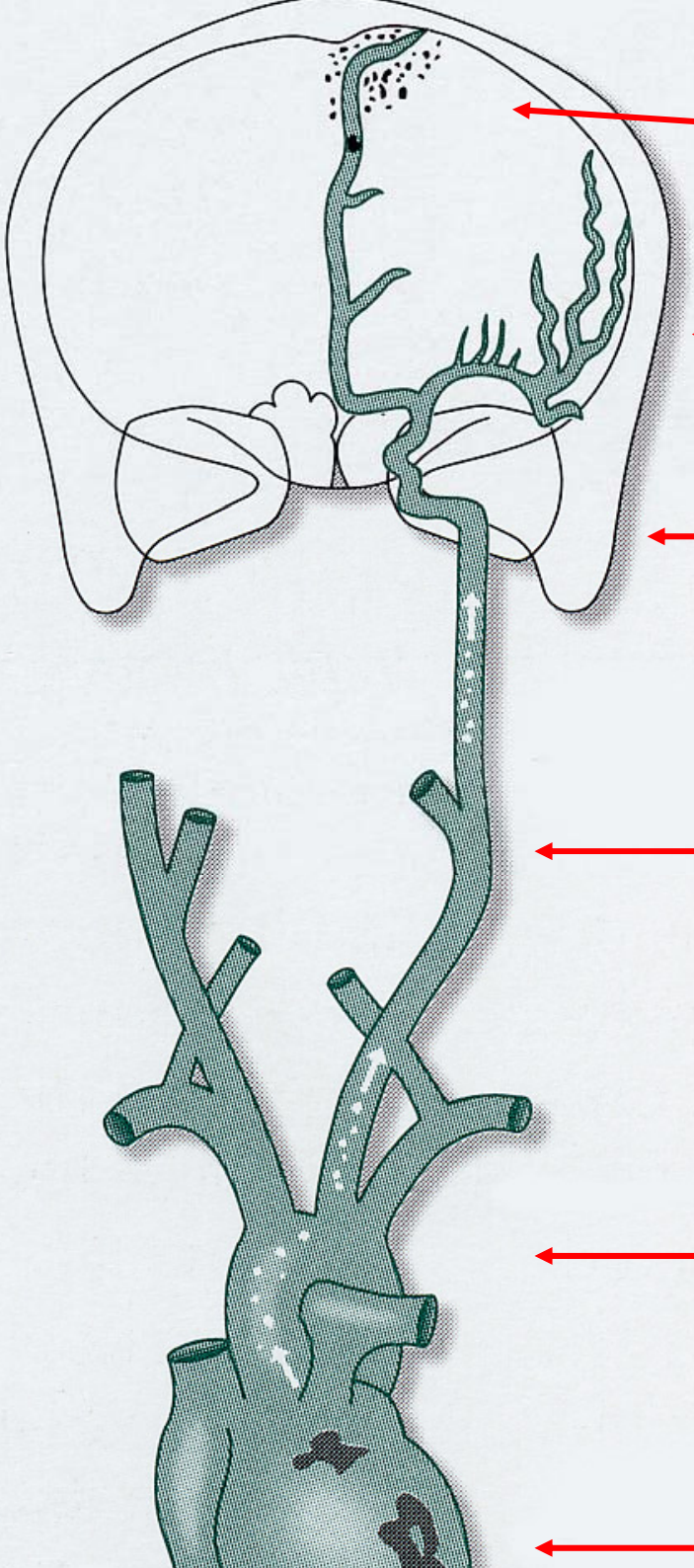
“Ictus cerebrale cardioembolico

prevenzione primaria e secondaria”

UNIVERSITA’ DEGLI STUDI DI ROMA

“TOR VERGATA”



Subtype	
Borderzone	5 %
Lacunar	20 %
Cryptogenic and rare causes	20 %
Artery-to-artery embolism	20 %
Aortic arch atheroma	15 %

Sorgenti cardioemboliche

Alto Rischio

- Trombosi atriale

Aritmie atriali
Fibrillazione Atriale
Flutter atriale
Sick sinus syndrome

Stenosi mitralica

- Trombosi endoventricolare sn

IMA
Cardiomiopatie dilatative

- Tumori cardiaci

Primitivi (mixoma, fibroelastoma)
Metastasi

- Vegetazioni

Infettive
Non infettive

- Protesi valvolari

- Ateromasia aortica complicata

Medio o incerto Rischio

- Anomalie del setto interatriale

PFO
DIA
Aneurisma SIA

- Ecocontrasto spontaneo

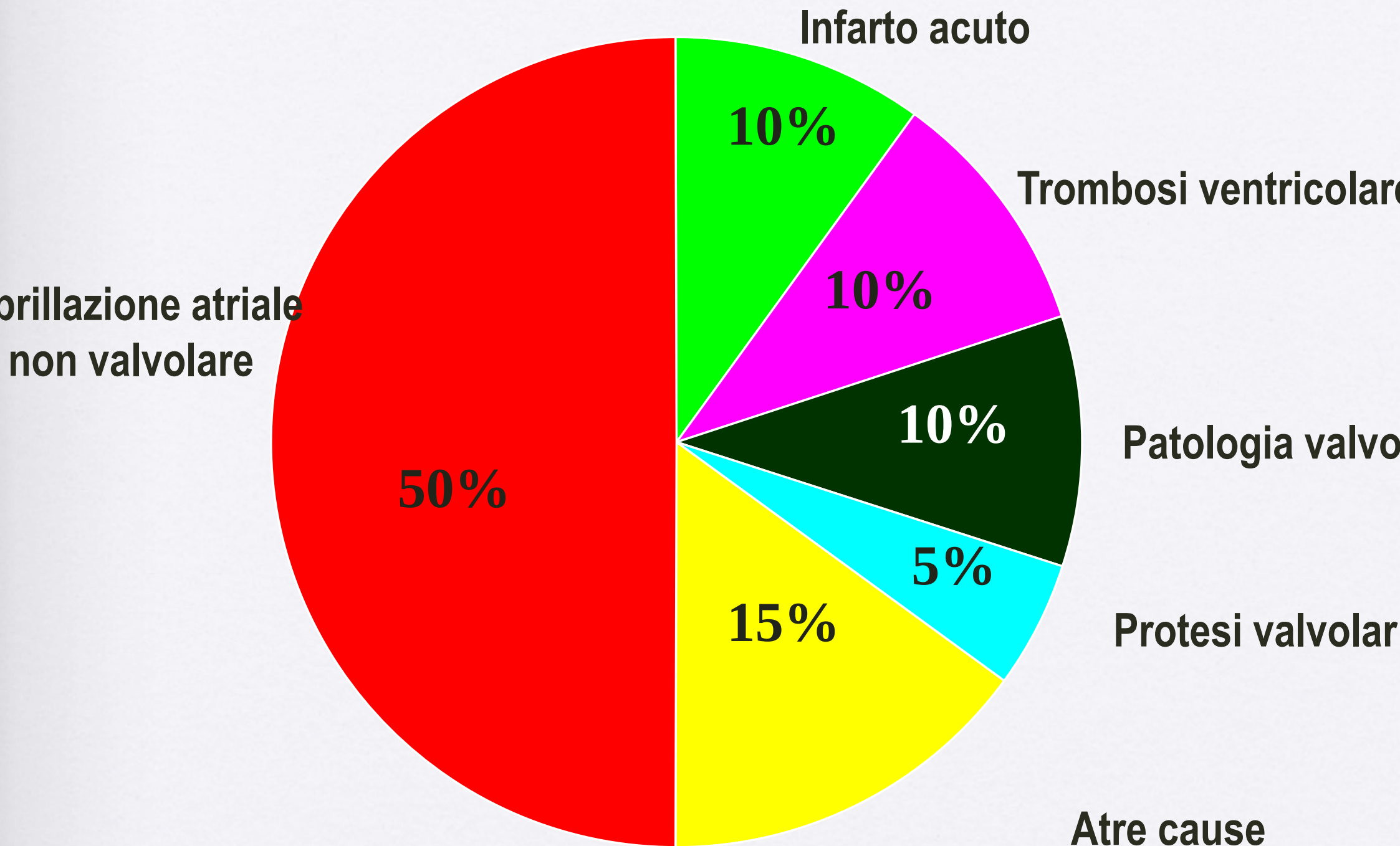
- Prolasso valvolare mitralico co
mixomatosi

- Calcificazioni valvolari

Calcificazioni anulus mitralico
Stenosi/sclerosi valv. Aortica

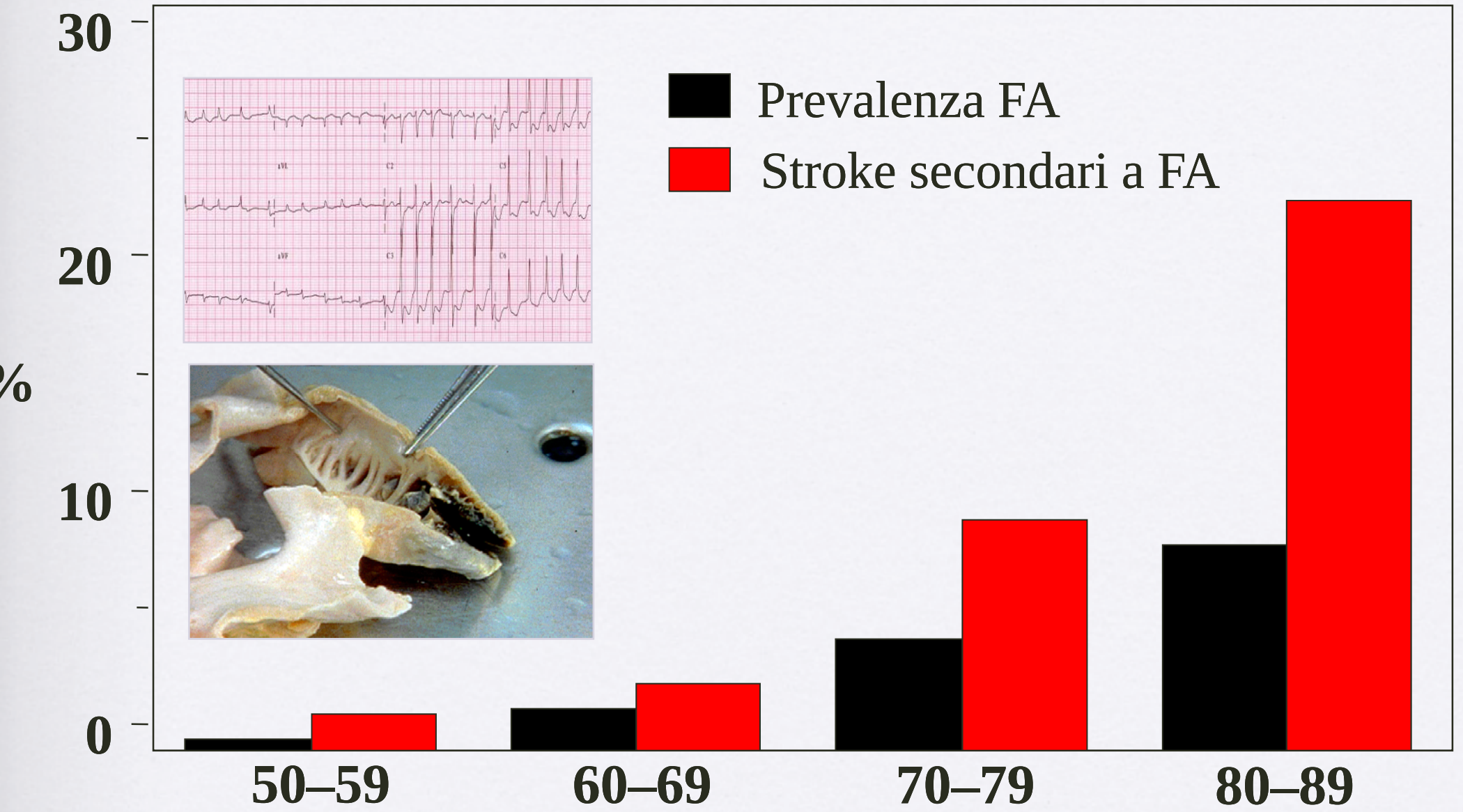
- *Strands* valvolari

Sorgenti cardioemboliche



Entità del rischio

Studio Framingham



Stroke from Atrial Fibrillation

AF is the most preventable cause of stroke:

