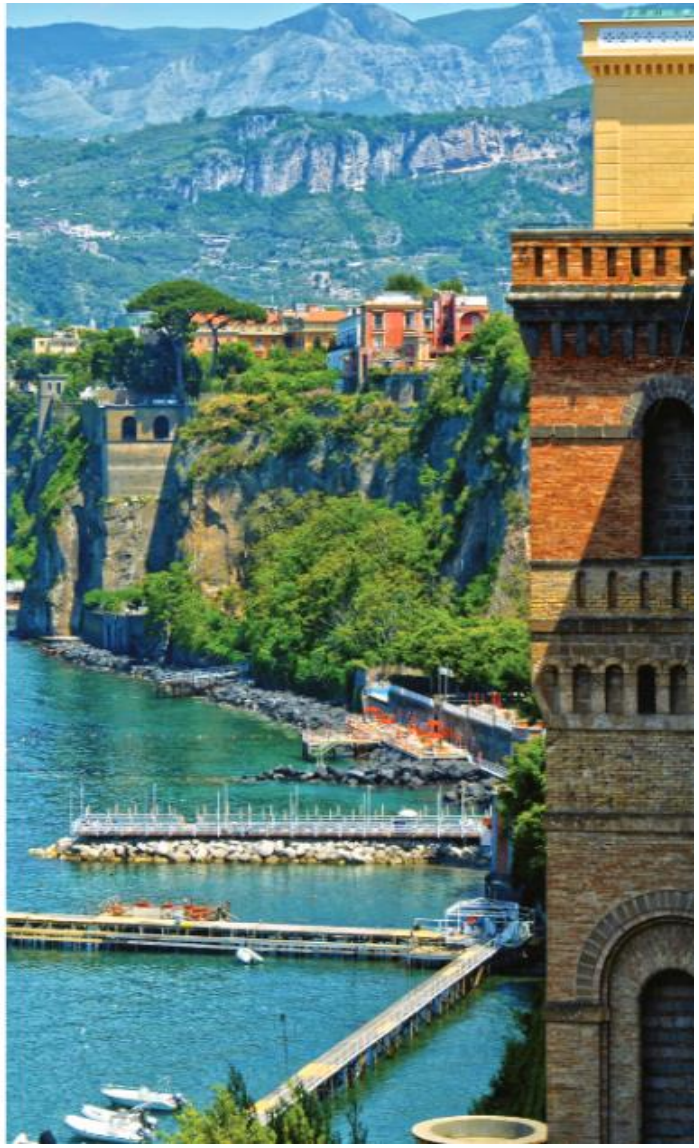
XXIX
CONGRESSO
NAZIONALE
ANCE



10 - 13 OTTOBRE 2019

Centro Congressi
Hilton Sorrento Palace
Sorrento (NA)

Terapia anticoagulante nella fibrillazione atriale:

