local investigators, which could affect the consistency of the diagnosis of AVD.
- The methodological approaches to defining vascular territories and outcome events carry certain limitations.

Conclusions

- AVD serves as a prognostic marker in individuals with recent stroke and AF, particularly when 3 to 4 territories are affected.
- The degree of vascular territory involvement directly correlates with an increased risk of combined and ischemic events.