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Atrial Cardiopathy and Ischemic Stroke: A Mechanism Unveiled by Ultrasound

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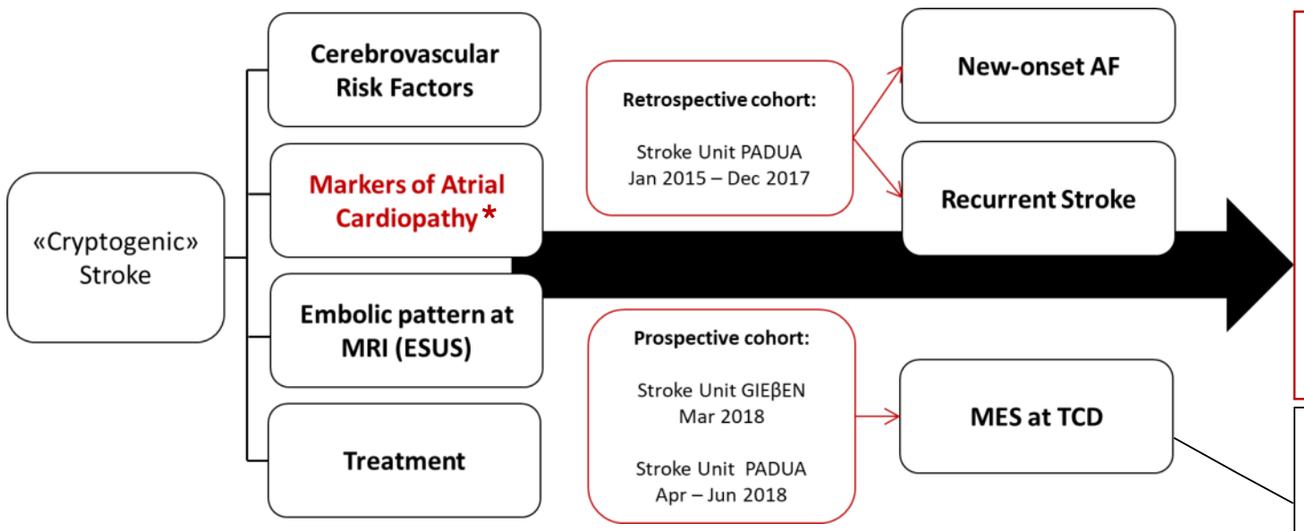
Background

Patients with cryptogenic stroke (CS) still receive an untargeted secondary prevention treatment. Atrial fibrillation (AF), which is considered one of the main disorders behind CS, is associated with left atrium derangements – collectively called **atrial cardiopathy** – which **could account by themselves for thrombogenesis and embolism in CS**.
This study aimed to investigate whether, in CS patients, atrial cardiopathy is related to AF detection, recurrent strokes, or to the presence of micro-embolic signals (MES) at trans-cranial Doppler (TCD), which are a surrogate marker for stroke risk.

Subjects and Methods

We enrolled all consecutive CS patients, first retrospectively (Padua, 2015-2017), and later prospectively (Padua/Giessen, March-June 2018). We assessed the presence of atrial cardiopathy markers. Medical records were reviewed to detect new-onset AF and recurrent strokes.



*** Markers of Atrial Cardiopathy:**
- Plasmatic level of atrial natriuretic peptide (**BNP**) > 100 ng/L;
- P-wave terminal force in V_1 (**$PFTV_1$**) at ECG > 5000 μV* ms;
- Presence of excessive supraventricular ectopic activity (**ESEA**) at 24h-Holter ECG, > 30/h; or paroxysmal supraventricular tachycardia (**PSVT**);
- Left atrial enlargement at trans-thoracic echo: **LAD** (diameter) > 3.8 cm F, > 4.3 cm M; **LAVI** (volume index) ≥ 32 ml/m^2

In the prospective cohort, a bilateral **60-minutes TCD monitoring** for MES detection of the middle cerebral artery was performed **within 24 hours** from stroke onset and repeated at 7 days.

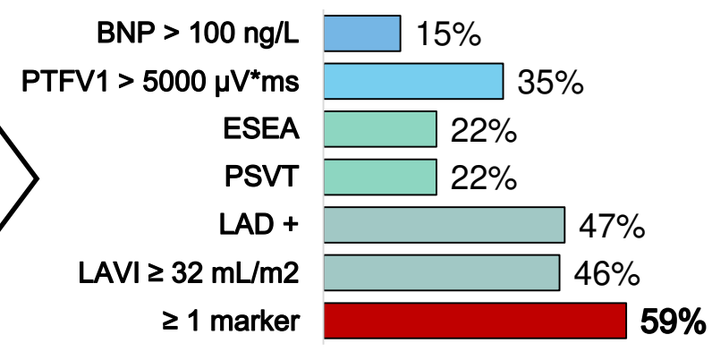
Results

Characteristics of the overall study population (n=169)

Cerebrovascular risk factors and stroke characteristics (%)

Male sex	60%	Coronary Heart Disease	9%
Age; mean ± sd	68.4 ± 12.9	Peripheral Vasculopathy	3%
Carotid stenosis ≤ 50%	69%	CHA_2DS_2-VASc score; median (IQR)	5 (3-5)
Previous stroke	5%	NIHSS at admission; mean ± sd	10.0 ± 6.6
Hypertension	72%	NIHSS at discharge; mean ± sd	3.4 ± 4.3
Diabetes	16%	Systemic thrombolysis with r-tPA	65%
Dyslipidemia	38%	Endovascular treatment	29%
Smoking	20%	Combined treatment	18%