nuove prospettive terapeutiche...
quello che le linee guida non dicono

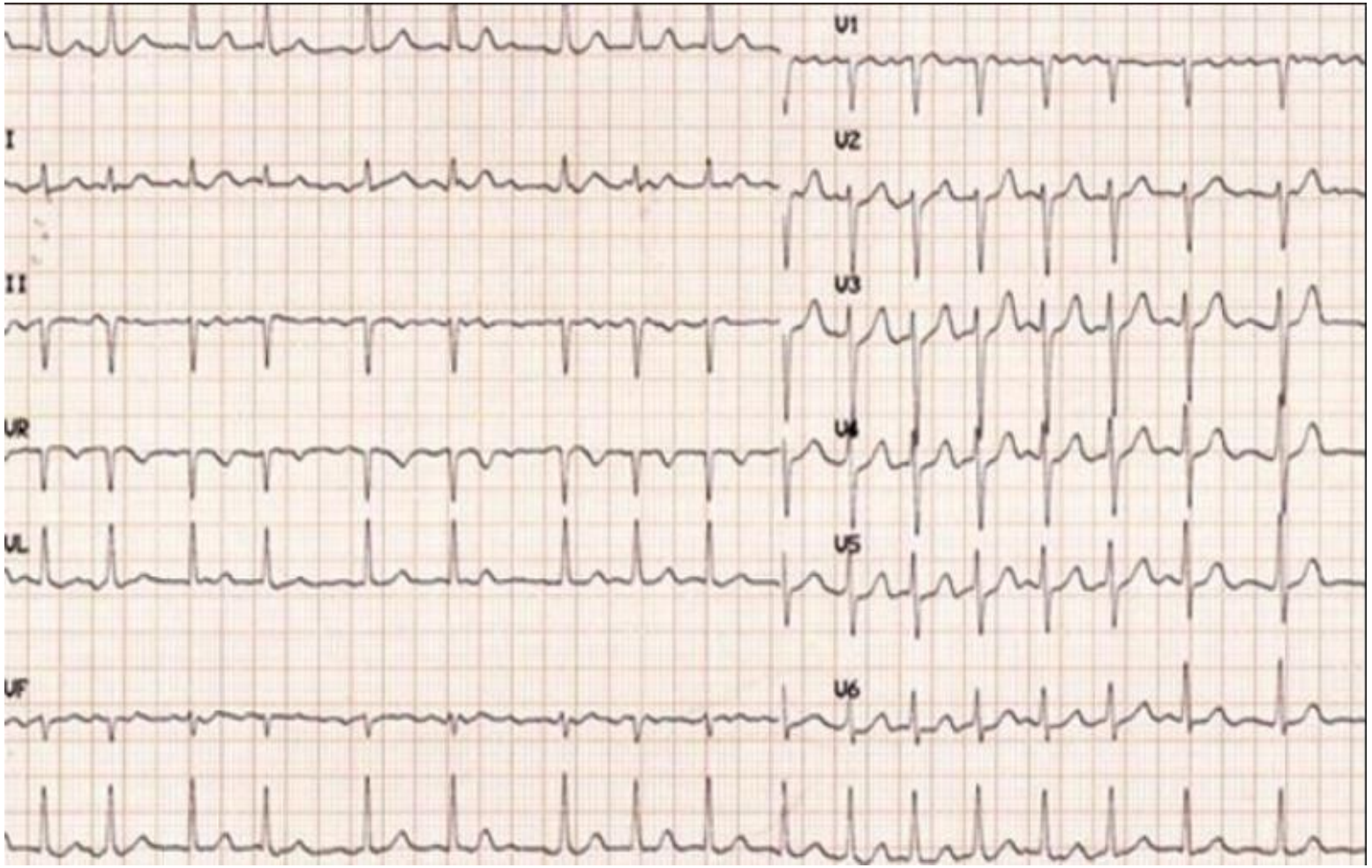
Dr. Ivana Pariggiano