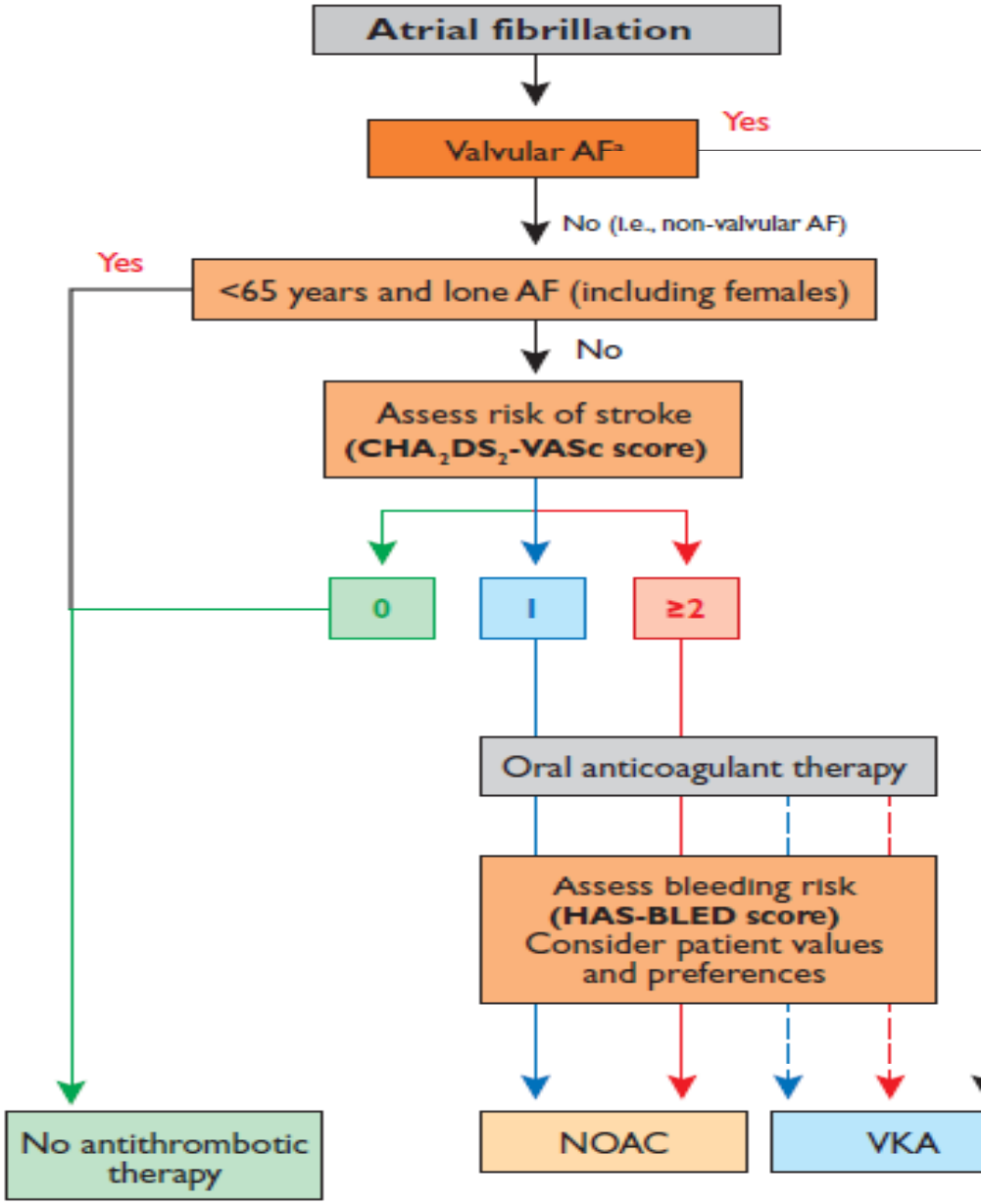
12-16 million will be on warfarin treatment by 2050 in the US

Clinical trials have shown stroke can be reduced:

- Placebo *vs* ASA = 19% ↓
- ASA *vs* warfarin = 30% ↓
- Placebo *vs* warfarin = 62% ↓
- **Dabigatran *vs* warfarin = 34% ↓**

able 3 Risk factors for ischaemic stroke/TIA/ ystemic embolism in patients with AF: the Swedish ohort Atrial Fibrillation study (adapted from Friberg *et al.*[25])

	Multivariate hazard ratios (95% CI)
Age (years) <65 65–74 ≥75	 1.0 (Reference) 2.97 (2.54–3.48) 5.28 (4.57–6.09)
Female sex	1.17 (1.11–1.22)
Previous ischaemic stroke	2.81 (2.68–2.95)
Intracranial bleeding	1.49 (1.33–1.67)
Vascular disease (any) • Myocardial infarction • Previous CABG • Peripheral artery disease	1.14 (1.06–1.23) 1.09 (1.03–1.15) 1.19 (1.06–1.33) 1.22 (1.12–1.32)
Hypertension	1.17 (1.11–1.22)
Heart failure (history)	0.98 (0.93–1.03)
Diabetes mellitus	1.19 (1.13–1.26)



Antiplatelet therapy with aspirin plus clopidogrel, or—less effectively—as only, should be considered in patients who refuse any OAC, or cannot to anticoagulants for reasons unrelated to bleeding. If there are contraindicatio OAC or antiplatelet therapy, left atrial appendage occlusion, closure or ex may be considered.

Recommendations for prevention of thromboembolism in non-valvular AF—general		
botic therapy to prevent thromboembolism is recommended for all patients with AF, except in those oth male and female) who are at low risk (aged <65 years and lone AF), or with contraindications.	I	
e of antithrombotic therapy should be based upon the absolute risks of stroke/thromboembolism and nd the net clinical benefit for a given patient.	I	
$_2DS_2$-VASc score is recommended as a means of assessing stroke risk in non-valvular AF.	I	
with a CHA_2DS_2-VASc score of 0 (i.e., aged <65 years with lone AF) who are at low risk, with none of the s, no antithrombotic therapy is recommended.	I	
with a CHA_2DS_2-VASc score ≥2, OAC therapy with: ted-dose VKA (INR 2–3); or ect thrombin inhibitor (dabigatran); or al factor Xa inhibitor (e.g. rivaroxaban, apixaban)[d] recommended, unless contraindicated.	I	
with a CHA_2DS_2-VASc score of 1, OAC therapy with ted-dose VKA (INR 2–3); or ect thrombin inhibitor (dabigatran); or al factor Xa inhibitor (e.g. rivaroxaban, apixaban)[d] ould be considered, based upon an assessment of the risk of bleeding complications and patient preferences.	IIa	
tients who are aged <65 and have lone AF (but still have a CHA_2DS_2-VASc score of 1 by virtue of their e low risk and no antithrombotic therapy should be considered.	IIa	
ients refuse the use of any OAC (whether VKAs or NOACs), antiplatelet therapy should be considered, bination therapy with aspirin 75–100 mg plus clopidogrel 75 mg daily (where there is a low risk of bleeding) effectively—aspirin 75–325 mg daily.	IIa	

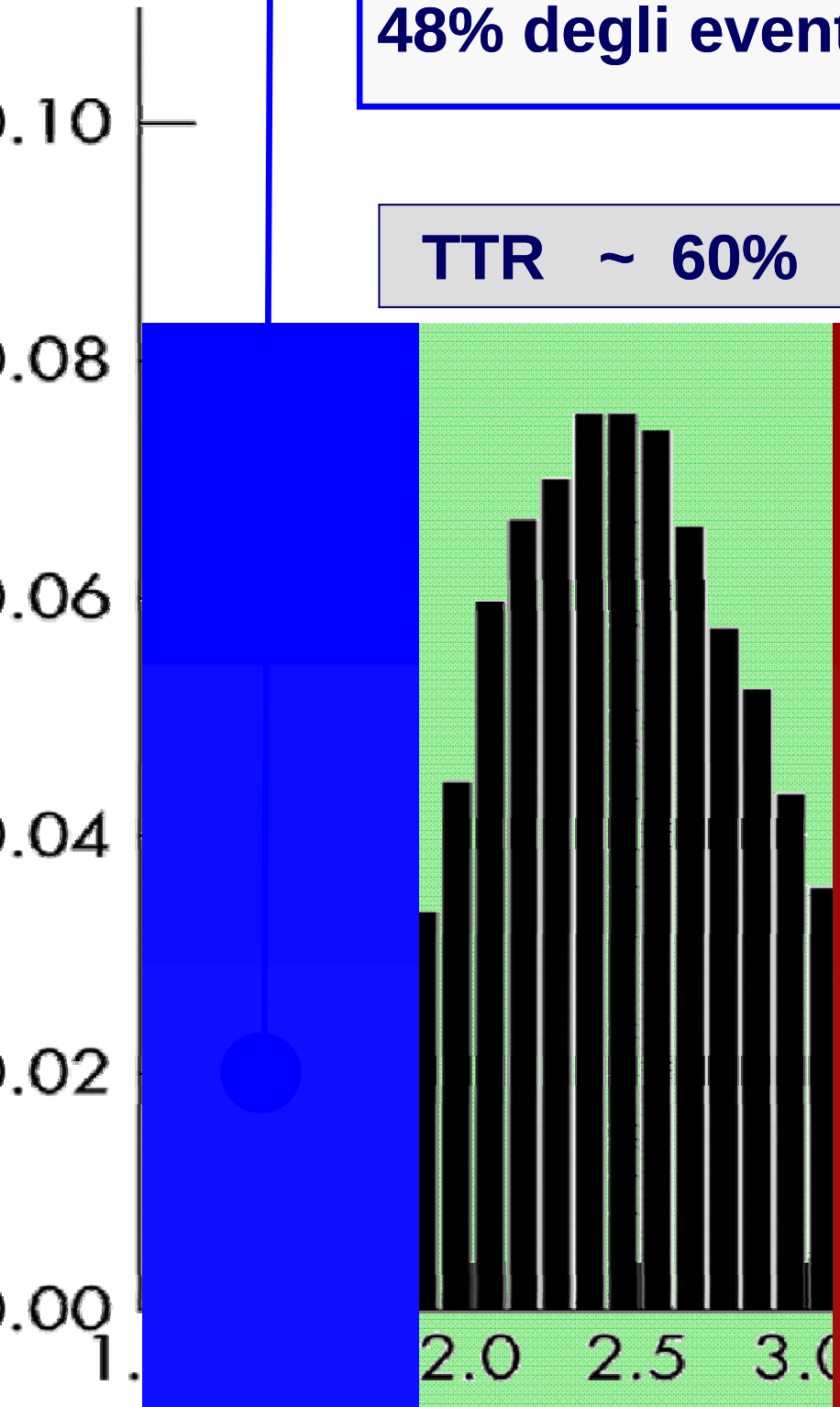
ies in keeping within therapeutic anticoagulation, experiencing side effects of VKAs, or inability to attend or ake INR monitoring, one of the NOACs, either: direct thrombin inhibitor (dabigatran); or oral factor Xa inhibitor (e.g. rivaroxaban, apixaban)[d] is recommended.	I
OAC is recommended, one of the NOACs, either: direct thrombin inhibitor (dabigatran); or oral factor Xa inhibitor (e.g. rivaroxaban, apixaban)[d] should be considered rather than adjusted-dose VKA (INR 2–3) for most patients with non-valvular AF, based their net clinical benefit.	IIa
dabigatran is prescribed, a dose of 150 mg b.i.d. should be considered for most patients in preference to b.i.d., with the latter dose recommended in: derly patients, age ≥ 80 ncomitant use of interacting drugs (e.g. verapamil) gh bleeding risk (HAS-BLED score ≥3) oderate renal impairment (CrCl 30–49 mL/min).	IIa
rivaroxaban is being considered, a dose of 20 mg o.d. should be considered for most patients in preference to o.d., with the latter dose recommended in: gh bleeding risk (HAS-BLED score ≥3) oderate renal impairment (CrCl 30–49 mL/min).	IIa
e and subsequent regular assessment of renal function (by CrCl) is recommended in patients following initiation NOAC, which should be done annually but more frequently in those with moderate renal impairment where hould be assessed 2–3 times per year.	IIa
s (dabigatran, rivaroxaban, and apixaban) are not recommended in patients with severe renal impairment (CrCl L/min).	III

ommendations	Class	L
Recommendations for prevention of thromboembolism in non-valvular AF—bleeding		
ssment of the risk of bleeding is recommended when prescribing antithrombotic therapy (whether with VKA, AC, aspirin/clopidogrel, or aspirin).	I	
HAS-BLED score should be considered as a calculation to assess bleeding risk, whereby a score ≥3 indicates 'high and some caution and regular review is needed, following the initiation of antithrombotic therapy, whether with or antiplatelet therapy (LoE = A). ectable risk factors for bleeding [e.g. uncontrolled blood pressure, labile INRs if the patient was on a VKA, omitant drugs (aspirin, NSAIDs, etc.), alcohol, etc.] should be addressed (LoE = B). of the HAS-BLED score should be used to identify modifiable bleeding risks that need to be addressed, but should e used on its own to exclude patients from OAC therapy (LoE = B).	IIa	A
risk of major bleeding with antiplatelet therapy (with aspirin–clopidogrel combination therapy and – especially in lderly – also with aspirin monotherapy) should be considered as being similar to OAC.	IIa	
Recommendations for prevention of thromboembolism in non-valvular AF—peri-cardioversion		
atients with AF of ≥48 h duration, or when the duration of AF is unknown, OAC therapy (e.g. VKA with INR 2-3 bigatran) is recommended for ≥3 weeks prior to and for ≥4 weeks after cardioversion, regardless of the method trical or oral/i.v. pharmacological).	I	
tients with risk factors for stroke or AF recurrence, OAC therapy, whether with dose-adjusted VKA (INR or a NOAC, should be continued lifelong irrespective of the apparent maintenance of sinus rhythm following oversion.	I	

