Conoscere e Curare il Cuore 2019

VENERDI' 1 MARZO

OLTRE IL CHA_2DS_2-VASC NELLA FIBRILLAZIONE ATRIALE. IL RUOLO DELL'ATRIO NEL RISCHIO DI ICTUS

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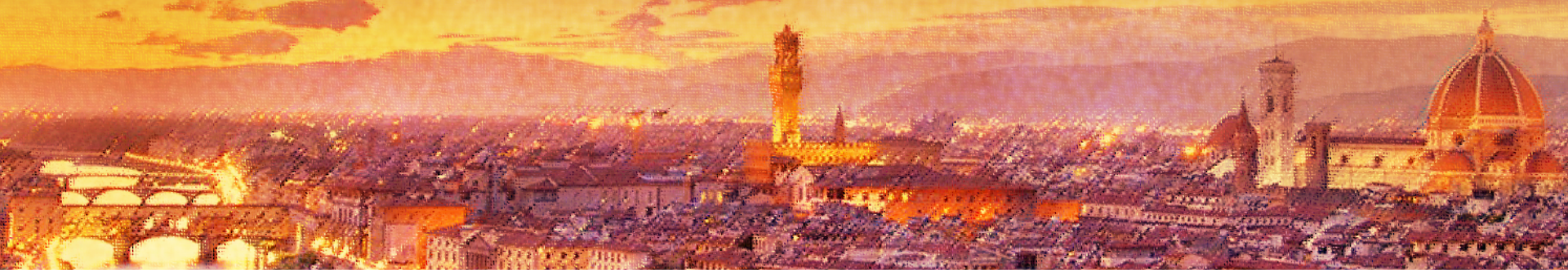


Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach - The Euro Heart Survey on Atrial Fibrillation

Stroke Risk Assessment in AF: the CHA_2DS_2-VASc Score

Stroke Risk Factor	Score
Congestive Heart Failure / LV Dysfunction	1
Hypertension	1
Age ≥75 years	**2**
Diabetes mellitus	1
Stroke / TIA / TE	2
Vascular Disease (MI, PAD, aortic plaque)	1
Age 65-74 years	**1**
Sex category (female)	1

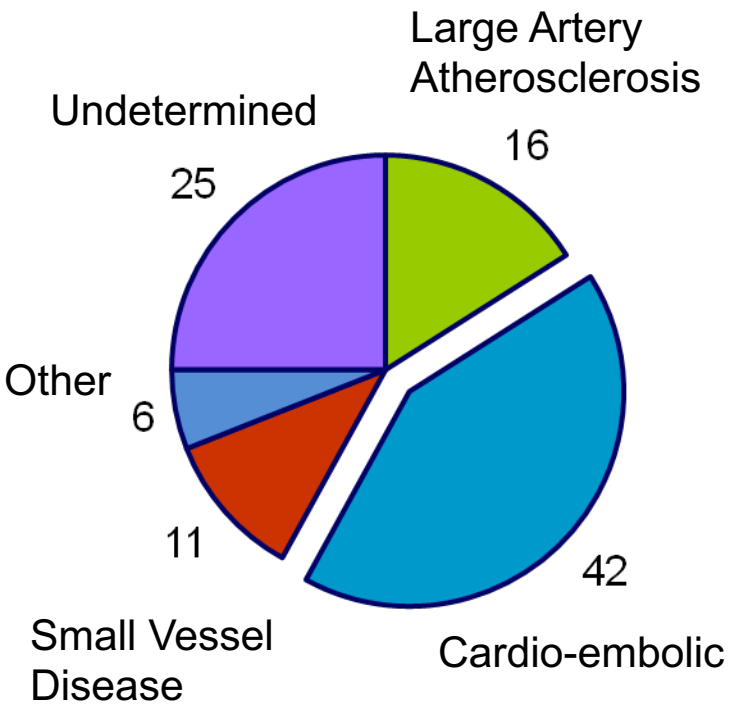
Maximum score = 9; Score >1 – OAC; **Score = 1** – ASA (75-325 mg) or OAC (preferred);
Score = 0 - ASA (75-325 mg) or None (preferred)

Lip, Chest, 2010

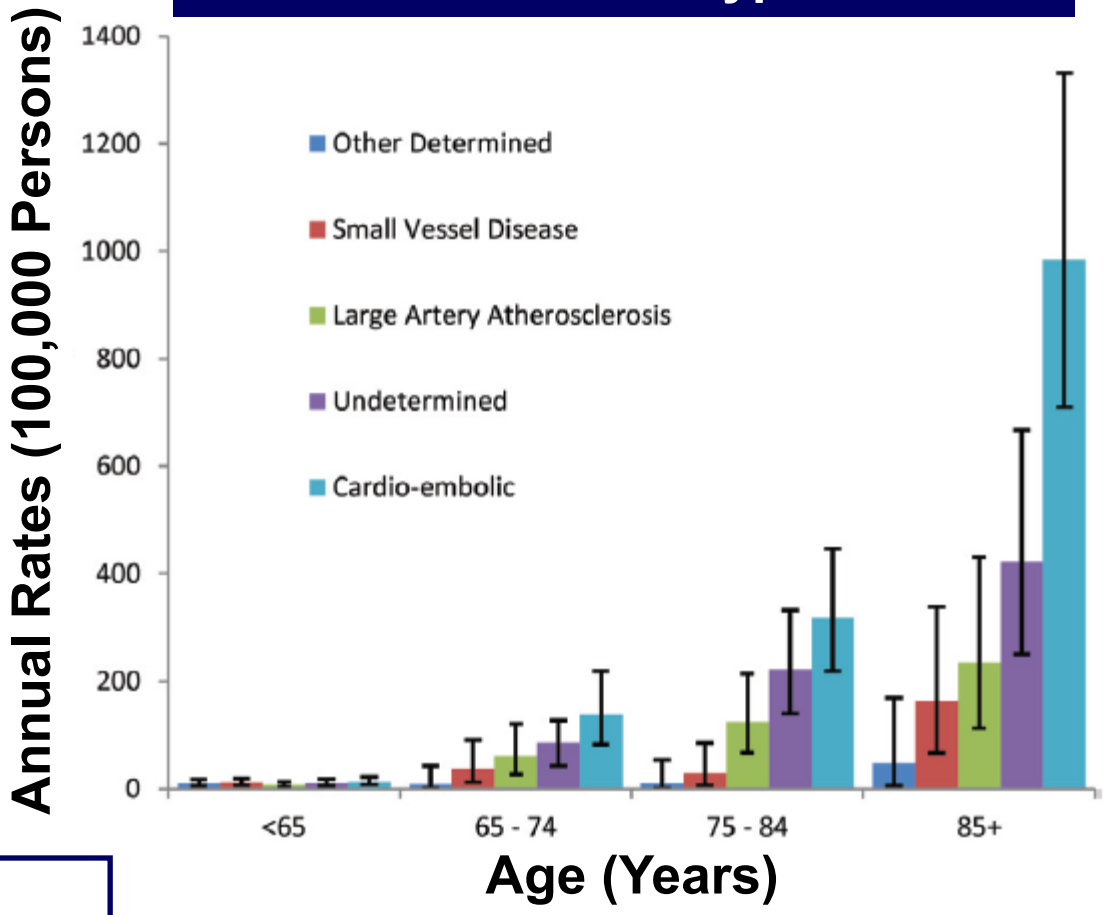
Adelaide Stroke Incidence Study

Declining Stroke Rates but Many Preventable Cardioembolic Strokes

Ischemic stroke (N=258) subtypes (%)



Age-specific incidence rates for ischemic stroke subtypes



Stroke incidence (ischemic + ICH):
215 per 100,000 person years; 2009-2010

Leyden JM. Stroke 2013

Ictus criptogenetico

- **Almeno una parte degli ictus criptogenetici è attribuibile a FA misconosciuta**
  - **Come diagnosticarla?**