Paziente di 70 anni U

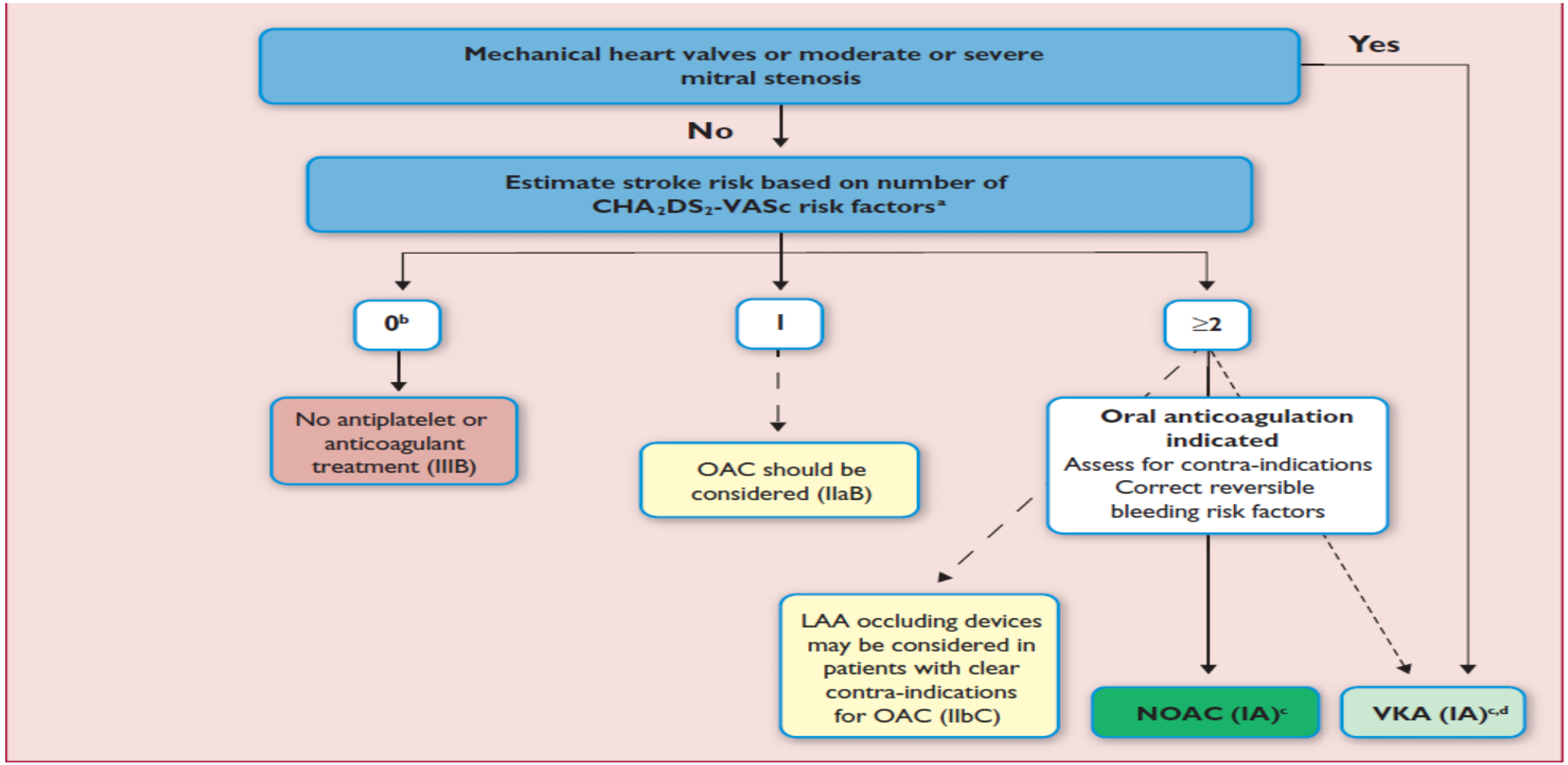
- Familiarità per CAD
- Ipertensione arteriosa sistemica
- Diabete mellito tipo 2,