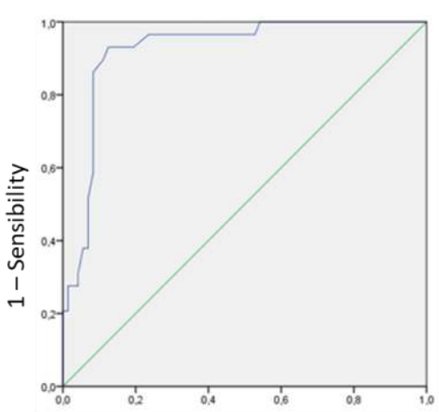
Distribution of atrial cardiopathy markers (% of patients with pathologic value)



Retrospective cohort (n=130): atrial cardiopathy and AF detection

Early AF detection (< 7 days): **18%**
[mean: 3.6 days]
Late AF detection (> 30 days): **15.4%**
[mean: 8.6 months]
Follow-up duration: 17.0 ± 10.8 months

Independent predictors of late AF detection at multivariate analysis:
- **ESEA** at Holter ECG **(p<0.001)**
- **LAVI ≥ 32ml/m^2** at echo **(p=0.003)**

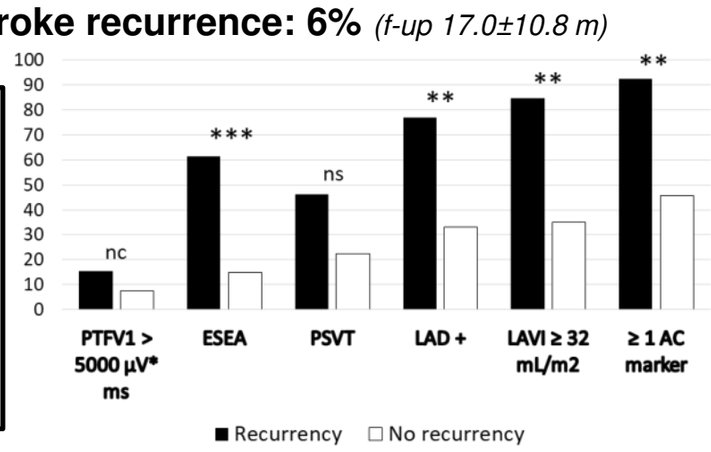


ROC curve for the predictive model: AUC 0.923; CI 95% 0.868-0.979 (p<0.001)

Retrospective cohort (n=130): atrial cardiopathy and recurrent stroke

Annualized rate of stroke recurrence: 6% *(f-up 17.0±10.8 m)*

Independent predictors of recurrent stroke at multivariate analysis:
- **ESEA: OR 8.8** (2.5-30.8, p=0.001)
- **LAVI ≥ 32 mL/m^2: OR 5.5** (1.0-32.1, p=0.05)

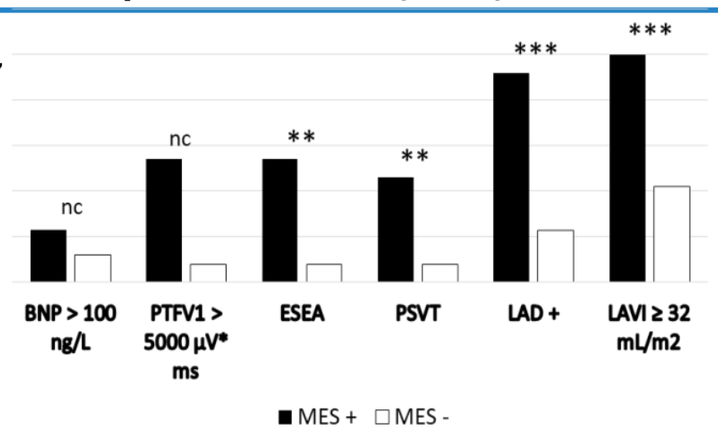


Distribution of atrial cardiopathy markers

Prospective cohort (n=39): atrial cardiopathy and MES at TCD monitoring

1° TCD monitoring (15.4±5.7 hours from onset):
33% of patients **had MES**
[rate: 1.7±0.9 MES/h*]*

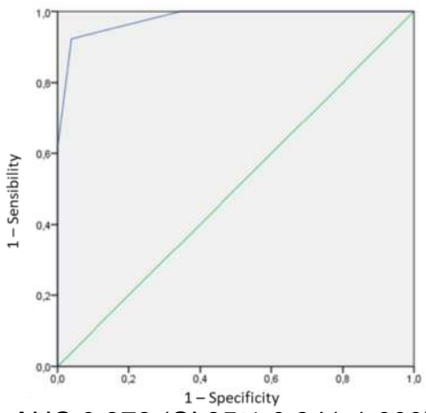
2° TCD monitoring (6.7±0.6 days from onset):
20% of patients **had MES**
[rate: 1.1±0.4 MES/h*]*



Distribution of atrial cardiopathy markers

Independent predictors of MES at TCD monitoring at multivariate analysis:
- **Age: RR 1.2** (IC 95% 1.0-1.5) **p=0.02**
- **LAD**: **RR 7.9** (IC 95% 2.1-30.3) **p=0.002**

ROC curve for predition of MES by an **«Atrial cardiopathy score»** → obtained by adding 1 point for every detected marker



AUC 0.979 (CI 95% 0.941-1.000) p<0.001

Conclusions

Atrial cardiopathy markers are related to the presence of MES in the acute phase of stroke and represent a risk factor for AF and recurrent stroke.

Main references: Watson T et al., Lancet 2009. Goette A et al., Heart Rhythm 2017. Korhonen M et al., PLOS ONE 2015.