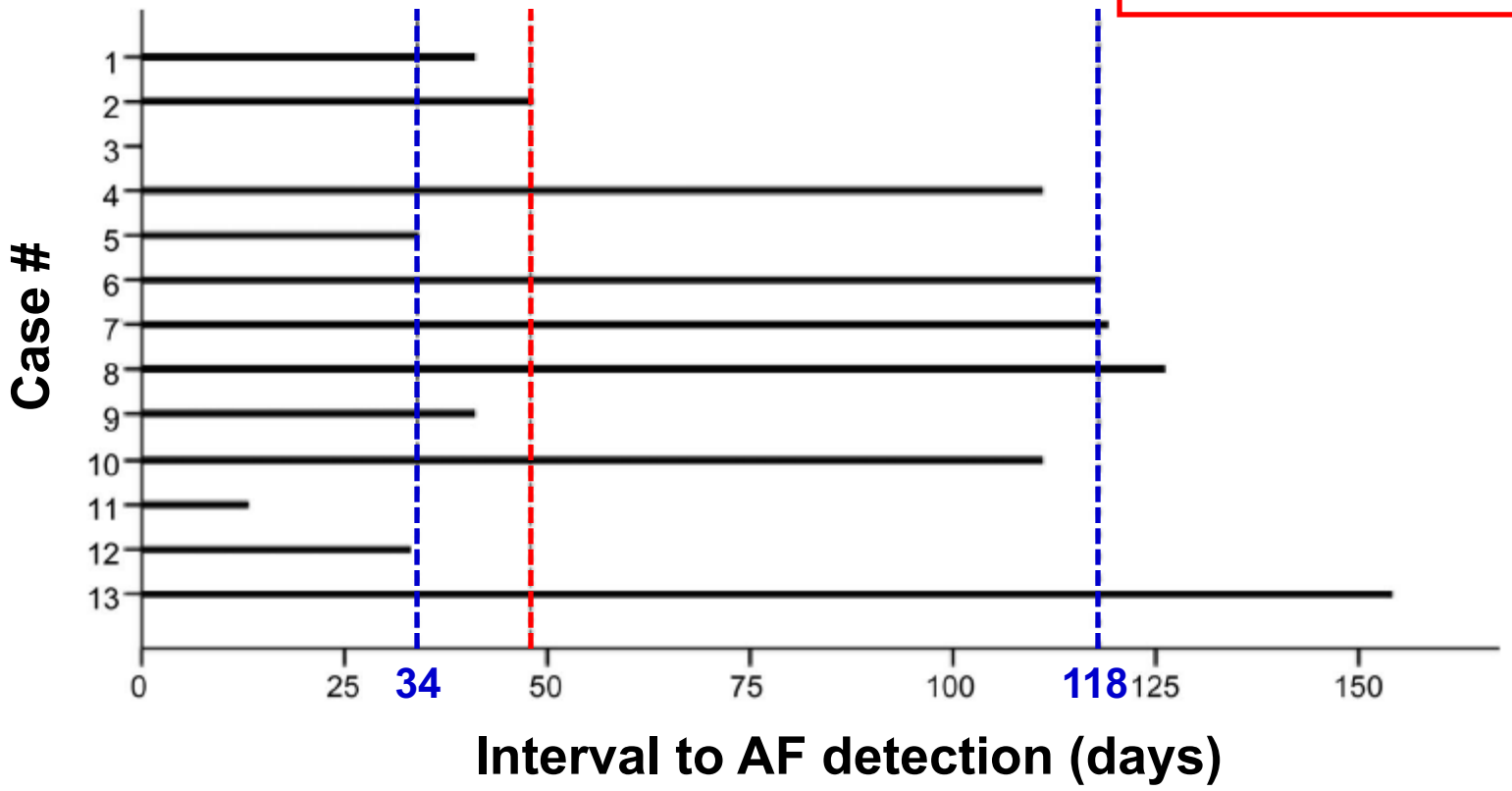
Incidence of atrial fibrillation detected by implantable loop recorders in unexplained stroke

AF detection rate: **25.5%** (N=13/51 cases)

Median duration of 1st detected AF: **6 minutes**

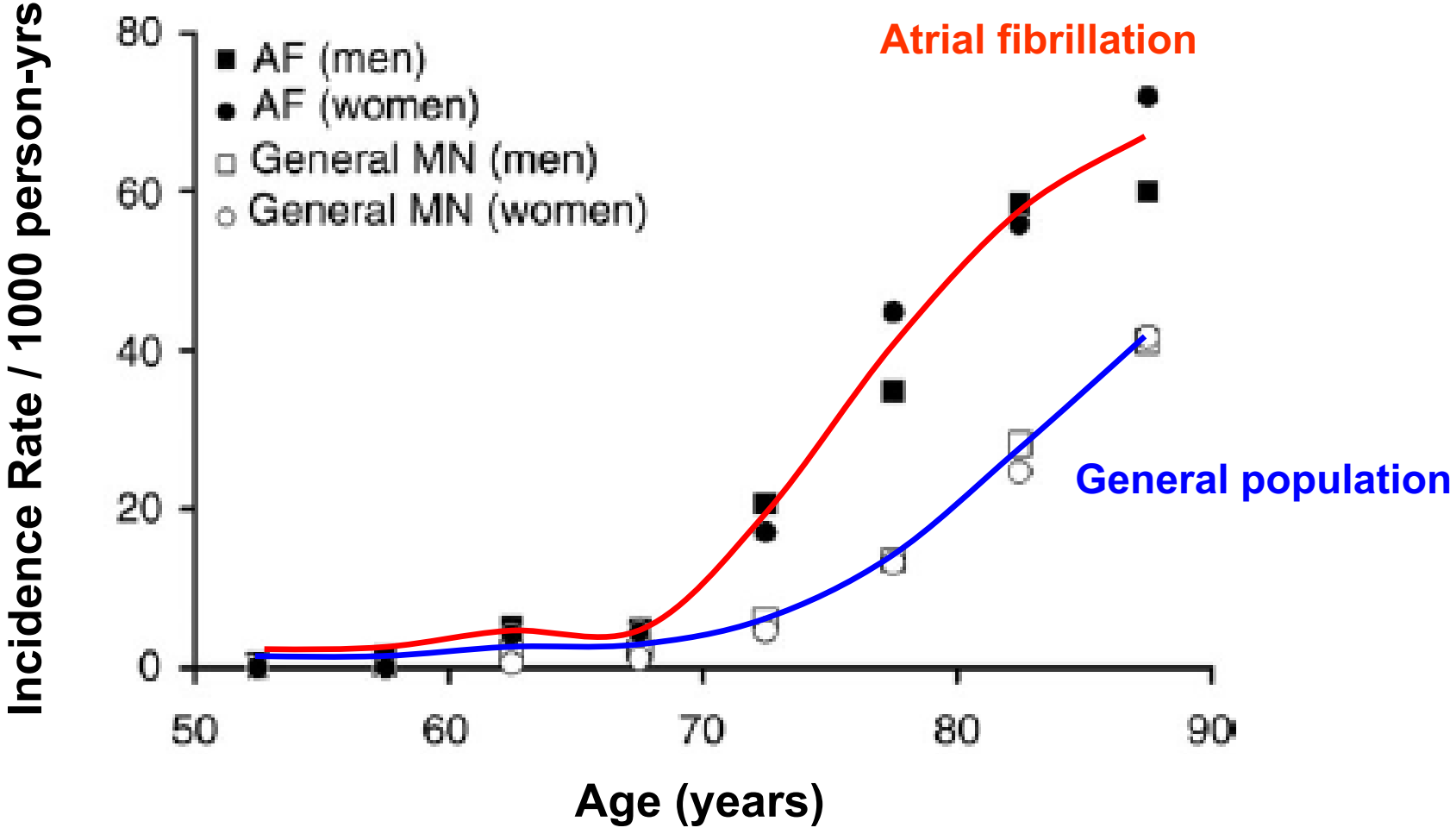
- ↑Age (59 vs. 49 y)
- ↑$CHADS_2$ (3 vs. 2)
- ↑APC per day
- ↑LA Volume
- ↑Inter-atrial block

Median duration recording: 48 days



Cotter PE. Neurology 2013

Risk of dementia in stroke-free patients diagnosed with atrial fibrillation: data from a community-based cohort



Miyasaka Y. *Eur Heart J*, 2007

Cambiamento nella epidemiologia

58% of all people with dementia live in countries currently classified by the World Bank as low or middle income countries. This proportion is estimated to increase to 63% in 2030 and 68% in 2050.