Storia di palpitazioni da alcuni mesi

ECG Holter si documentano episodi di FA



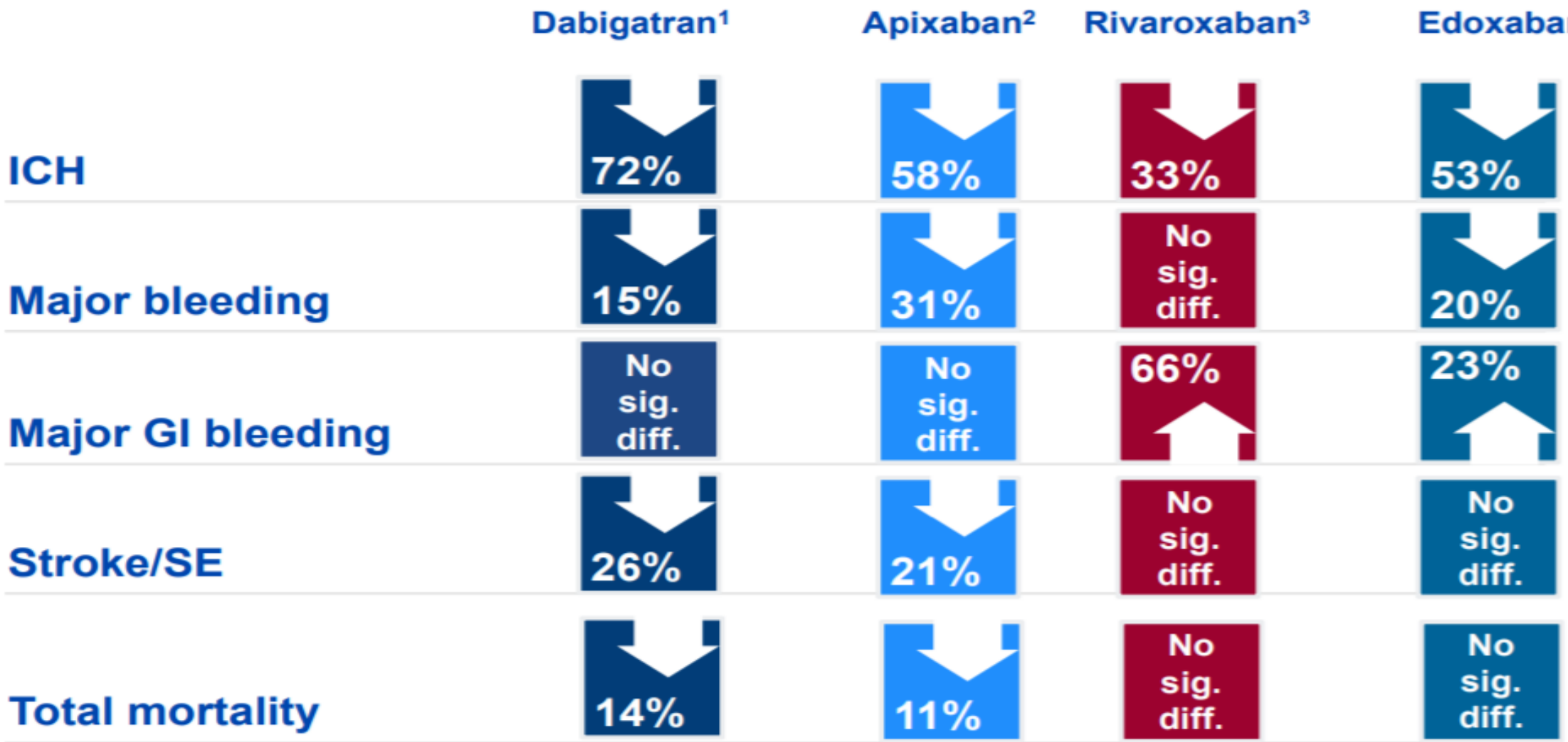
2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS



AF = atrial fibrillation; LAA = left atrial appendage; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulation; VKA = vitamin K antagonist.
[a]Congestive heart failure, Hypertension, Age ≥75 years (2 points), Diabetes, prior Stroke/TIA/embolus (2 points), Vascular disease, age 65–74 years, female Sex.
[b]Includes women without other stroke risk factors.
[c]IIaB for women with only one additional stroke risk factor.
[d]IB for patients with mechanical heart valves or mitral stenosis.