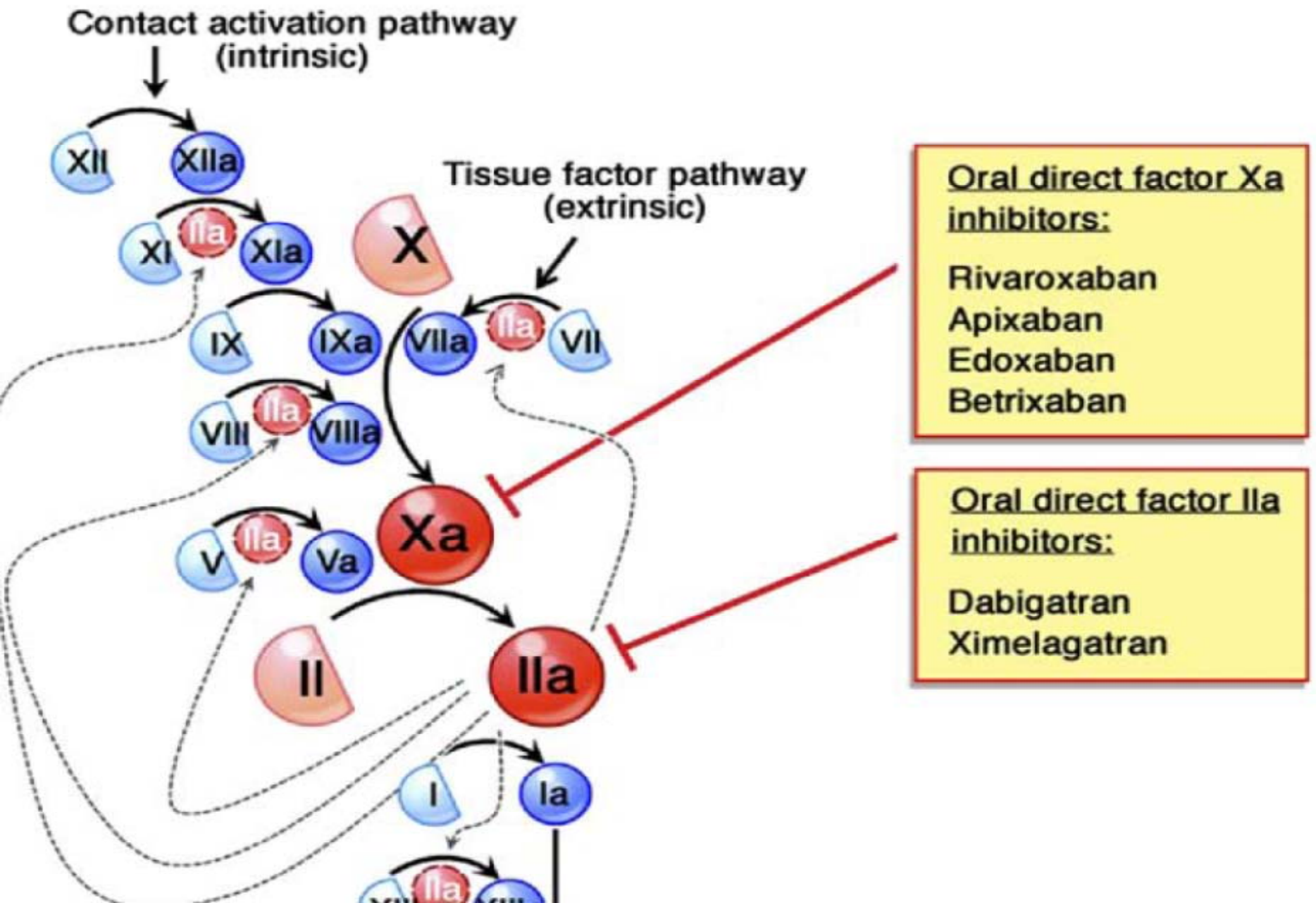
48% degli eventi tromboembolici

44% degli eventi emorrag

TTR ~ 60%



Nell'ictus o TIA cardioembolico associat a cardiopatie e valvulopat emboligene è indicata la terapia anticoagulante orale mantenendo l'INR tra 2 e 3.


Contact activation pathway
(intrinsic)
XII
XIIa
XI
IIa
XIa
Tissue factor pathway
(extrinsic)
X
IX
IXa
VIIa
IIa
VII
VIII
IIa
VIIIa
V
IIa
Va
Xa
II
IIa
I
Ia
IIa
Oral direct factor Xa inhibitors:
Rivaroxaban
Apixaban
Edoxaban
Betrixaban
Oral direct factor IIa inhibitors:
Dabigatran
Ximelagatran

Similar Yet Different

	Dabigatran[1,2,3,7]	Rivaroxaban[3,4,7]	Apixaban[3,5,7]	Edoxaban[3,6,]
Mechanism of action	Direct thrombin inhibitor	Direct Xa inhibitor	Direct Xa inhibitor	Direct Xa inhibito
Current Indications (Canada)	• Stroke prevention in AF (Oct/2010) • VTE prophylaxis post orthopaedic surgery (Mar/2009)	• VTE prophylaxis post orthopaedic surgery (Sep/2008)	None	None
Prodrug	Prodrug	No	No	No
Bioavailability	6 %	> 80 %	66 %	>50 %
Tmax	2 hrs	2-4 hrs	3 hrs	1-2 hrs
Half-life	14-17 hours	7-11 hours	8-15 hours	9-11 hours
Dosing Frequency	QD (orthopaedic) BID (AF)	QD (orthopaedic & AF)	BID (orthopaedic & AF)	QD (AF)
Excretion	80% renal, 20% fecal	66% renal (33% unchanged, 33% inactive metabolites); 33% fecal	70% fecal; 25% renal	Predominantly renal
Food Interactions	None	None	None	None

# of Patients With Atrial Fibrillation (Update on Dabigatran)

Table 2 Recommendation for emerging antithrombotic agents

2011 Focused update recommendation	Comments
Class I	
1. Dabigatran is useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolization who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure (creatinine clearance <15 mL/min) or advanced liver disease (impaired baseline clotting function).[3] *(Level of Evidence: B)*	New recommendation

# of Patients With Atrial Fibrillation (Update on Dabigatran

Table 3. Recommendation for Combining Anticoagulant With Antiplatelet Therapy

2011 Focused Update Recommendation	Comments
Class IIb	
1. The addition of clopidogrel to aspirin (ASA) to reduce the risk of major vascular events, including stroke, might be considered in patients with AF in whom oral anticoagulation with warfarin is considered unsuitable due to patient preference or the physician's assessment of the patient's ability to safely sustain anticoagulation.[10] *(Level of Evidence: B)*	New recommendation

Dabigatran: Not Without Issues

1. No anticoagulant effect if missed dose
   - 2% discontinuation rate due to GI distress
   - Cost of drug ($240/mo *vs* $4/mo for warfarin)
2. No test to assess anticoagulation
3. Difficult to modulate dose
4. Bleeding in the elderly and renal impaired patients
5. ‘Real world’ untested populations
6. Drug interactions
7. Limited data on bridging between anticoagulants
8. No specific antidote
9. 0.2% increase in myocardial infarction
10. Off-label use

Who is "NOT" a good candidate for dabigatran?

Dabigatran is probably NOT the best anticoagulant choice for patients who have

- Consistently therapeutic INRs on warfarin
    - Patients with a higher time in therapeutic range (TTR) (e.g. >60-80%) will derive the least benefi compared to continued warfarin therapy
- Renal dysfunction (Avoid in patients with CrCl <30 mL/min; For CrCl 15-30 mL/min can use reduced dose this regimen has not been well studied)
- History of significant GI disease or GI bleeding (i.e. peptic ulcer disease, poorly controlled GERD)
- Hepatic dysfunction
- Medication non-compliance
- No prescription insurance and/or unable to afford co-pay

UNIVERSITY OF UTAH HEALTH CARE | Thrombosis

Patients in whom dabigatran has not been well studied

Heart valve disorder or heart valve replacement

Increased bleeding risk (recent major surgery; planned surgery or procedure; history of intracranial, intraocula

intraspinal, retroperitoneal, or intra-articular bleeding, GI hemorrhage within the last year; gastroduodenal ul

disease; hemorrhagic disorder; recent use of fibrinolytic agents; uncontrolled hypertension)

Patients undergoing atrial fibrillation ablation

Renal dysfunction (CrCl <30 mL/min)

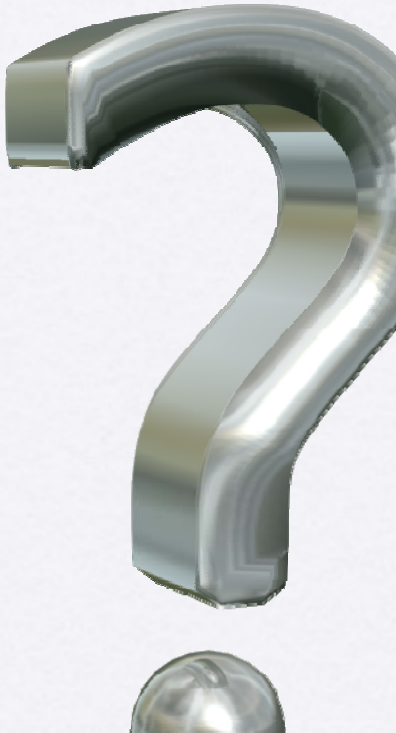
Liver disease (increased AST/ALT/Alk Phos >2x upper limit of normal, hepatitis A, B, C)

Pregnant women

Anemia/Thrombocytopenia

QUESTIONI APERTE:

- **Mancanza di antidoti specifici**
- **Semplificazione eccessiva della terapia (*uso inappropriato ?*)**
- **Mancanza di test coagulativi efficaci in circostanze d'urgenza**
- **Monitoraggio della "*compliance*" dei pazienti**
- **Comportamento nell'insufficienza renale**
- **Gestione perioperatoria**
- **Costi**
- **Quale paziente trattare ?**



2012 focused update of the ESC Guidelines for the management of atrial fibrillation

Left atrial appendage closure

Recommendations for LAA closure/occlusion/excision

Recommendations	Class[a]	Level[b]	Ref[c]
Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.	IIb	B	115, 118
Surgical excision of the LAA may be considered in patients undergoing open heart surgery.	IIb	C	

LAA = left atrial appendage.
[a]Class of recommendation.
[b]Level of evidence.
[c]References.

about this procedure. For more detailed information on the evidence, see the overview, available at www.nice.org.uk/IP310aoverview

Guidance

Current evidence suggests that percutaneous occlusion of the left atrial appendage (LAA) is efficacious in reducing the risk of thromboembolic complications associated with non-valvular atrial fibrillation (AF). With regard to safety, there is a risk of life-threatening complications from the procedure, but the incidence of these is low. Therefore, this procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit.

on-site cardiac surgery.

device-related adverse events resulting from rocedure should be reported to the cines and Healthcare products Regulatory cy (MHRA).

established by transoesophageal echocardiography (TOE). An appropriately sized device is selected and deployed in the mouth of the LAA where it is expanded to fit the space.

2.2.2 The position and patency of the occlusion device may be confirmed postoperatively using echocardiographic imaging.

2.4.5 Delivery wire fracture requiring su was reported in 1 patient in the c 75 patients.

2.4.6 The RCT of 707 patients reported effusion successfully treated surg pericardiocentesis in 5% (22/463 effusion not requiring drainage in oesophageal tear in less than 1% procedure-related arrhythmia in l 1% (1/463) of patients treated by percutaneous occlusion.

2.4.7 Perforation of the right femoral a accessing the right femoral vein a thrombus at the time of the proc the implantation of the device wa 1 patient each in the case series

2.4.8 The Specialist Advisers considered adverse events to include the ina an incorrectly positioned device b means, so requiring emergency s persistent atrial septal defect.

2.5 Other comments

2.5.1 The Committee noted that the pu included different occlusion devic mindful that clinical outcomes ma be the same with all devices.

2.5.2 The Committee noted that new p products are in development for the risk of thromboembolism asso

3 Further information

3.1 For related NICE guidance see ww

Information for patients

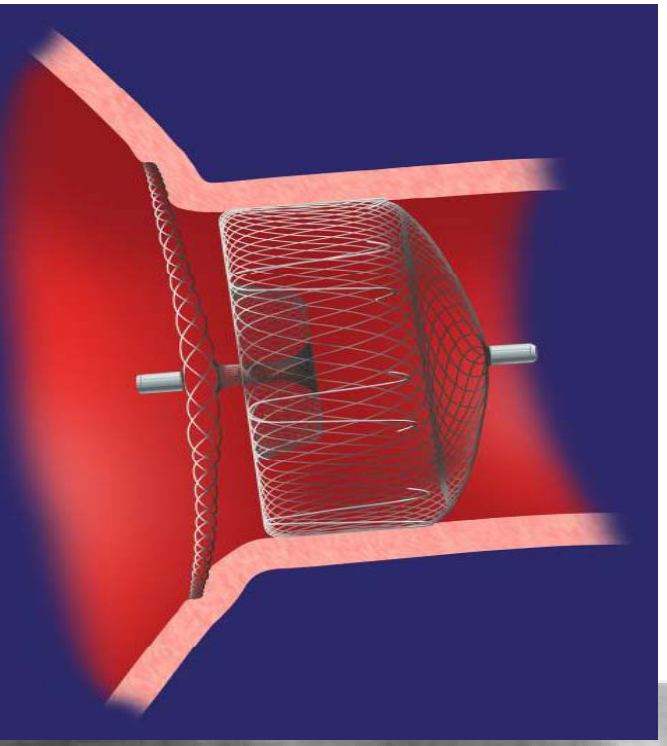
NICE has produced information on this pro patients and carers ('Understanding NICE g explains the nature of the procedure and t issued by NICE, and has been written with in mind. See www.nice.org.uk/guidance/IP