Figure 2.4
The growth in numbers of people with dementia (millions) in high income (HIC) and low and middle income countries (LMIC)

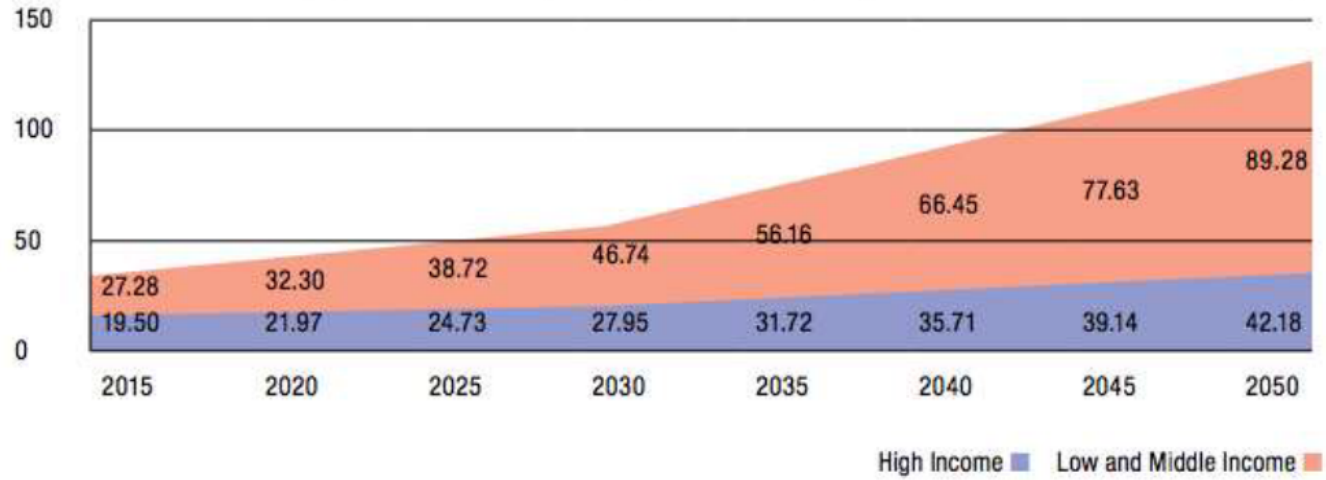


Table 2.8
Numbers of people with dementia (millions) according to the 2015 World Bank income classification

World Bank Income Group	Number of People with Dementia (millions)							
	2015	2020	2025	2030	2035	2040	2045	2050
Low Income	1.19	1.42	1.68	2.00	2.41	2.90	3.55	4.35
Lower Middle Income	9.77	11.52	13.72	16.35	19.48	23.12	27.18	31.54
Upper Middle Income	16.32	19.36	23.33	28.39	34.28	40.43	46.90	53.39
High Income	19.50	21.97	24.73	27.95	31.72	35.71	39.14	42.18
World	46.78	54.27	63.45	74.69	87.88	102.15	116.78	131.45

Table 6.3
Worldwide costs of dementia in 2010 and 2015 (billion US$), based on World Bank country classification 2010

Year for cost estimates (basis for prevalence estimates)	2010 (WAR 2010)		2015 (WAR 2015)	
World Bank Country Classification Year	2010		2010	
	US$ (billions)	Per cent	US$ (billions)	Per cent
Low income	4.4	0.7%	6.6	0.8%
Lower middle income	29.2	4.8%	57.1	7.0%
Upper middle income	32.5	5.4%	84.5	10.3%
High income	537.9	89.1%	669.6	81.9%
Total	604.0	100.0%	817.9	100.0%

Atrial fibrillation and incidence of dementia

A systematic review and meta-analysis

The most recent review on vascular risk factors and dementia suggested multiple plausible biological mechanisms that might explain the association between AF and dementia

- ➔ Fluctuations in cardiac output in AF may contribute to thromboembolic damage and chronic cerebral hypoperfusion
- ➔ Some studies suggest that there is a link between cerebrovascular disease and both Alzheimer dementia and silent microinfarcts, which could contribute to the pathogenesis of AD
- ➔ There may also be increased expression of amyloid precursor proteins secondary to ischemic insults or cerebrovascular insufficiency which leads to AD
- ➔ **Furthermore, the influence of anticoagulation therapy on cognitive impairment is unclear as role of anticoagulation therapy in prevention of dementia in AD has not yet been studied**

Kwok CS, Neurology 2011

E’ ora di rivedere il paradigma FA/ictus tromboembolico?

the causality of the association AF—ischemic stroke—is questioned by the reported lack of temporal relation between stroke events and AF paroxysms or atrial high-rate episodes detected by implantable loop recorders or devices.

The Asymptomatic AF and Stroke Evaluation in Pacemaker Patients and the AF Reduction Atrial Pacing Trial (ASSERT)

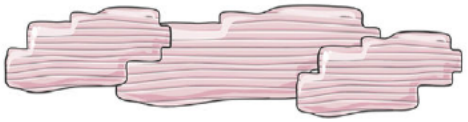
- Subclinical AF was associated with increased stroke risk
- Lack of a temporal relationship between AF and stroke
- Many patients show AF for the first time after their stroke
- Challenge of the concept that AF itself is the necessary and sufficient cause of stroke in patients with this dysrhythmia

Un nuovo paradigma per il cardiologo:

LA CARDIOMIOPATIA ATRIALE

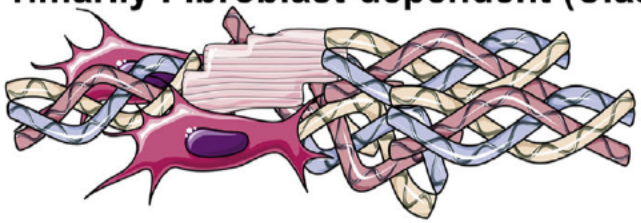
Classificazione isto-patologica delle cardiomiopatie atriali

Primarily Cardiomyocyte-dependent (Class I)



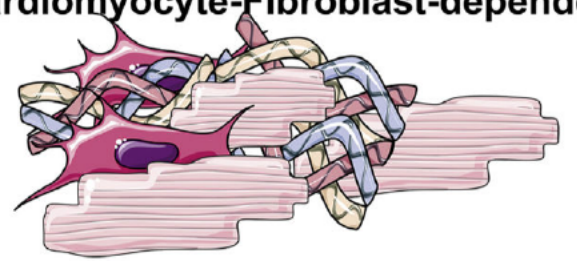
- lone AF
- genetic diseases
- diabetes mellitus

Primarily Fibroblast-dependent (Class II)



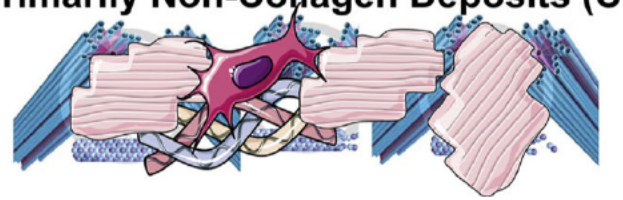
- aging
- cigarette smoking

Mixed Cardiomyocyte-Fibroblast-dependent (Class III)