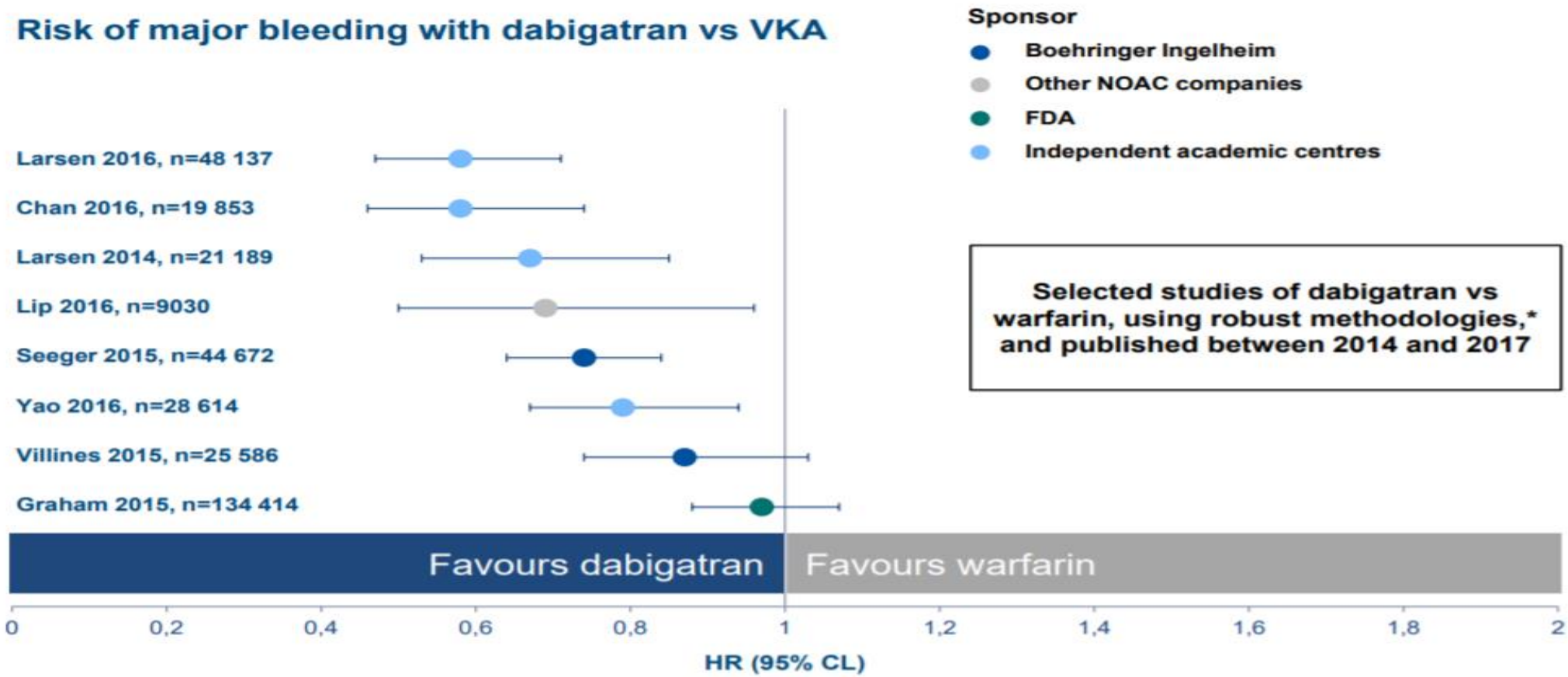
European Heart Journal, Volume 37, Issue 38, 7 October 2016

Risk reductions vs warfarin



1. Lip GY et al. Thromb Haemost 2014; 2. Granger CB et al. NEJM 2011; 3. Patel MR et al. NEJM 2011; 4. Giugliano RP et al. NEJM 2013

Practice-Based Data Consistently Confirm the Favourable Safety Profile of Dabigatran vs Warfarin



*Robustness assessed based on sample size, new-user design, use of propensity score matching, and/or adjustment for patient characteristics. Sample sizes for comparison of dabigatran vs warfarin; Definition of major bleeding may differ across studies.