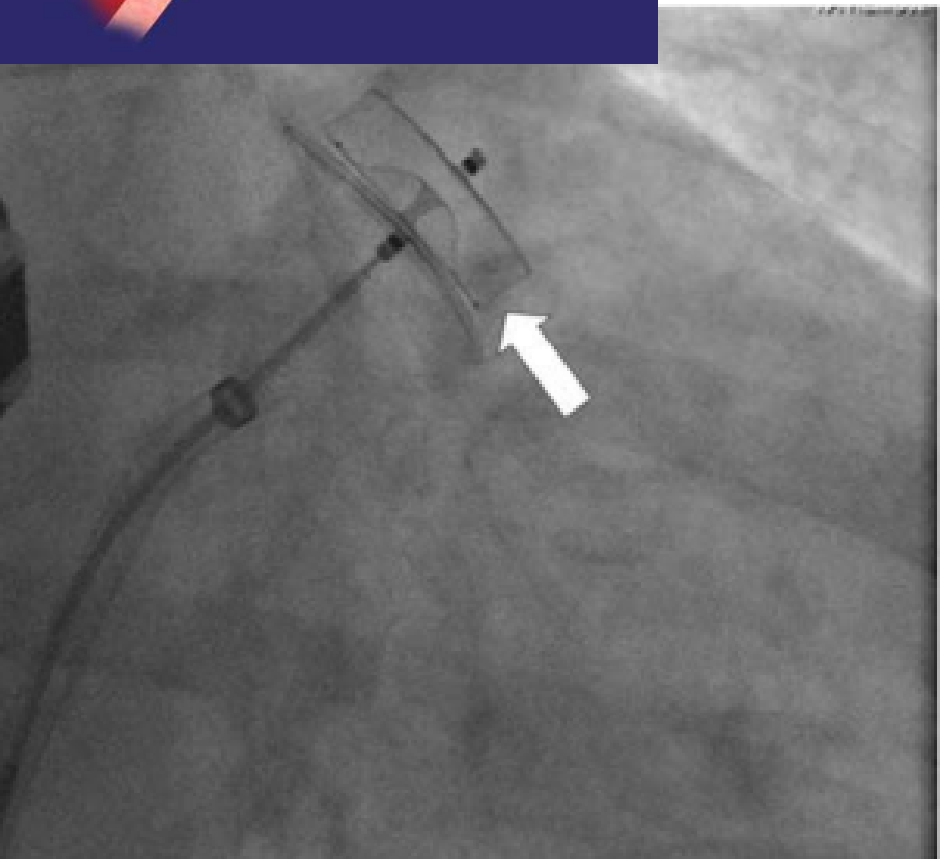
Ordering printed copies
Contact NICE publications (phone 0845 003 7783 or email publications@nice.org.uk) and quote reference n this guidance or N2206 for the 'Understanding NICE guidance'.

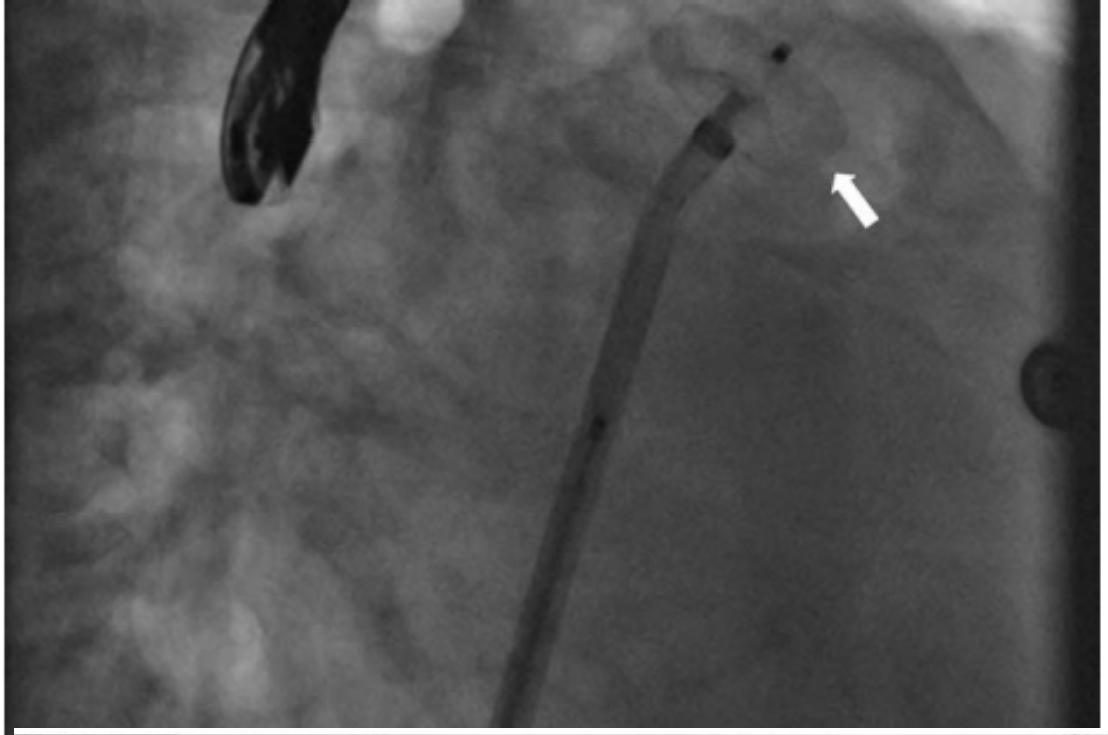
This guidance represents the view of NICE, which was arrived at after careful consideration of the available eviden professionals are expected to take it fully into account when exercising their clinical judgement. This guidance doe override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstance patient, in consultation with the patient and/or guardian or carer.

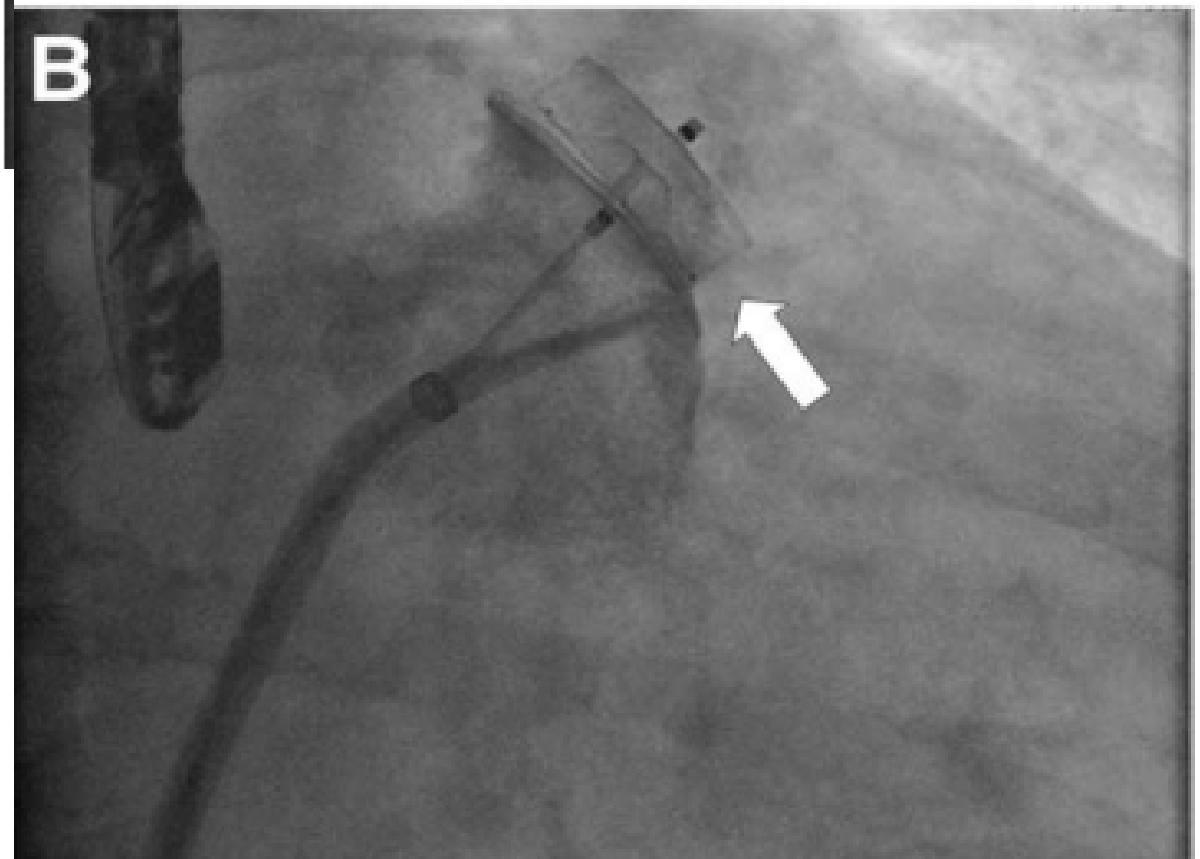
Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and p reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to a discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interp

(ACI)