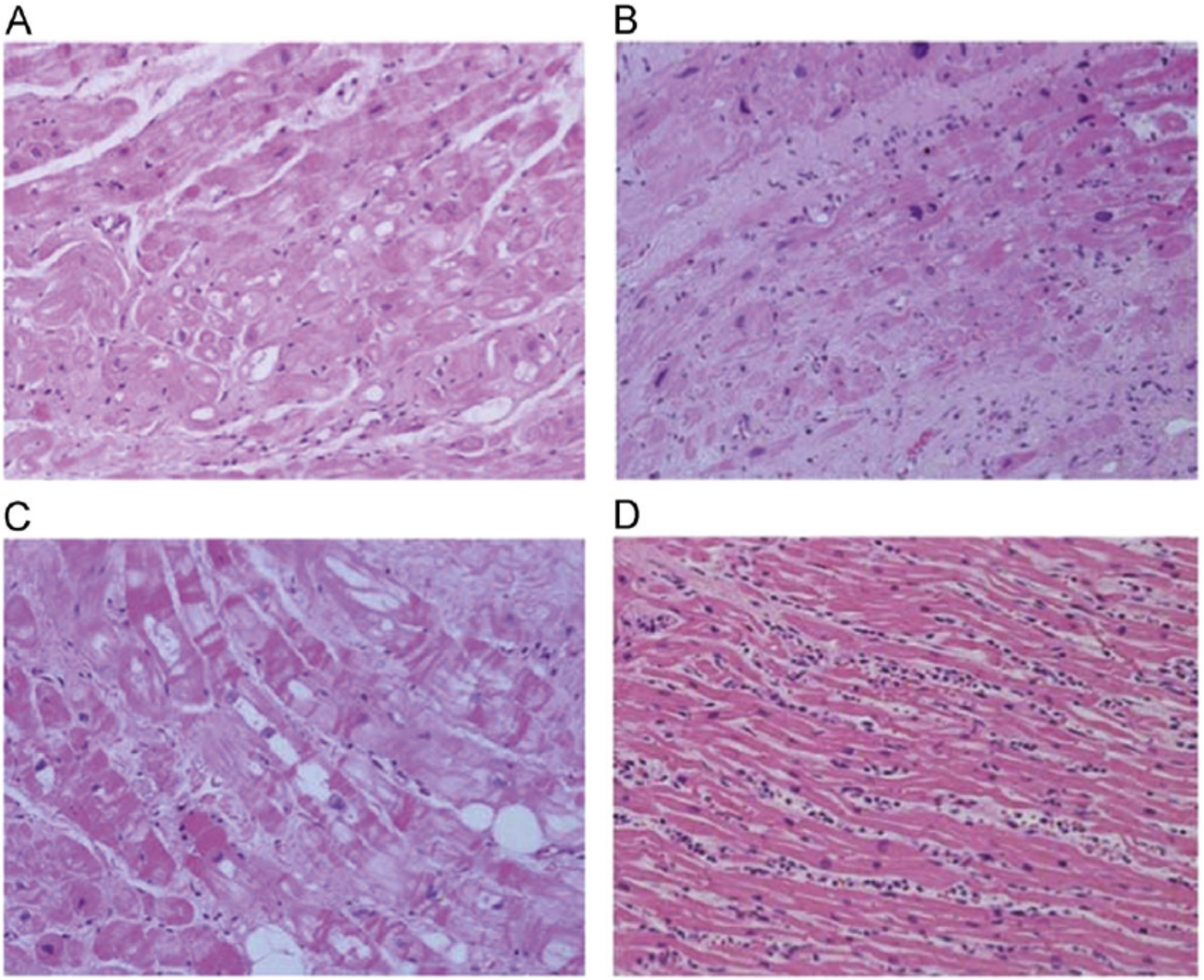
- CHF
- valvular diseases

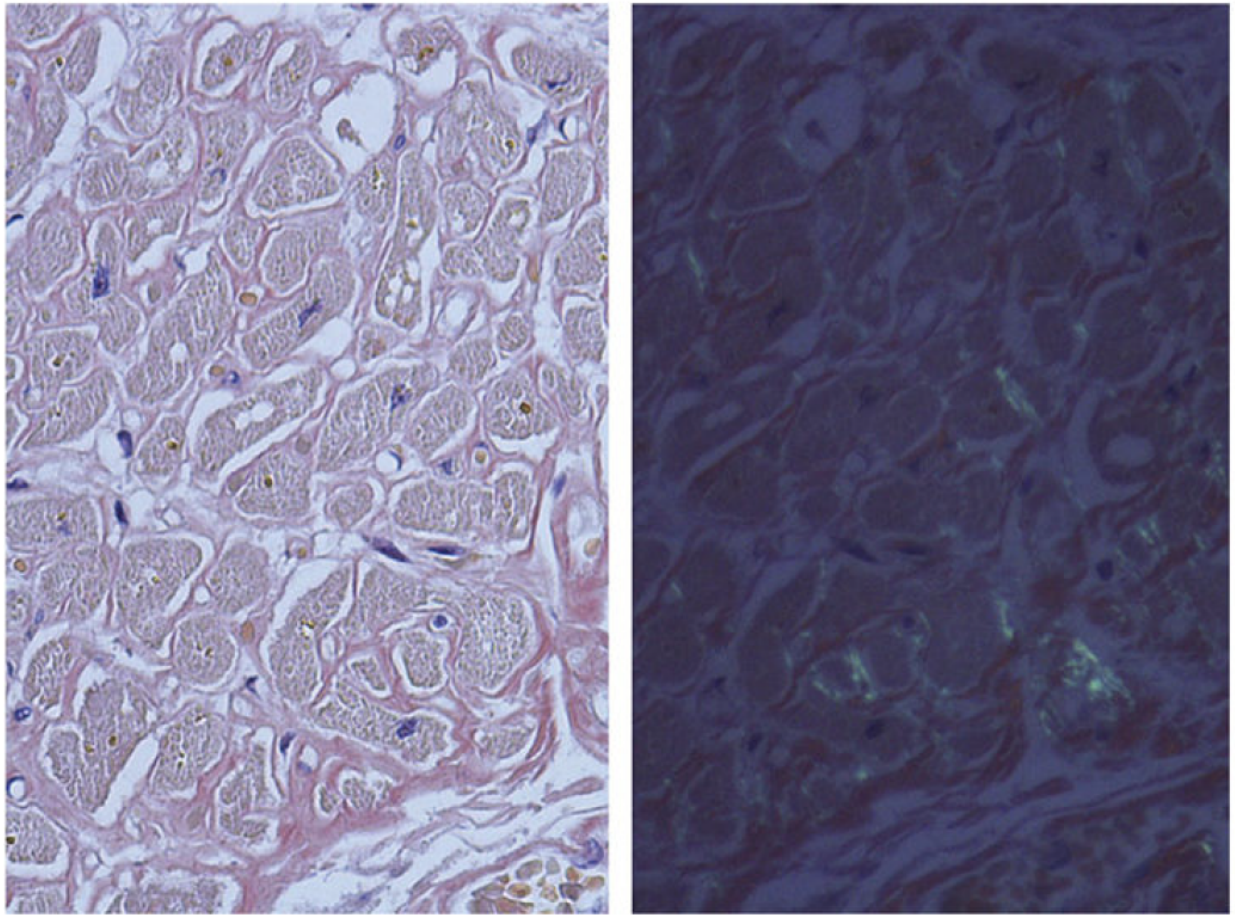
Primarily Non-Collagen Deposits (Class IV)



- isolated atrial amyloidosis
- granulomatosis
- inflammatory Infiltrates
- glycosphingolipids

Goette et al. Heart Rhythm. Author manuscript; available in PMC 2018 January 01.


A
B
C
D



Condizioni determinanti alterazioni istopatologiche delle pareti atriali

FA isolata (”lone”): quando non sono riconoscibili patologie predisponenti. In questa condizione ci può essere una predisposizione genetica[10] , con alterazioni isto-patologiche riconoscibili di classe II e III.
Amiloidosi atriale isolata
Produzione di ANP anomalo: presente in alcune forme di tachiaritmie atriali e cardiomiopatie atriali
Distrofie muscolari ereditarie
Cardiomiopatia atriale da scompenso cardiaco
Sindrome delle apnee ostruttive
Rimodellamento indotto da FA
FA indotta da farmaci
Miocardite
Cardiomiopatie atriali da alterazioni genetiche della ripolarizzazione
Invecchiamento
Ipertensione
Obesità
Diabete
Valvulopatie

Fattori di rischio per FA (1)

Età avanzata

Malattie cardiovascolari:

- Ipertensione
- Diabete mellito, resistenza all'insulina e sindrome metabolica
- Infarto miocardico
- Scompenso cardiaco congestizio
- Valvulopatie e pregressi interventi di cardiochirurgia

Abuso di alcolici

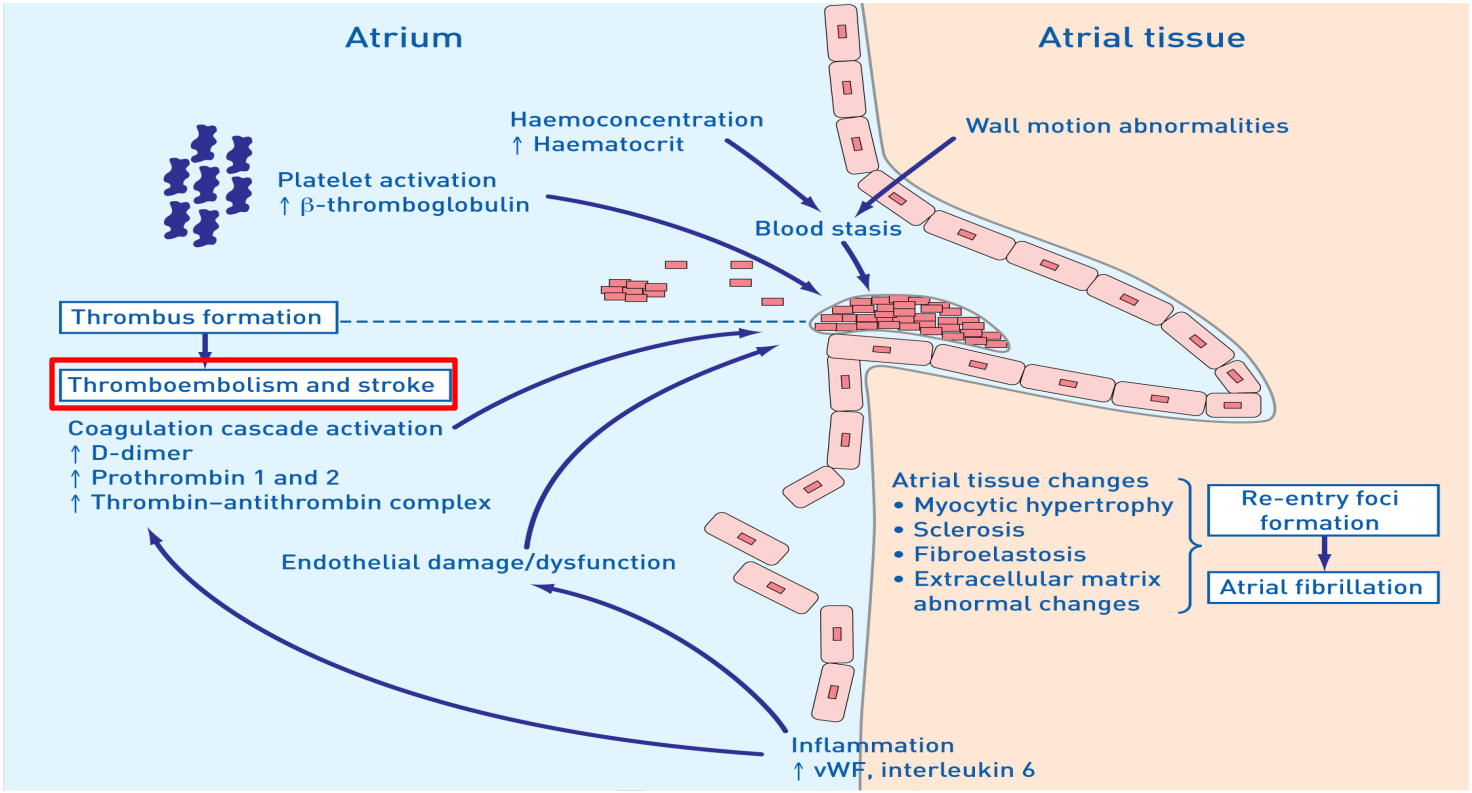
Anamnesi familiare positiva per FA

Sesso femminile

Blocco interatriale (evidenze successive al 2007)

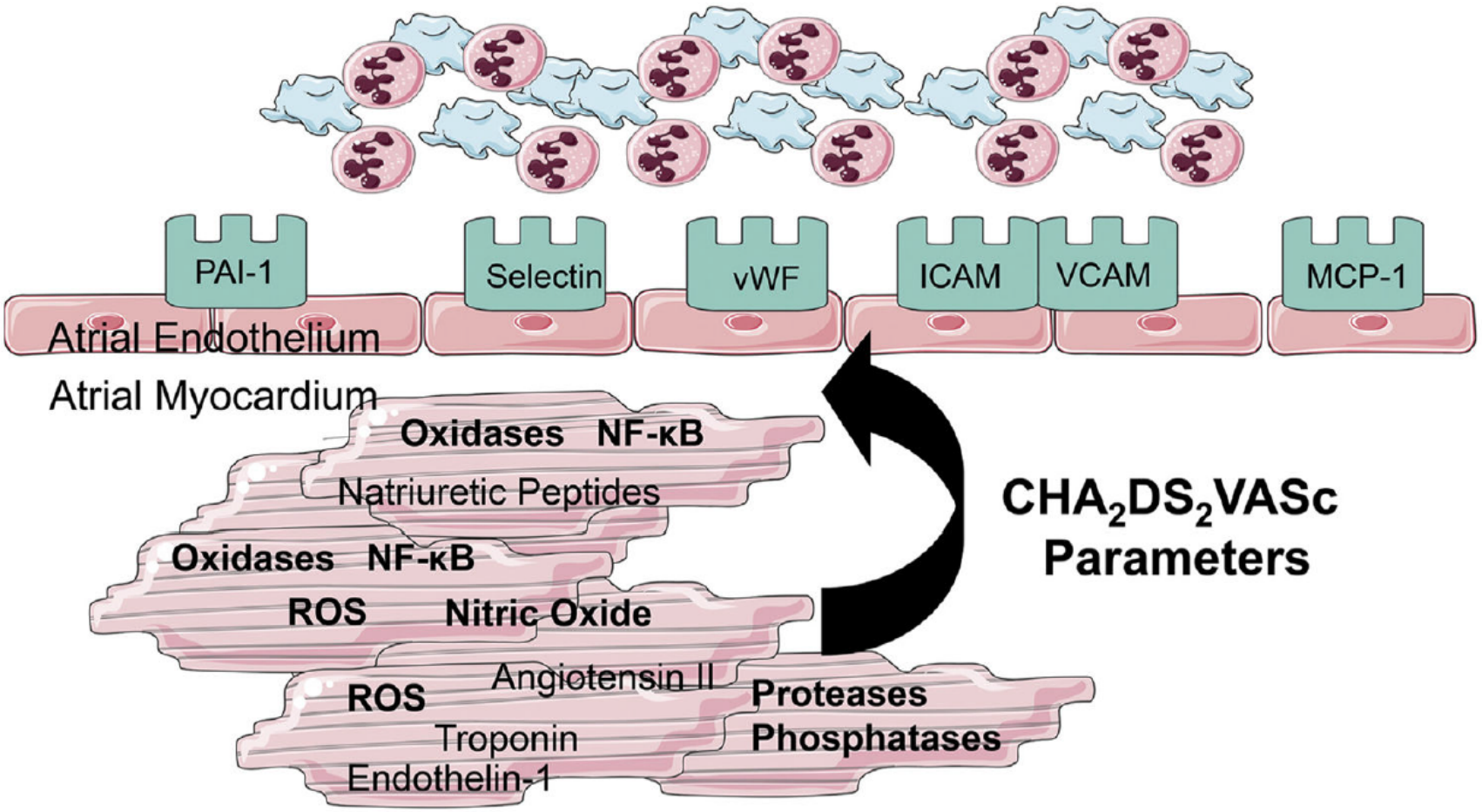
Sawin CT et al. N Engl J Med 1994;331:1249–52;
Kannel WB & Benjamin EJ. Med Clin North Am 2008;92:17–40