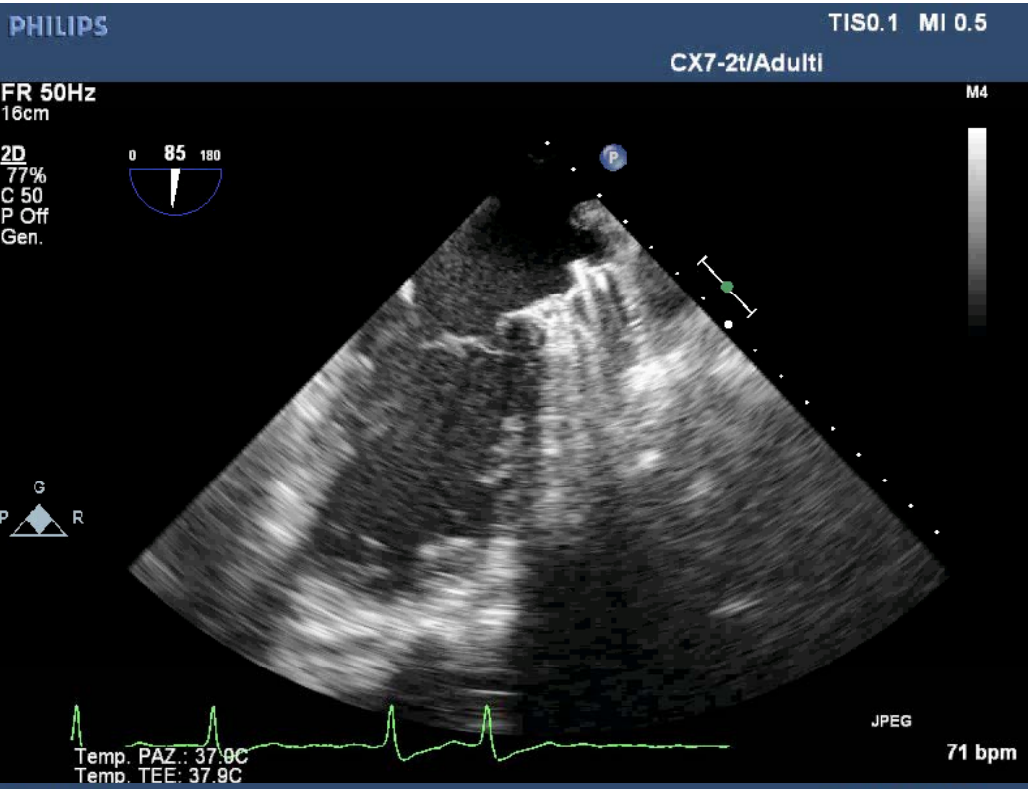


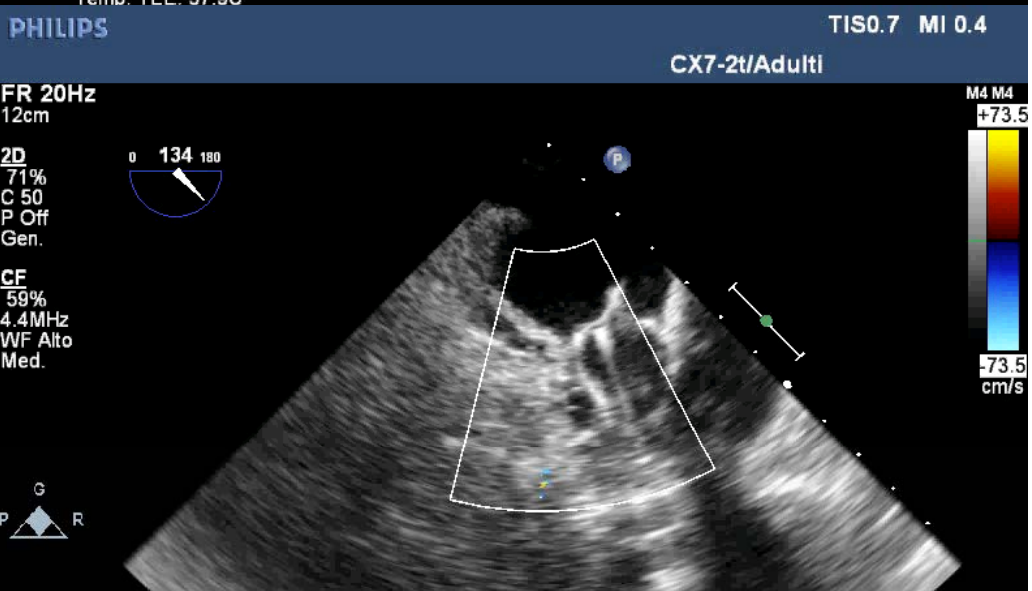


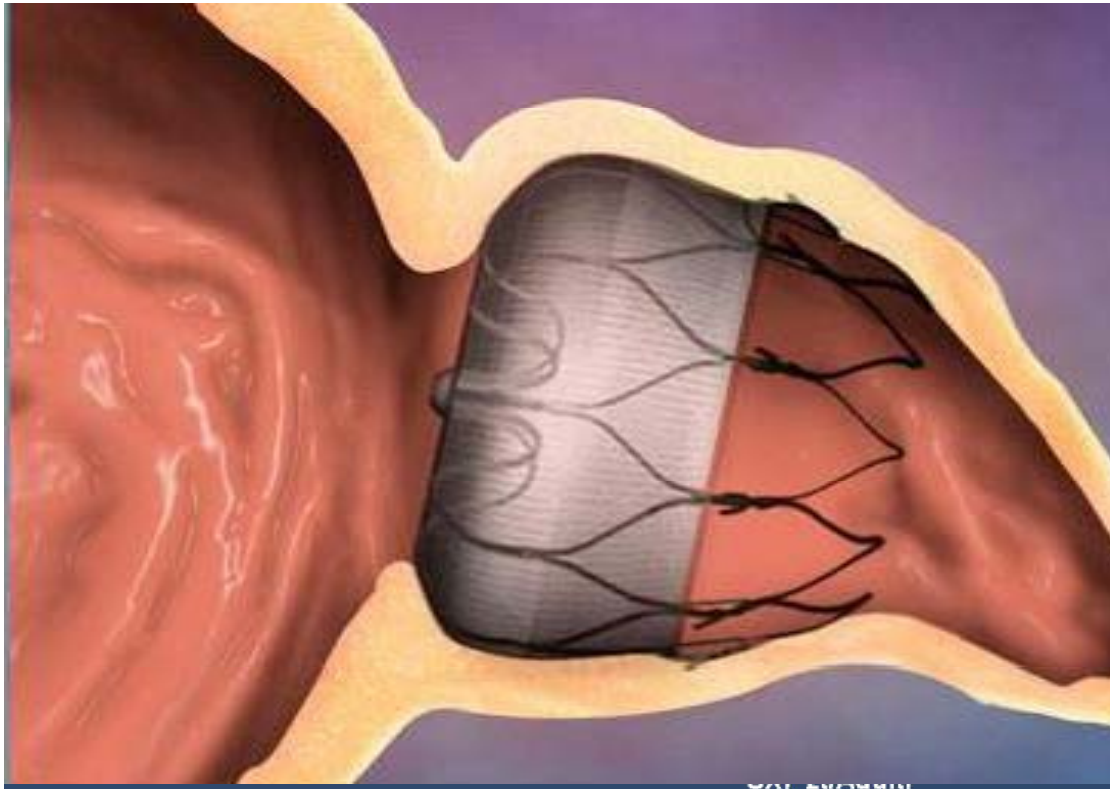


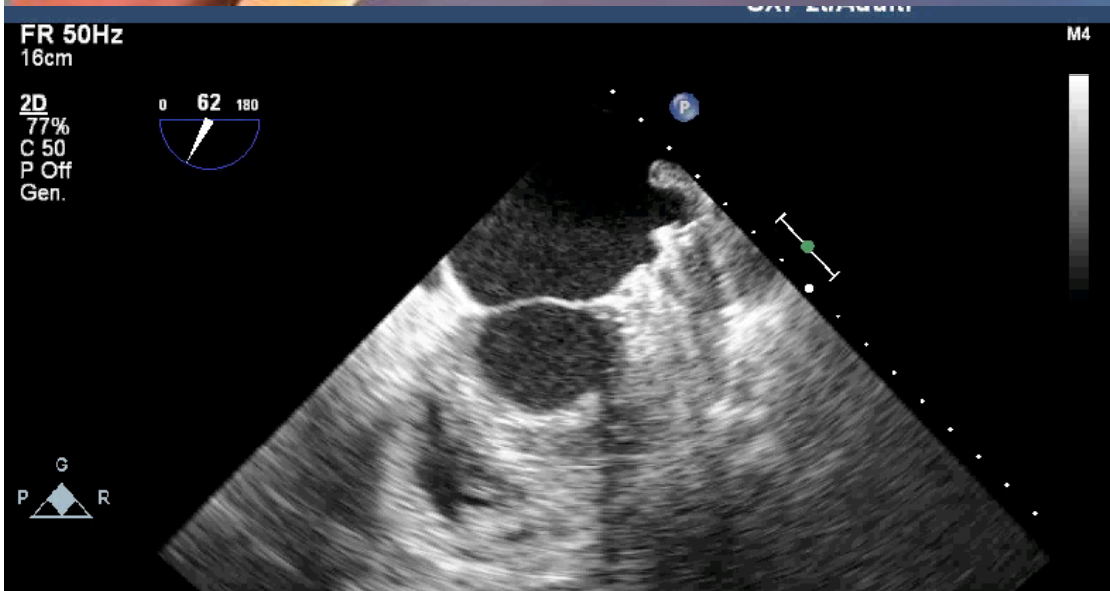


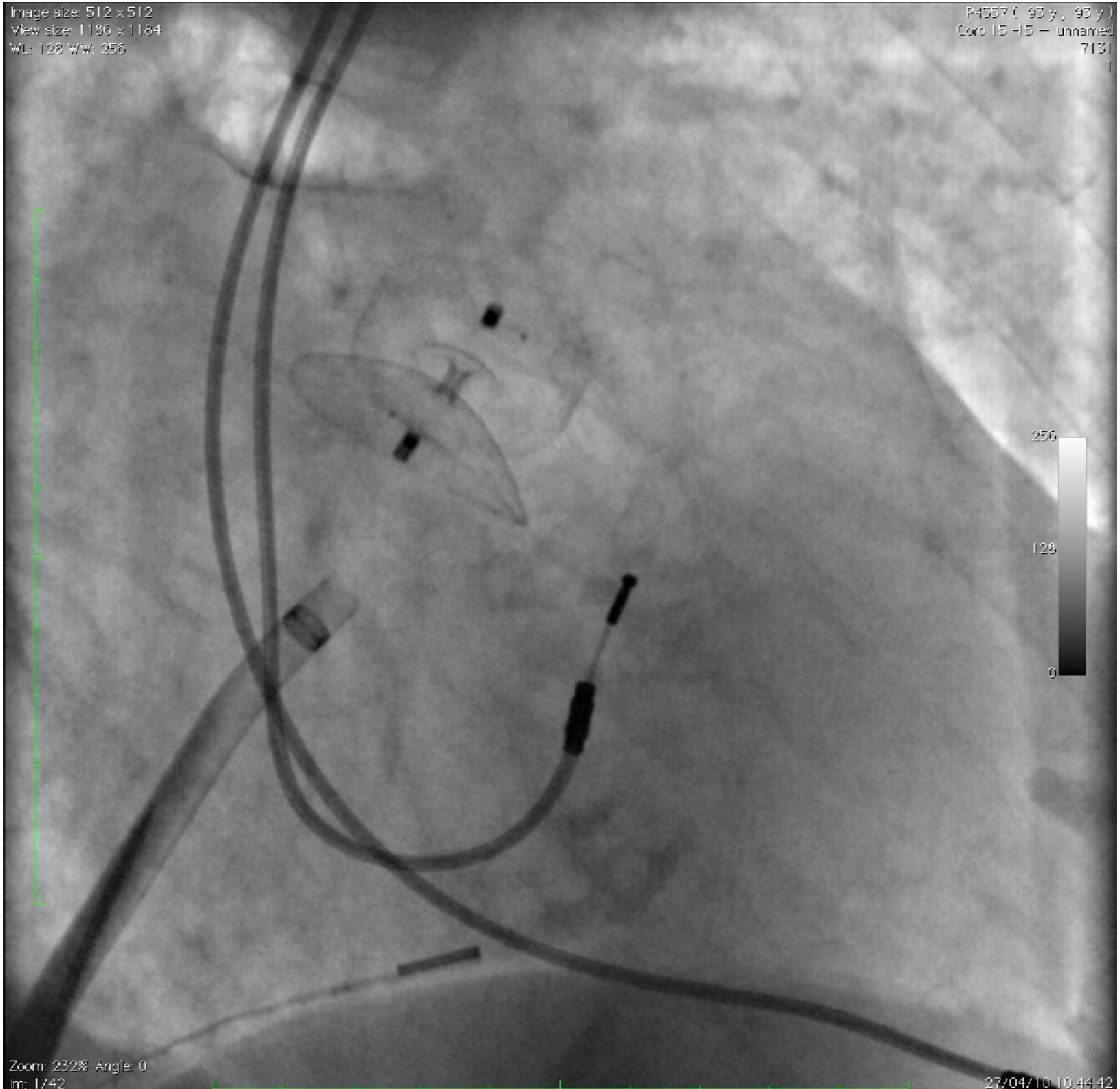
Release Criteria Details (PASS)



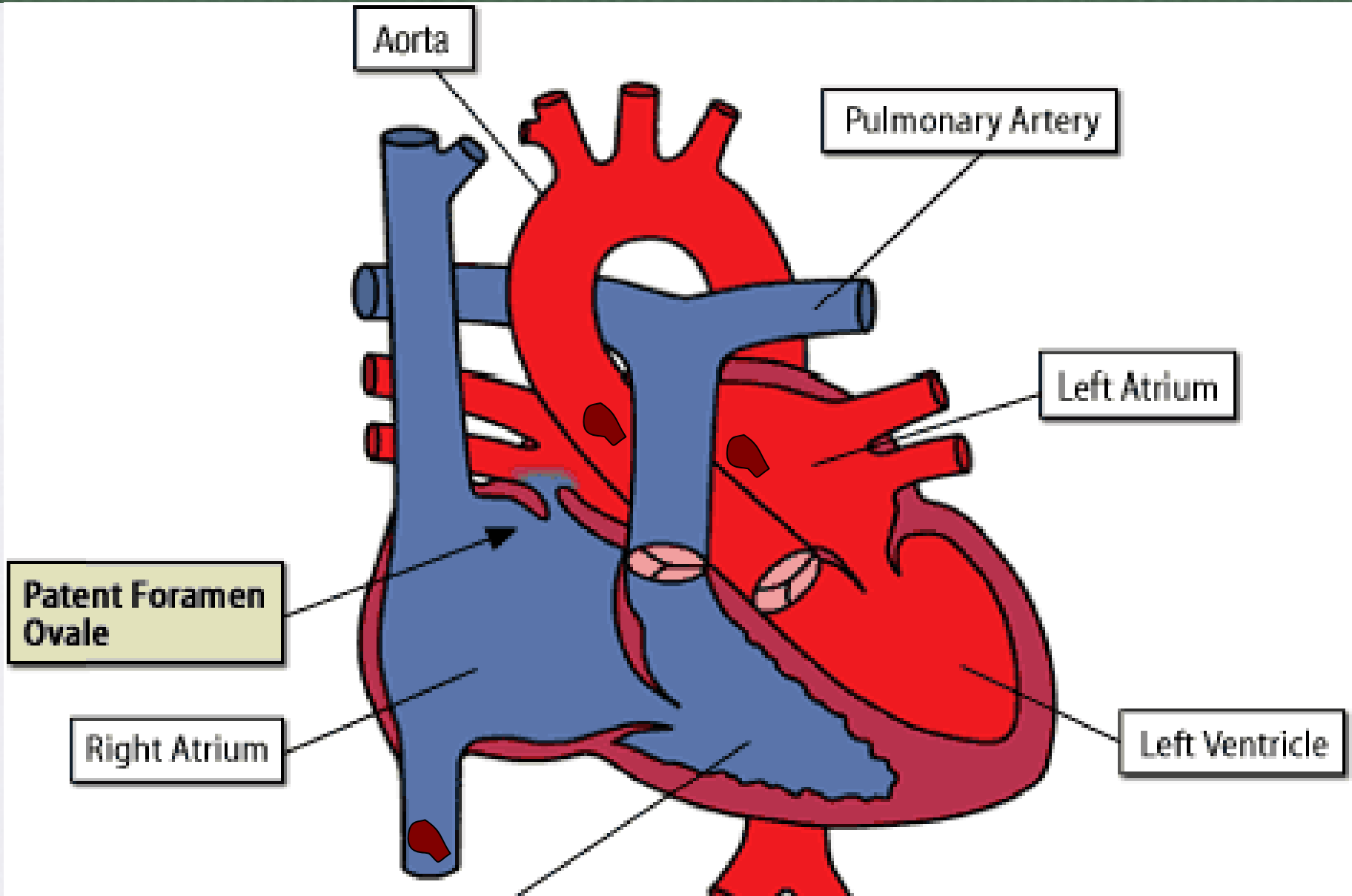







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Pervietà del Forame Ovale: embolia paradossa