Fisiopatologia della trombogenesi nella FA



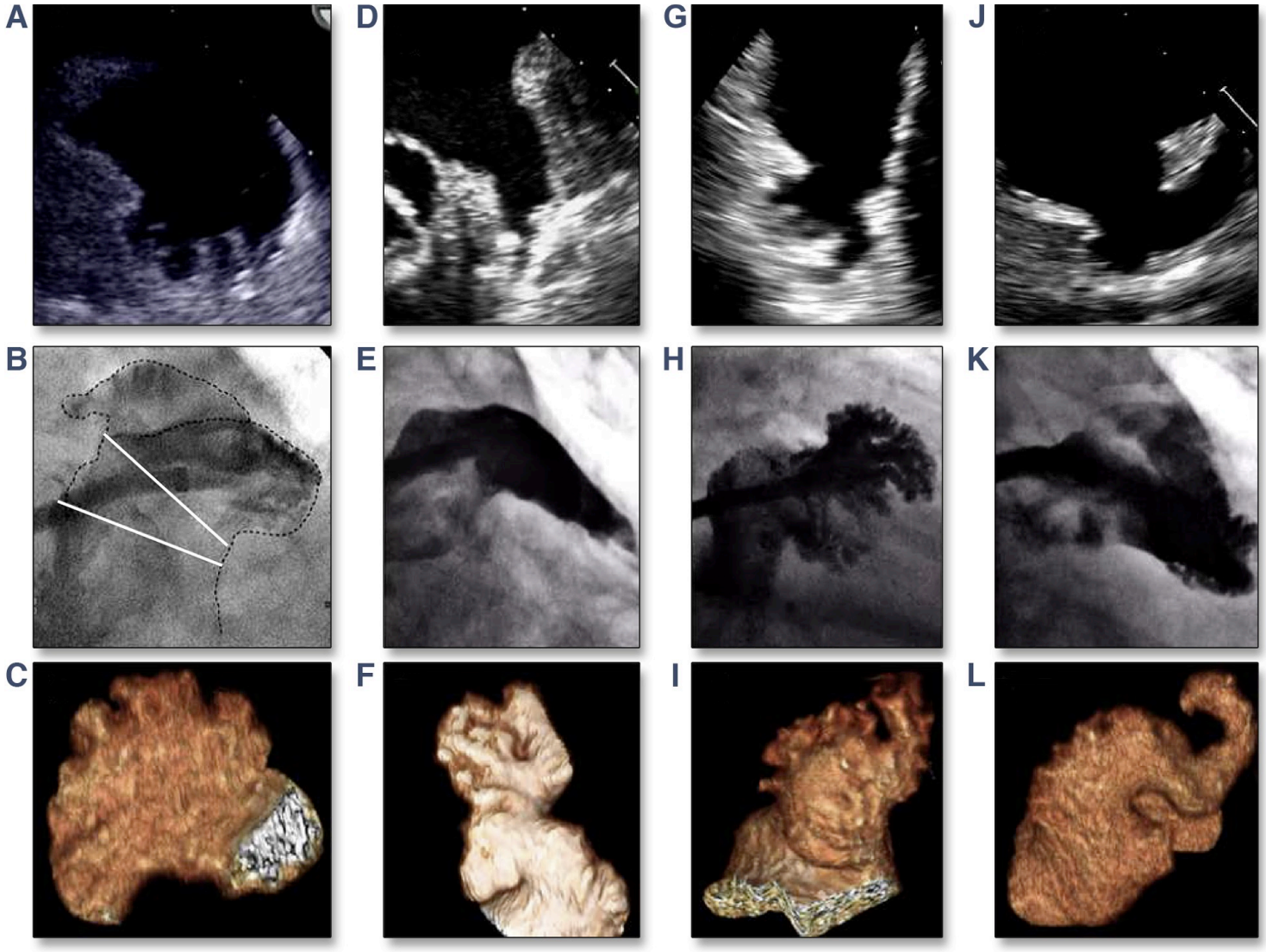
vWF = fattore di Von Willebrand

Watson T et al. Lancet 2009;373:155–66



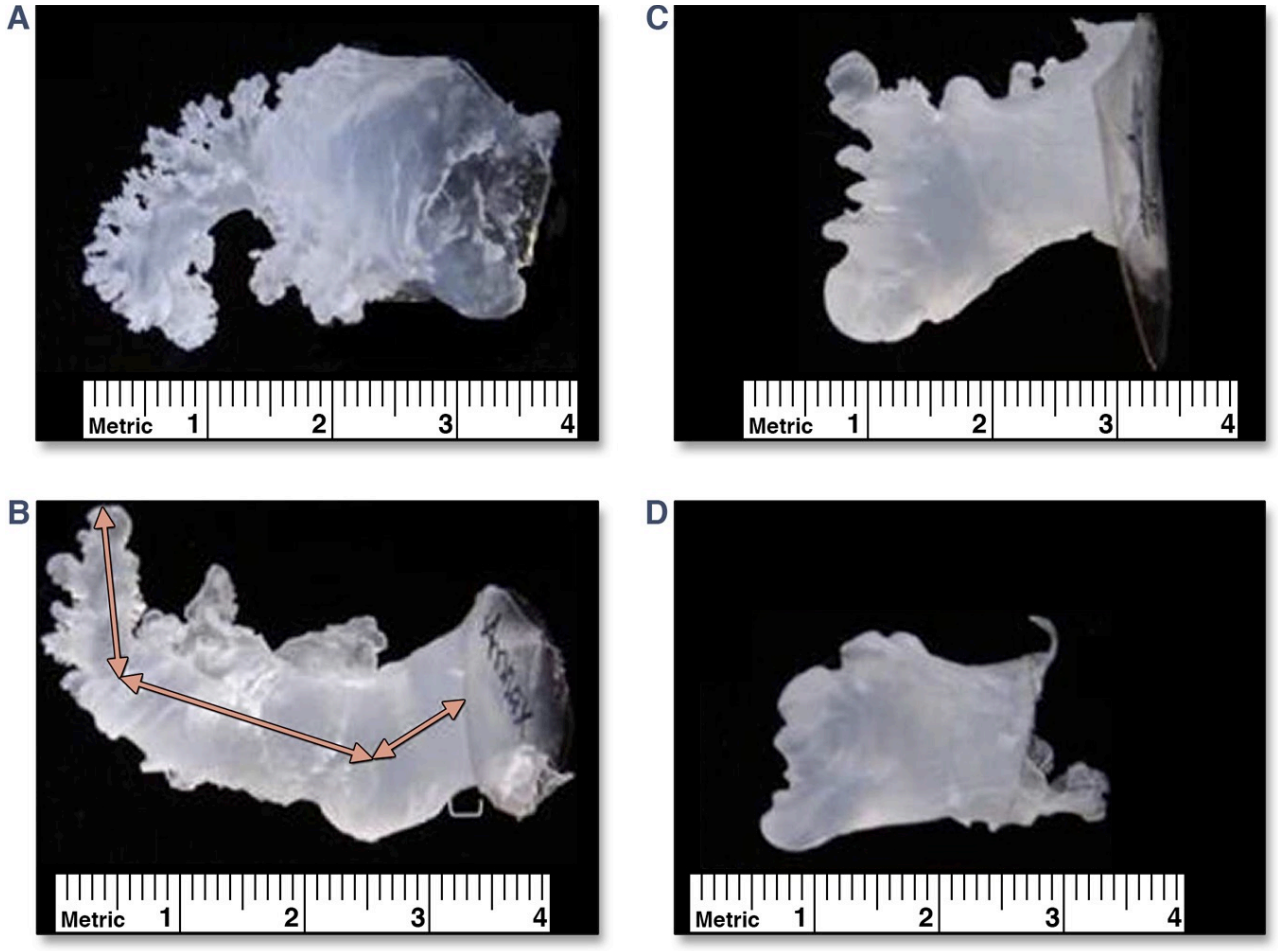
Goette et al. Heart Rhythm. Author manuscript; available in PMC 2018 January 01.

The 4 different LAA morphologies as shown by TEE (top), cine angiography (middle), and 3D computed tomography (bottom). Cauliflower (A to C), windsock (D to F), cactus (G to I), and chicken wing (J to L).



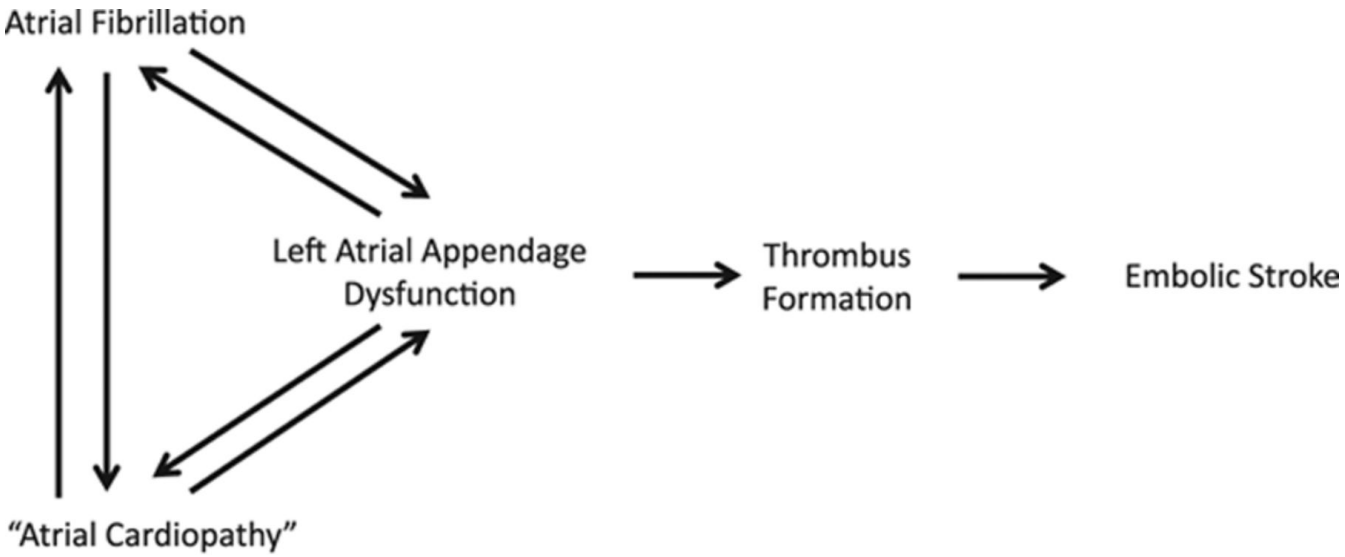
Endocasts Obtained From 2 Explanted Hearts Showing the Different LAA Intraluminal Morphologies

(A) Chicken wing. (B) Windsock. (C) Cauliflower. (D) Cactus. A, B and C, D are pairs of the same casts but viewed from different perspectives showing the overlap that exists regarding LAA morphology.



Patients with Chicken Wing LAA morphology are less likely to have an embolic event even after controlling for comorbidities and CHADS2 score. If confirmed, these results could have a relevant impact on the anticoagulation management of patients with a low-intermediate risk for stroke/TIA.

- LAA can be considered the cause of many currently cryptogenic strokes.
- Measurements of LAA function can be performed by TTE.
- Including these measurements in the diagnostic evaluation of patients with cryptogenic stroke may help understand the recurrent stroke risk and potentially improve stroke prevention strategies.

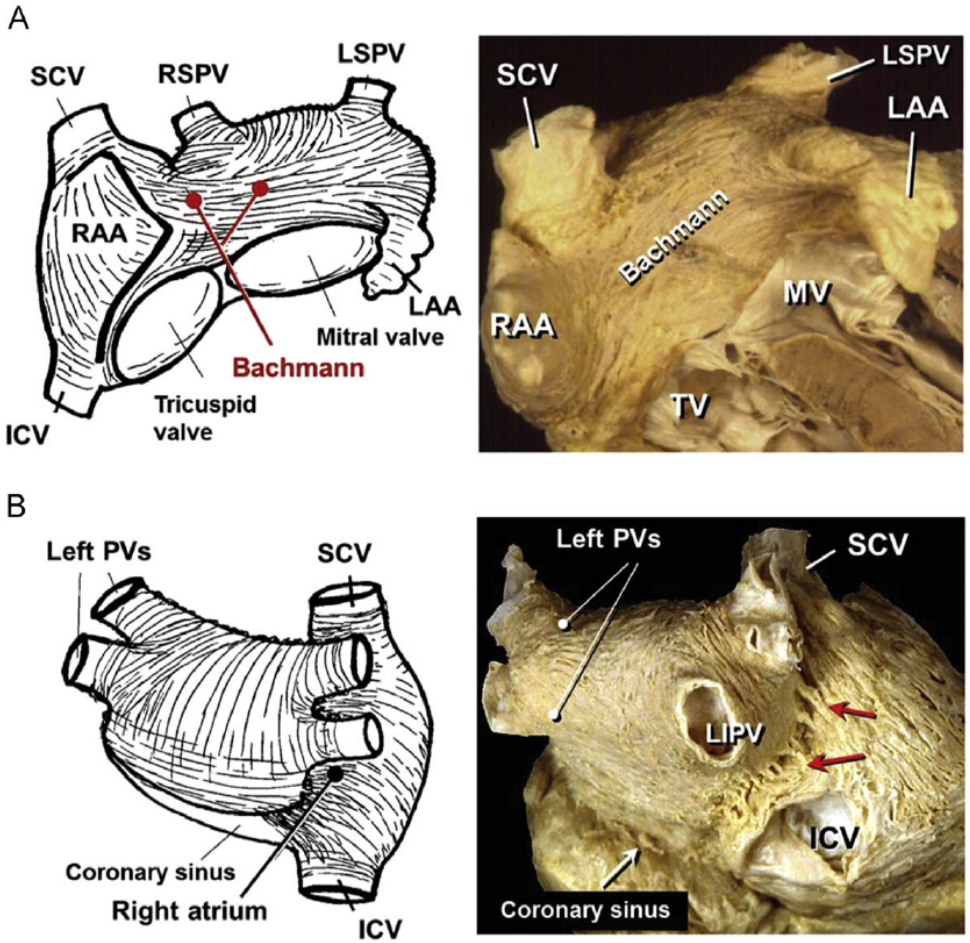


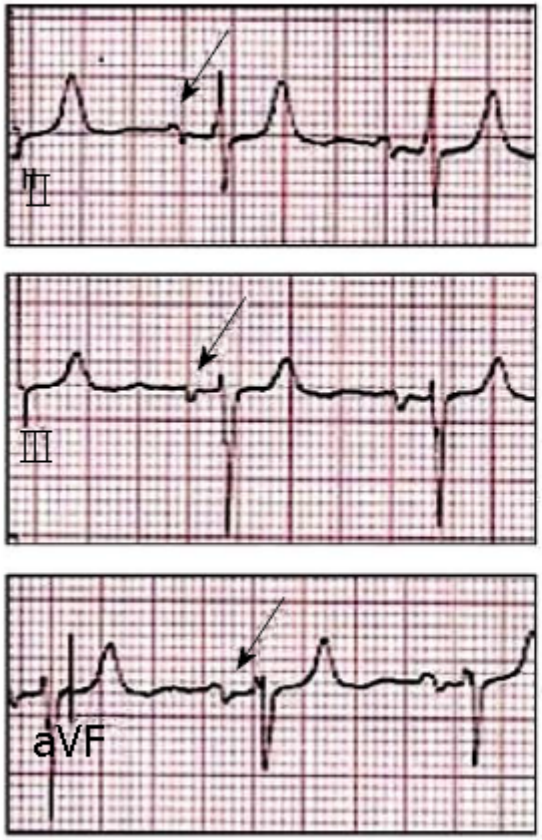
Atrial cardiopathy: evidence of markers of atrial dysfunction such as elevated N-terminal proBNP, evidence of p-wave dispersion on ECG, increased left atrial size, and paroxysmal supraventricular tachycardia.