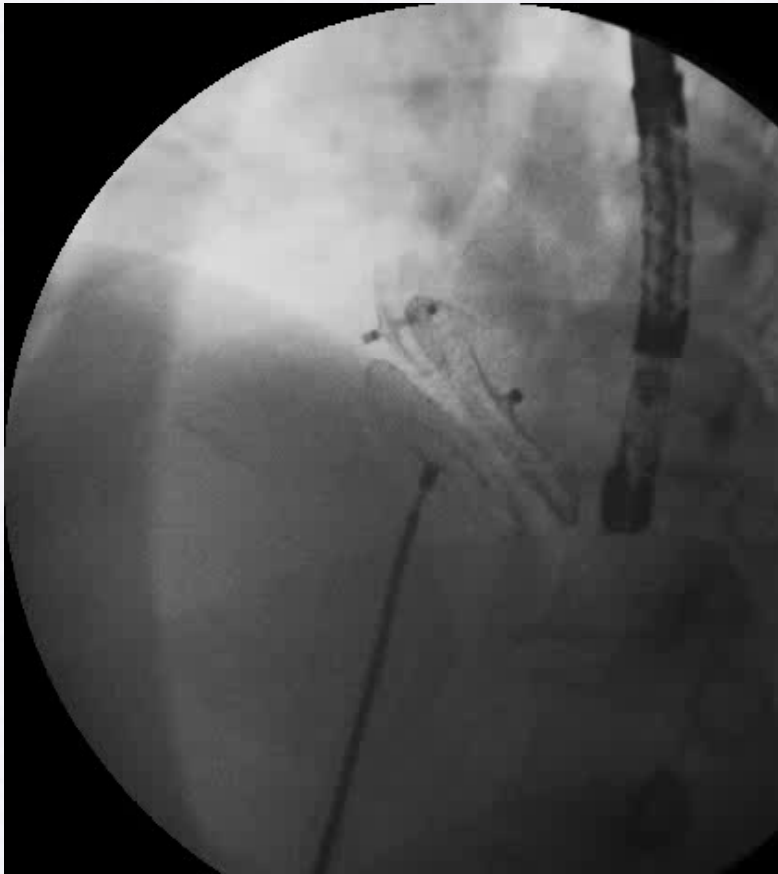


Meccanismi di stroke

Embolia paradossa a partenza da TVP

→ dimostrata in 5-10% casi

Trombosi in situ nel “tunnel”

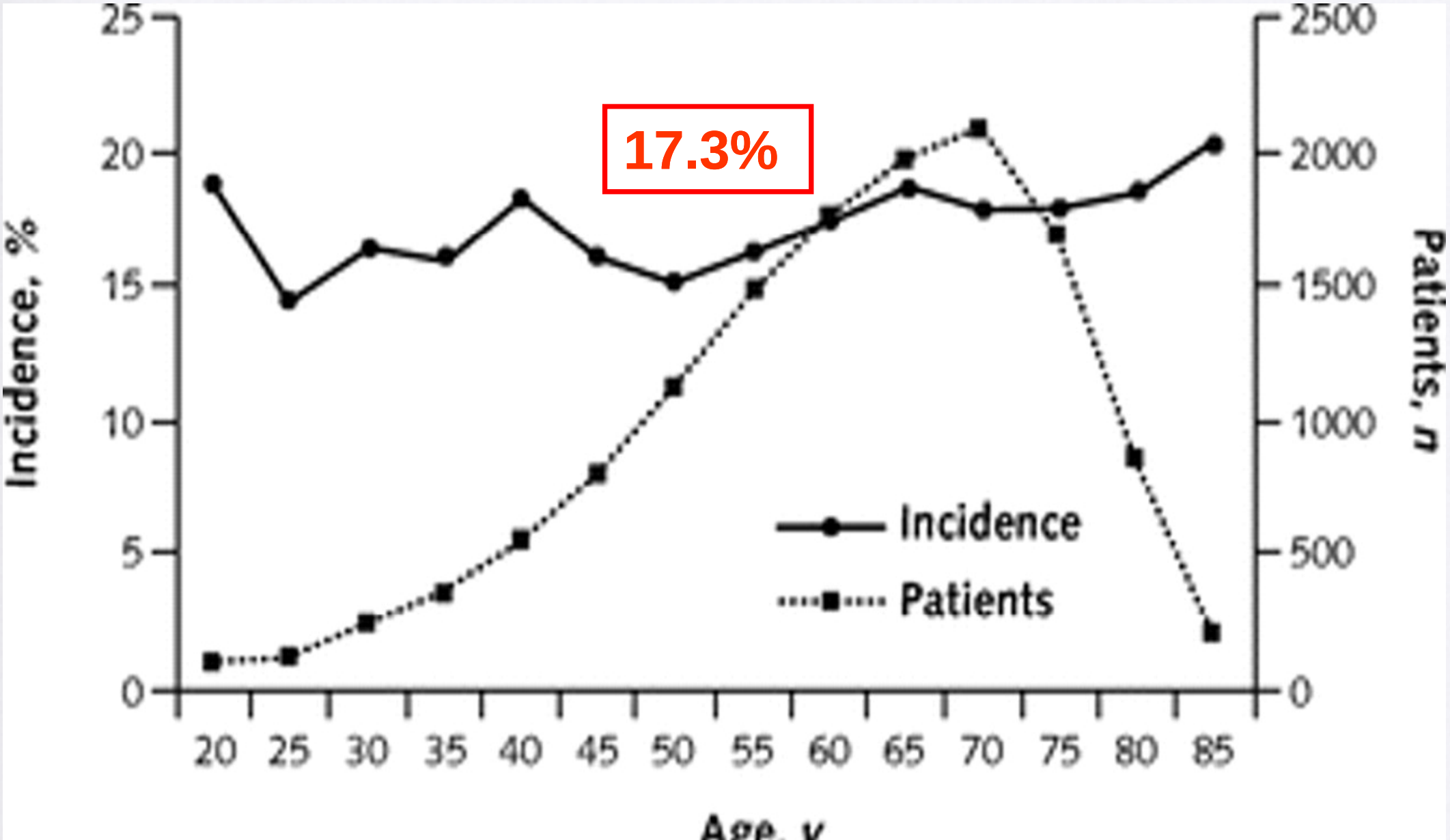


Aritmie atriali

Stato di ipercoagulabilità

Prevalenza nella "popolazione generale"

Incidence of asymptomatic patent foramen ovale, by age, in 13 261 patients undergoing cardiothoracic surgery





ei pazienti con ictus ischemico o TIA e forame ovale ervio, esenti da trombosi venose profonde e al primo vento tromboembolico è indicato il trattamento con ASA

Nei casi di ictus o TIA e:

–FOP associato ad ASI e primo evento;
–FOP e TVP o diatesi trombofilica;
–FOP isolato, con shunt di grosse dimensioni, e multipli eventi ischemici;

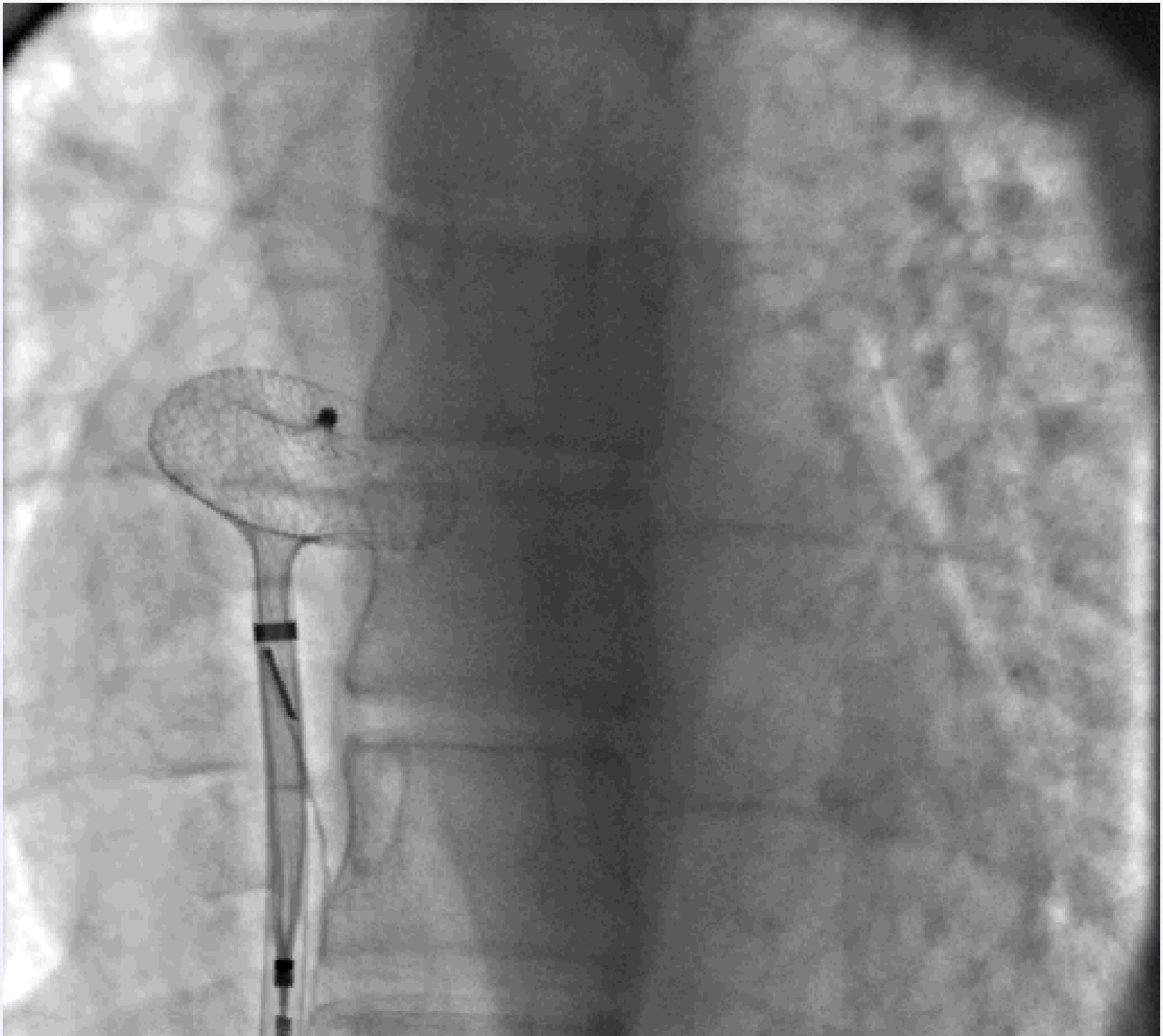
dopo avere escluso altre eziologie è indicato scegliere, sulla base del rapporto tra rischi e benefici, tra terapia anticoagulante (INR 2-3) e la chiusura transcatetere



ei casi di ictus o TIA e:

FOP associato ad ASI al primo evento ma con TVP o diate
ombofiliche controindicazioni alla TAO;
FOP con sintomatologia recidivante nonostante TAO;

opo avere escluso altre eziologie è indicata la chiusu
anscatetere, in caso di fallimento, la chiusura chirurgica



RESPECT

CLINICAL TRIAL

RANDOMIZED EVALUATION OF RECURRENT STROKE COMPARING PFO CLOSURE TO ESTABLISHED CURRENT STANDARD OF CARE TREATMENT

JOHN D. CARROLL, MD, JEFFREY L. SAVER, MD, DAVID E. THALER, MD, PH
RICHARD W. SMALLING, MD, PHD, SCOTT BERRY, PHD, LEE A. MACDONAL
MD, DAVID S. MARKS, MD, MBA, DAVID L. TIRSCHWELL, MD

ubpopulation Differential Treatment Effect

roup	Device Group	Medical Group	Hazard Ratio and 95% CI		Pvalue (Log Rank)
	no. of patients/total number (%)				
	9/499 (1.8%)	16/481 (3.3%)		0.492 (0.217, 1.114)	0.0825
	4/230 (1.7%)	5/210 (2.4%)		0.698 (0.187, 2.601)	0.5901
	5/262 (1.9%)	11/266 (4.1%)		0.405 (0.140, 1.165)	0.0828
	5/268 (1.9%)	10/268 (3.7%)		0.448 (0.153, 1.311)	0.1321
	4/231 (1.7%)	6/213 (2.8%)		0.571 (0.161, 2.024)	0.3789
e or moderate	7/247 (2.8%)	6/244 (2.5%)		1.034 (0.347, 3.081)	0.9527
al	2/247 (0.8%)	10/231 (4.3%)		0.178 (0.039, 0.813)	0.0119
al aneurysm					
	2/180 (1.1%)	9/169 (5.3%)		0.187 (0.040, 0.867)	0.0163
	7/319 (2.2%)	7/312 (2.2%)		0.889 (0.312, 2.535)	0.8259
t topography					
l	5/280 (1.8%)	12/269 (4.5%)		0.366 (0.129, 1.038)	0.0487
p	2/57 (3.5%)	1/70 (1.4%)		1.762 (0.156, 19.93)	0.6429
	2/157 (1.3%)	3/139 (2.2%)		0.558 (0.093, 3.340)	0.5167
dical regimen					
lant	4/132 (3.0%)	3/121 (2.5%)		1.141 (0.255, 5.098)	0.8628

onclusion

r carefully selected patients with history of cryptogenic stroke and
O, the RESPECT Trial provides evidence of benefit in stroke risk
luction from closure with the AMPLATZER PFO Occluder over medic
nagement alone

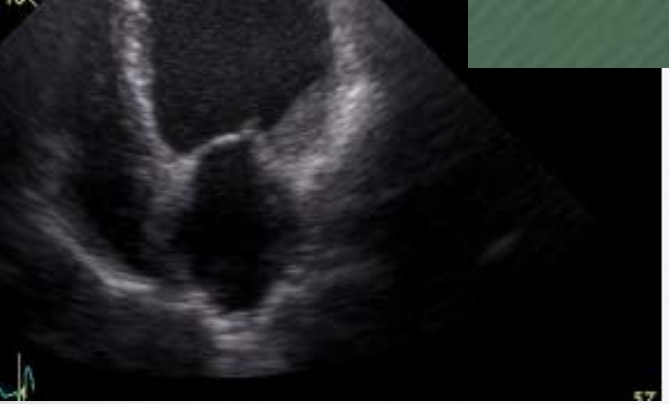
rimary analysis of ITT cohort was not statistically significant but trended
wards superiority while secondary analyses suggested superiority