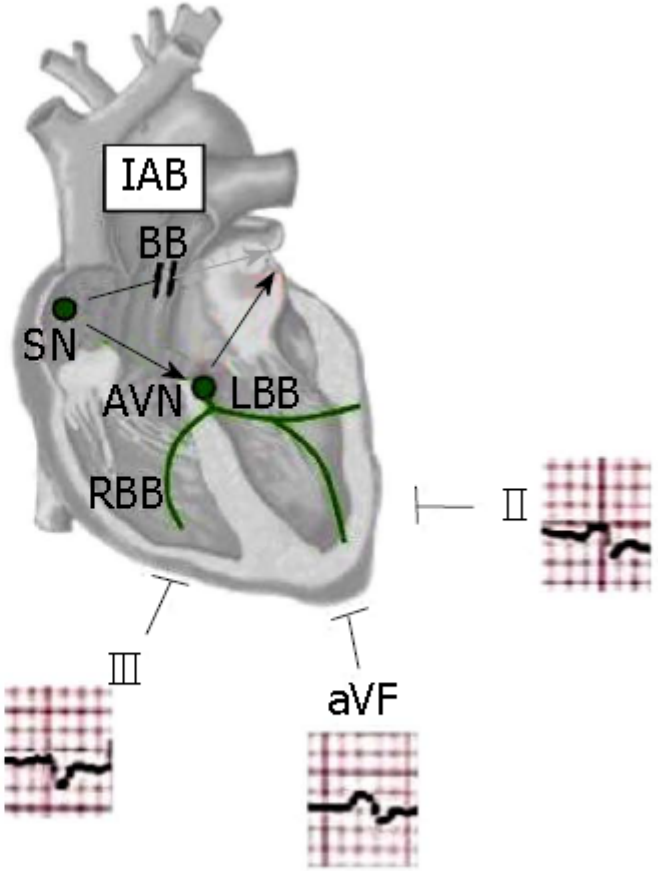
Left Atrial Appendage Function and Stroke Risk, Volume: 46, Issue: 12, Pages: 3554-3559, DOI: (10.1161/STROKEAHA.115.011273)

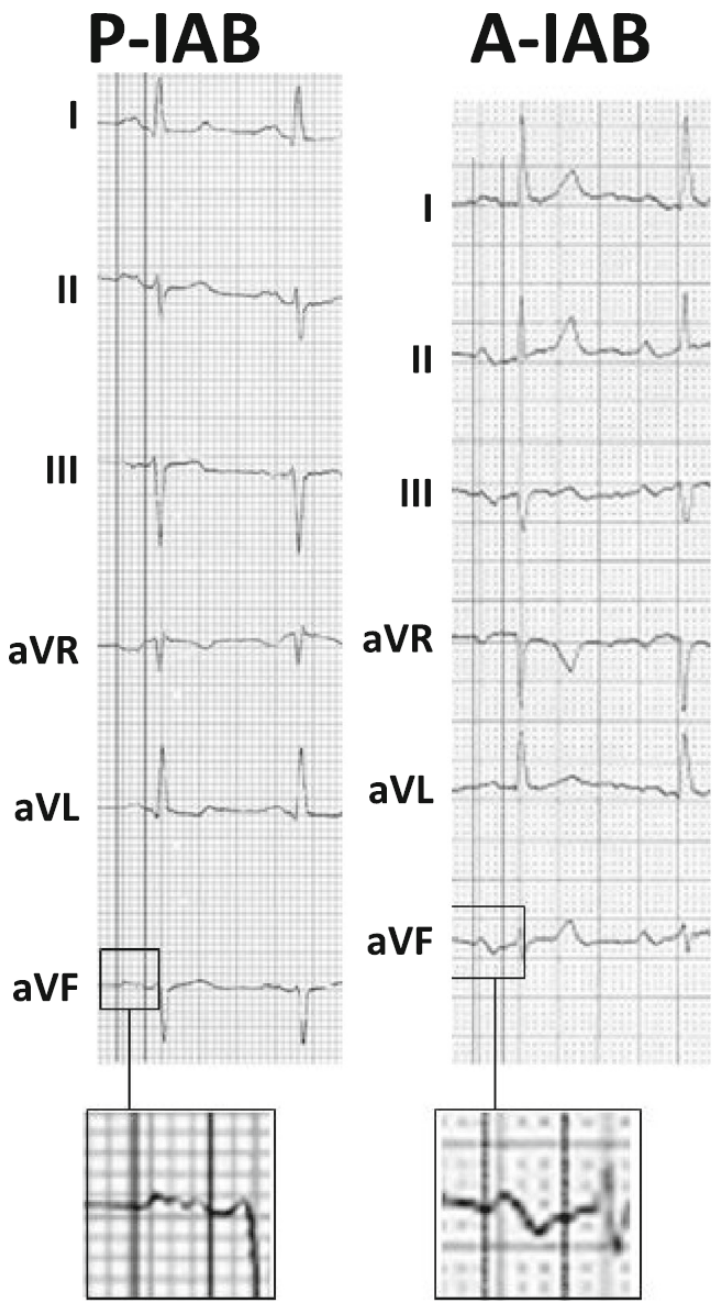
Un nuovo paradigma per il cardiologo

IL BLOCCO INTERATRIALE (IAB)


A
SCV
RSPV
LSPV
RAA
LAA
Mitral valve
Bachmann
Tricuspid valve
ICV
SCV
LSPV
LAA
Bachmann
MV
RAA
TV
B
Left PVs
SCV
Coronary sinus
Right atrium
ICV
Left PVs
SCV
LIPV
ICV
Coronary sinus


II
III
aVF


IAB
BB
SN
AVN
LBB
RBB
II
III
aVF



Bayés de Luna et al. BMC Cardiovascular Disorders (2017) 17:211. DOI 10.1186/s12872-017-0650-y

Principali studi (1979-2016) su IAB come fattore di rischio per Ictus

- Wu *et al*[(2016) CHADS2 and CHA2DS2-VASc scores may be predictors of risk of ischemic stroke or TIA in patients with IAB without atrial fibrillation
- Martinez-Selles (2015) Advanced IAB is a pre-atrial fibrillation condition associated with premature atrial beats.
- O'Neal (2016) IAB was associated with incident ischemic stroke
- O'Neal (2016) IAB is a useful marker to identify high risk subjects for developing atrial fibrillation
- Pirinen (2015) Routine ECG provides useful information for directing the workup of a young IS patient. In addition to AF, P-terminal force in particular showed a strong association with etiology of high-risk source of cardioembolism
- Enriquez (2015) Left atrium was larger in aIAB (46.2 ± 5.9 mm *vs* 43.1 ± 6.0 mm; *P* = 0.01) 35.8% of patients developed new-onset AF
- Cotter (2013) IAB was an independent predictor of AF
- Ariyarajah (2007) IAB could be a novel risk for embolic stroke
- Ariyarajah (2007) In patients with comparable echocardiographic parameters, IAB remained associated with atrial fibrillation after 15-mo follow-up
- Lorbar (2005) IAB may represent a new factor for stroke
- Jairat (2001) Patients with IAB must be followed for atrial enlargement, potential thrombosis, and the onset of AF

Characteristics associated with an increase of thromboembolic risk in patients without documented arrhythmias.

- - CHA2DS2-VASc ≥ 2
- - More than 40 atrial premature beats/h and/or runs in Holter monitoring
- - Advanced interatrial block with P ≥ 160 ms

Martínez-Sellés M, *et al.* Anticoagulation in patients at risk without documented arrhythmias. *J Geriatr Cardiol* 2017; 14: 166□168. doi:10.11909/j.issn.1671-5411.2017.03.004

CONCLUSIONI 1

- L’atrio sinistro è la prima fonte di rischio cardioembolico
- La cardiomiopatia atriale è la condizione predisponente al cardioembolismo
- L’ictus cardioembolico avviene anche senza FA dimostrabile
- Condizioni cliniche note possono predisporre alla FA
- L’ecg può aiutare nel rilevare la propensione a FA
- Il blocco interatriale è presente nel 25-40 % oltre i 70 anni e triplica il rischio di FA nei soggetti normopeso

CONCLUSIONI 2

- L’ictus ischemico nel 30% dei casi è criptogenetico
- In presenza di cardiomiopatia atriale (rilevabile con imaging), profilo di rischio elevato e /o IAB considerare TAO anche in assenza di dimostrata FA
- LAA è il sito più comune di formazione di trombi nell'atrio sinistro. La terapia anticoagulante può rivelarsi vantaggiosa per i pazienti senza fibrillazione atriale ma evidenza convincente di disfunzione della LAA

I quesiti con cui vi lascio (ma con risposta vicina)

1. Il modello FA/Ictus va rivisto?
2. Esiste un «profilo di rischio embolico» identificabile al difuori della FA?
3. Esiste una indicazione a prevenzione del rischio di ictus con i NAO al difuori della FA?
4. Possiamo sperare di diventare molto vecchi conservando il nostro cervello?

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