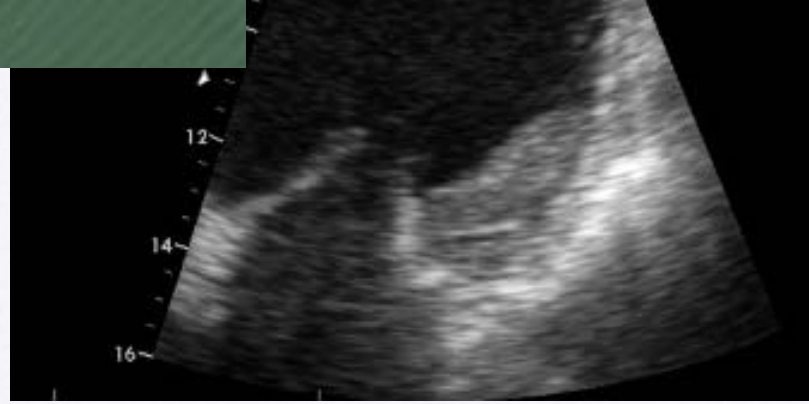
troke risk reduction was observed across the totality of analyses with rate
anging from 46.6% - 72.7%

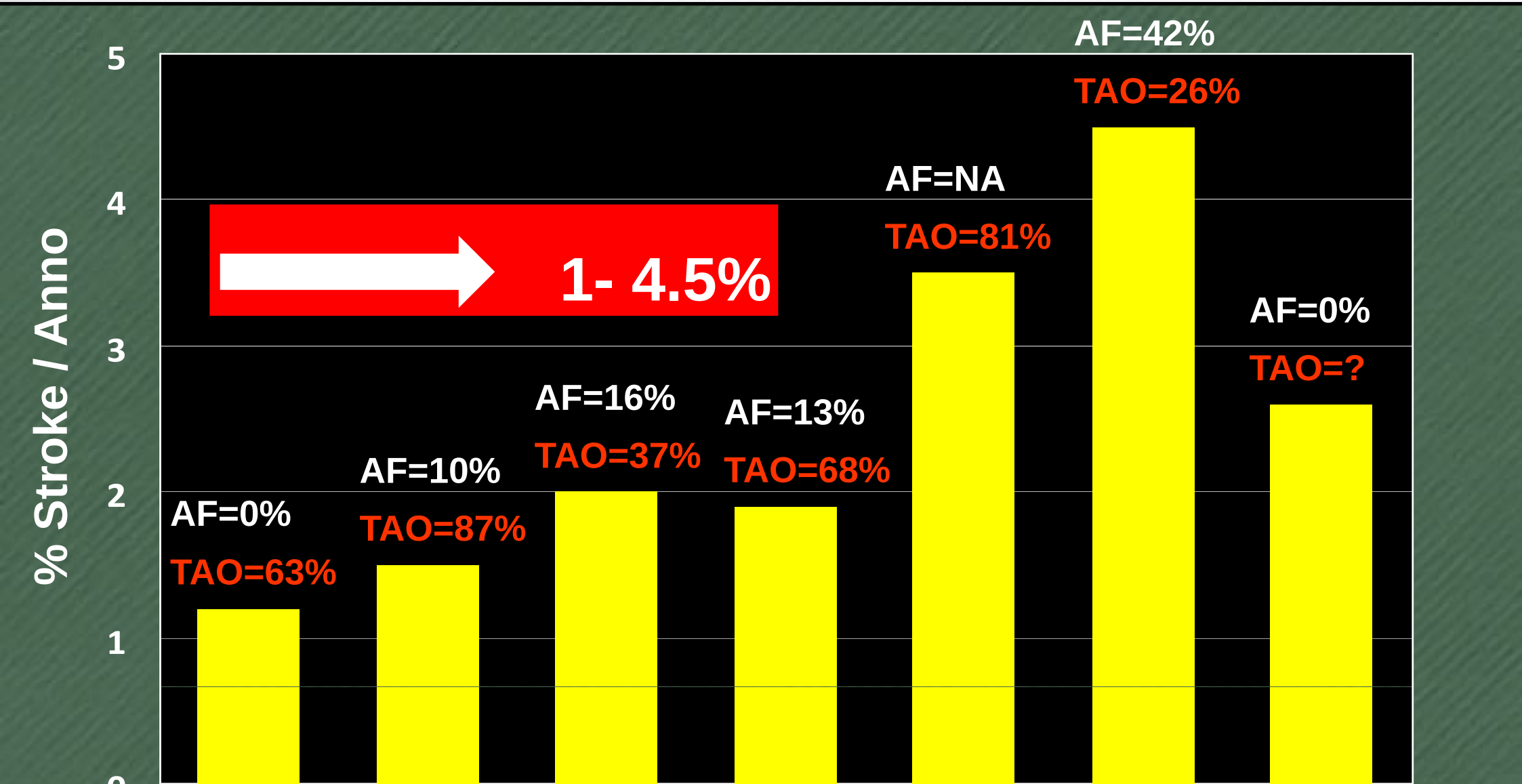
O closure with the AMPLATZER PFO Occluder exposes patients to a
y low risk of device- or procedure-related complications

sults of the RESPECT Trial have substantial import for the treatment
tients with a history of cryptogenic stroke and PFO

low-up of patients is on-going and will continue to provide additional
ger term information regarding benefits, risks, and differential






% Stroke / Anno
5
4
3
2
1
1- 4.5%
AF=0%
TAO=63%
AF=10%
TAO=87%
AF=16%
TAO=37%
AF=13%
TAO=68%
AF=NA
TAO=81%
AF=42%
TAO=26%
AF=0%
TAO=?

Quali sono i fattori di rischio?

- Fibrillazione atriale
- Storia di tromboembolia (9-10%/aa)
- Trombosi ventricolare sinistra
- Severità dello scompenso
- Entità della disfunzione VS
- Sesso femminile
- Eziologia ischemica vs non ischemica

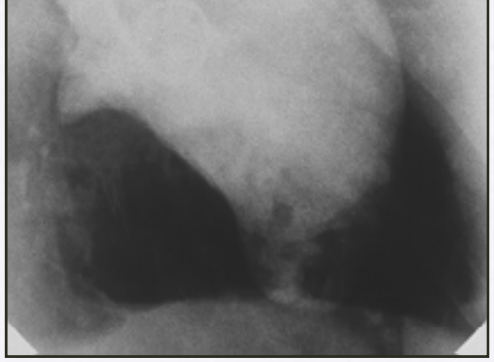
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

Increased embolic risk in patients with left ventricular thrombi.

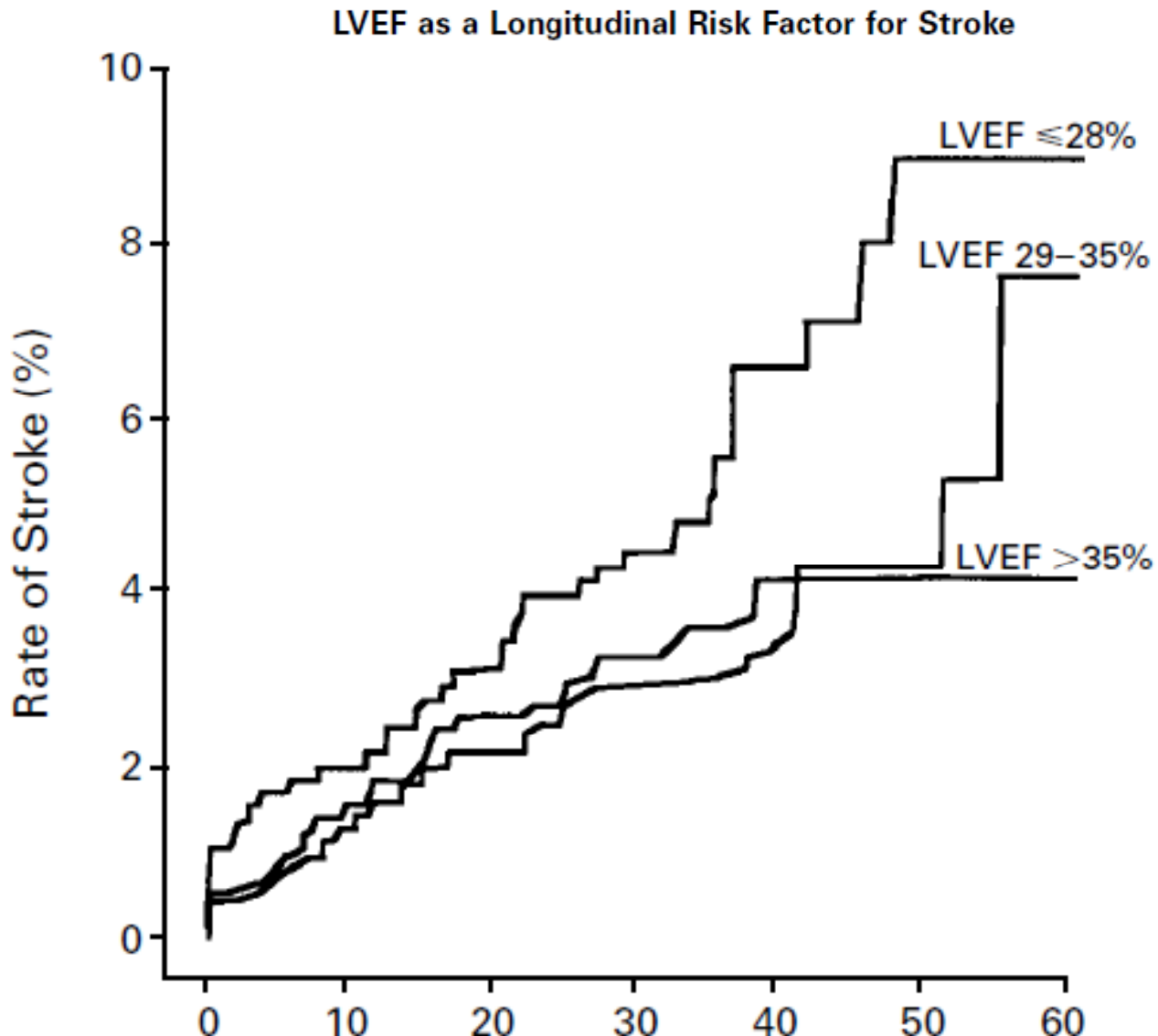
J R Stratton and A D Resnick

Circulation. 1987;75:1004-1011



ABSTRACT Although left ventricular thrombi are associated with an increased embolic risk in th first few weeks after acute myocardial infarction, the long-term risk remains undefined. To ascertai the incidence of strictly defined systemic emboli, we followed 85 patients with echocardiographicall documented left ventricular thrombi. At the time of the entry echocardiogram, most patients (n = 57 had remote myocardial infarction, while 19 had recent (<1 month) infarction, and nine had idiopathi cardiomyopathy. Because of the difficulty in classifying events as embolic in patients with advance atherosclerosis, a matched control group of 91 patients without thrombi was also studied. The thrombu and control groups were similar with regard to recent myocardial infarction, remote infarction, anterio infarction, ejection fraction, atrial fibrillation, echocardiographic referral for source of emboli, an warfarin therapy. During a mean follow-up of 22 months after echocardiography, embolic event occurred in 13% (11 of 85) of patients with thrombi compared with 2% (two of 91) of control patients (< .01). The actuarial probability of being embolus free at 2 years after echocardiography was 86% i patients with thrombi compared with 97% in control patients ($p < .01$). All embolic events occurre greater than 1 month after myocardial infarction (range 1 to 96 months). The only clinical or echocar diographic features predictive of embolization were protrusion and mobility of thrombus (both p < .02). We conclude that the incidence of embolic events is definitely increased in patients with le ventricular thrombi compared with control subjects during long-term follow-up. The increased emboli risk is not restricted to the immediate postinfarction period, documenting that chronic thrombi continu to embolize. Whether long-term anticoagulation can reduce the embolic rate with an acceptable risk c bleeding remains to be determined.

VENTRICULAR DYSFUNCTION AND THE RISK OF STROKE AFTER MYOCARDIAL INFARCTION



ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

1.3 Thrombo-embolism prophylaxis

ombo-embolism prophylaxis in patients with HF and AF should based on the Cardiac failure, Hypertension, Age ≥75 ubled), Diabetes, Stroke (Doubled)-Vascular disease, Age 74 and Sex category (Female) (CHA_2DS_2-VASc) score (see e 17), in keeping with the 2010 ESC AF guidelines.[166,179] t patients with systolic HF will have a risk score consistent a firm indication for (score ≥2), or preference for, an oral coagulant (score = 1), although bleeding risk must also be con- red (see below).

Table 17 Assessment of stroke risk in patients v atrial fibrillation

CHA_2DS_2-VASc	
Congestive HF or LVEF ≤40%	1
Hypertension	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke, transient ischaemic attack, or thrombo-embolism	2
Vascular disease (previous myocardial infarction, peripheral artery disease, or aortic plaque)	1
Age 65–74 years	1
Sex category (i.e. female sex)	1
Maximum score	9
CHA_2DS_2-VASc score = 0: recommend no antithrombotic therapy.	
CHA_2DS_2-VASc score = 1: recommend antithrombotic therapy with or anticoagulation or antiplatelet therapy, but preferably oral anticoagulati	
CHA_2DS_2-VASc score = 2: recommend oral anticoagulation.	

CHA_2DS_2-VASc = Cardiac failure, Hypertension, Age ≥75 (Doubled), D

The Hypertension, Abnormal renal/liver function (1 point each), Stroke, Bleeding history or predisposition, Labile INR, Elderly (>65), Drugs/alcohol concomitantly (1 point each) (HAS-BLED score) (*Table 18*) is recommended to assess bleeding risk, in keeping with the 2010 ESC AF guidelines.[166,180] A substantial proportion of patients with HF will have a score ≥3, indicating that careful consideration should be given before prescribing an oral anticoagulant and that regular review is needed (and correctable risk factors addressed) if an oral anticoagulant is given.

Some new anticoagulant drugs such as the oral direct thrombin inhibitors and oral factor Xa inhibitors are contraindicated in severe renal impairment (creatinine clearance <30 mL/min).[181–183] This is clearly a concern in many patients with HF and, if these drugs are used, serial monitoring of renal function is required. There is no known way to reverse the anticoagulant action of these new drugs.

Quali pz trattare con TAO?

Warfarin is reccomended:

with HF and permanent, persistent or paroxismal AF **(without contraindicat**

s I, level of evidence A

ents with intracardiac thrombus detected by imaging or evidence of syste
ization

s I, level of evidence C

atients with severe systolic disfunction ??? ⟶ WATCH, WAR

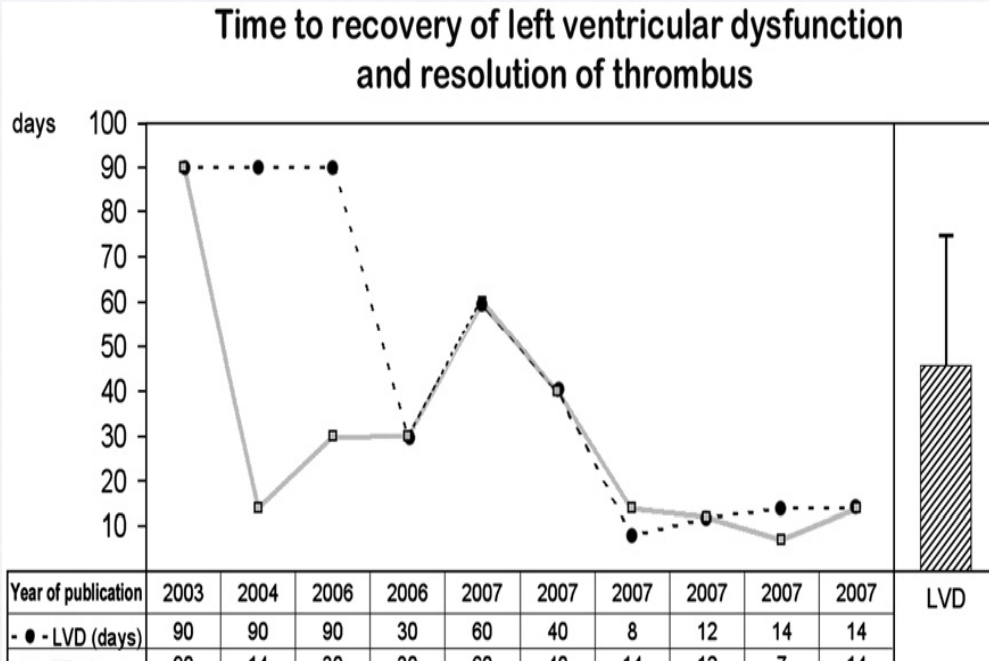
atients with *high risk cardiomyopathy (n.c. non compaction cmp)* ???

Trombosi ventricolare sn

00 casi descritti di Takotsubo (2.5%)
complicanze cardiemboliche (0.8%)



years)	64.3±12.1
en (%)	86.7
F mean value (%)	37.6±7.7
tion of thrombus	apex
thrombus (%)	46.7
v. of LV dysfunction (days)	41.4±34.9
lution of TF (days)	28.9±25.9
mic embolization (%)	33.3



K-dependent clotting factors II, VII, IX, X and anticoagulant proteins C and S, while dabigatran directly inhibits factor II (thrombin). Here are some of the other important differences for you to consider:

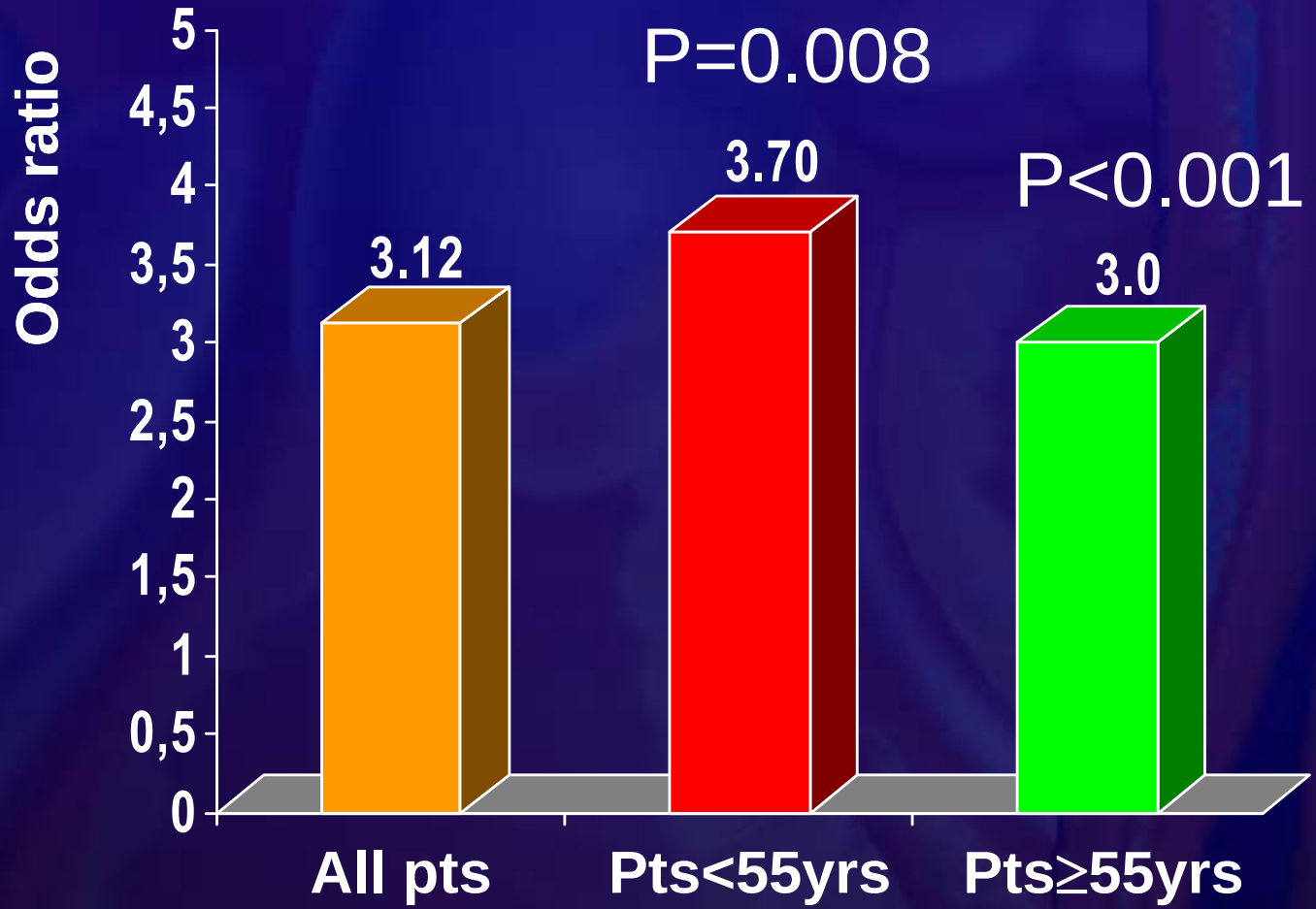
	Coumadin® (warfarin)	**Pradaxa® (dabigatran etexilate)**
	Variable; dosed once daily to target INR range	150 mg twice daily
lation	Tablet	Capsule
e	**36 hours**	**12-17 hours** in normal renal function
y Route of ation	Hepatic	Renal (80%) • **Avoid** or need dose adjustment for CrCl 15-30 mL/min • **CONTRAINDICATED** in CrCl <15 mL/min
onitoring	Yes	None – THE INR is NOT adequately sensitive to the effects of dabigatran
Laboratory	No	Yes—renal function monitoring at baseline and then

	Coumadin® (warfarin)	Pradaxa® (dabigatran etexilate)
se	Variable; dosed once daily to target INR range	150 mg twice daily
		Dabigatran has effects on the aPTT –but results CANNOT be used to guide management. The Ecarin clotting time (ECT) and Thrombin Time (TT are the most sensitive laboratory methods to assess dabigatran effects in urgent clinical situations. Their routine use is NOT indicated.
ecial Diet	Intake of Vitamin K-containing foods must be consistent	No
ecial medication structions	No	Do not chew, break, or open capsules as this increase bioavailability by 75% Take with food if dyspepsia occurs Once medication bottle has been opened, must use within 30 days
ug Interactions	Many	Few Avoid concomitant use of dabigatran and rifampin or other P-gp inducers (interaction results in decreased efficacy of dabigatran due to p-glycoprotein induction

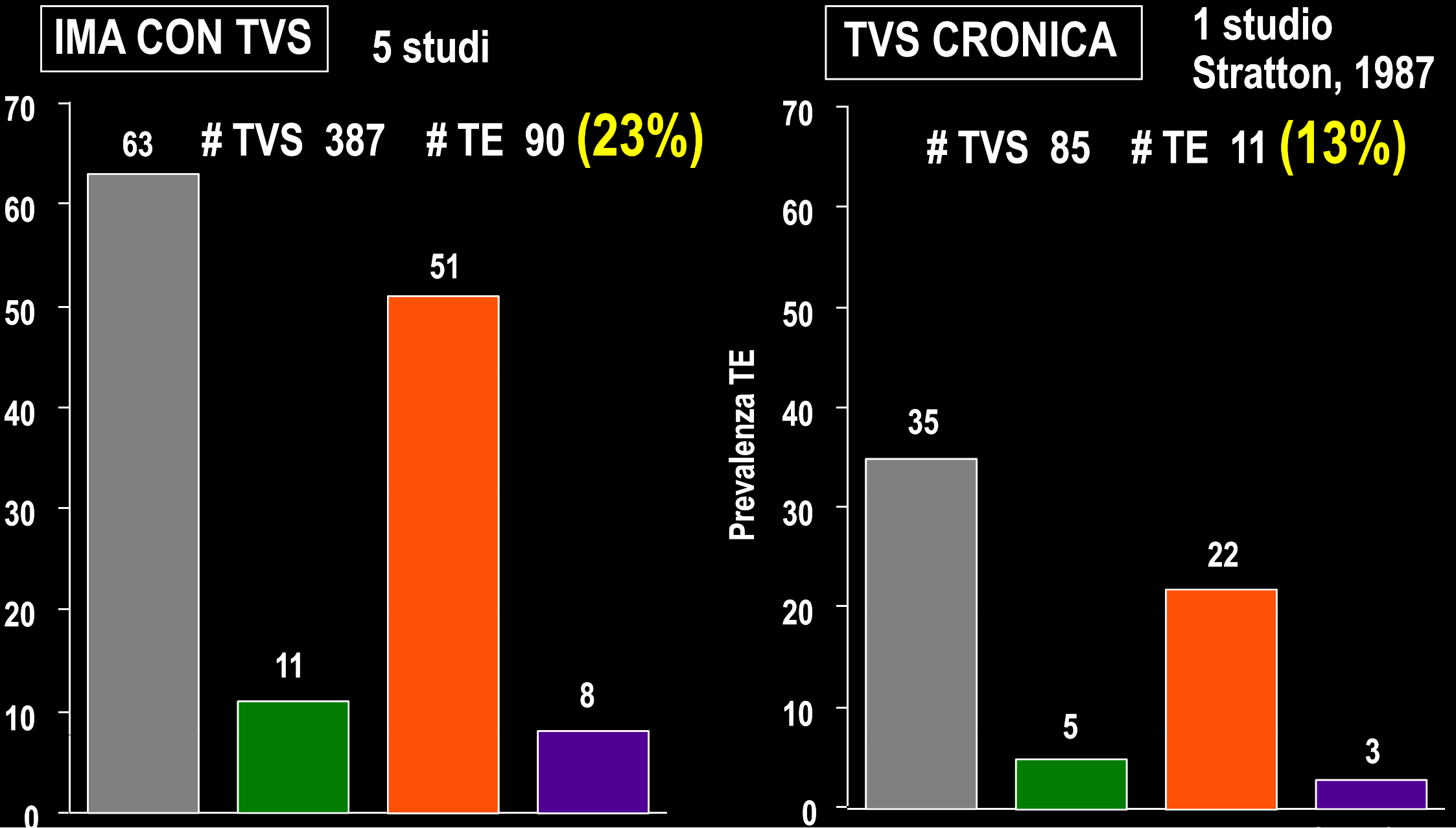
PFO e stroke criptogenetico

Patent foramen Ovale and cryptogenetic stroke in older patient

503 pts (227 cryptogenetic stroke; 276 stroke of known cause



Trombosi ventricolare sn



Entità della disfunzione Vsn