Recommendations for stroke prevention in patients with atrial fibrillation

Recommendations	Class[a]	Level[b]	Ref[c]
Oral anticoagulation therapy to prevent thromboembolism is recommended for all male AF patients with a CHA_2DS_2-VASc score of 2 or more.	I	A	38, 318–321, 354, 404
Oral anticoagulation therapy to prevent thromboembolism is recommended in all female AF patients with a CHA_2DS_2-VASc score of 3 or more.	I	A	38, 318–321, 354, 404
Oral anticoagulation therapy to prevent thromboembolism should be considered in male AF patients with a CHA_2DS_2-VASc score of 1, considering individual characteristics and patient preferences.	IIa	B	371, 375–377
Oral anticoagulation therapy to prevent thromboembolism should be considered in female AF patients with a CHA_2DS_2-VASc score of 2, considering individual characteristics and patient preferences.	IIa	B	371, 376, 377
Vitamin K antagonist therapy (INR 2.0–3.0 or higher) is recommended for stroke prevention in AF patients with moderate-to-severe mitral stenosis or mechanical heart valves.	I	B	274, 435–440
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a vitamin K antagonist.	I	A	39, 318–321, 404
When patients are treated with a vitamin K antagonist, time in therapeutic range (TTR) should be kept as high as possible and closely monitored.	I	A	395, 432, 441-444
AF patients already on treatment with a vitamin K antagonist may be considered for NOAC treatment if TTR is not well controlled despite good adherence, or if patient preference without contra-indications to NOAC (e.g. prosthetic valve).	IIb	A	39, 318, 319, 404, 408
Combinations of oral anticoagulants and platelet inhibitors increase bleeding risk and should be avoided in AF patients without another indication for platelet inhibition.	III (harm)	B	429, 445
In male or female AF patients without additional stroke risk factors, anticoagulant or antiplatelet therapy is not recommended for stroke prevention.	III (harm)	B	368, 371, 376, 377
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III (harm)	A	38, 429, 430
NOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) are not recommended in patients with mechanical heart valves (Level of evidence B) or moderate-to-severe mitral stenosis (Level of evidence C).	III (harm)	B C	318–321, 400, 404

AF = atrial fibrillation; CHA_2DS_2-VASc = Congestive Heart failure, hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex (female); INR = international normalized ratio; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulation; TTR = time in therapeutic range; VKA = vitamin K antagonist.

[a]Class of recommendation.

[b]Level of evidence.

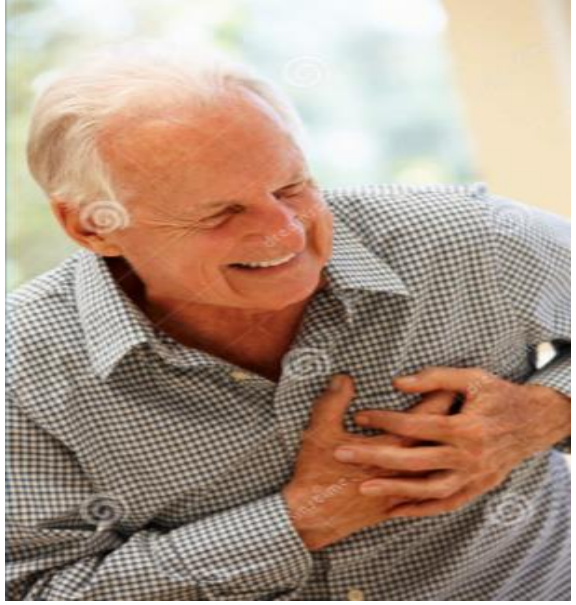
[c]Reference(s) supporting recommendations.

European Heart Journal, Volume 37, Issue 38, 7 October 2016

- CHA2DS2VASc: 3
- HASBLED 2
- eGFR: 58 ml/min
- Ecocardiogramma : Vss ipertrofico con funzione sistoloca no , assenza di valvulopatie , atrio lievemente dilatato,

- Inizio Terapia con **Dabigatran 150 mg x 2**

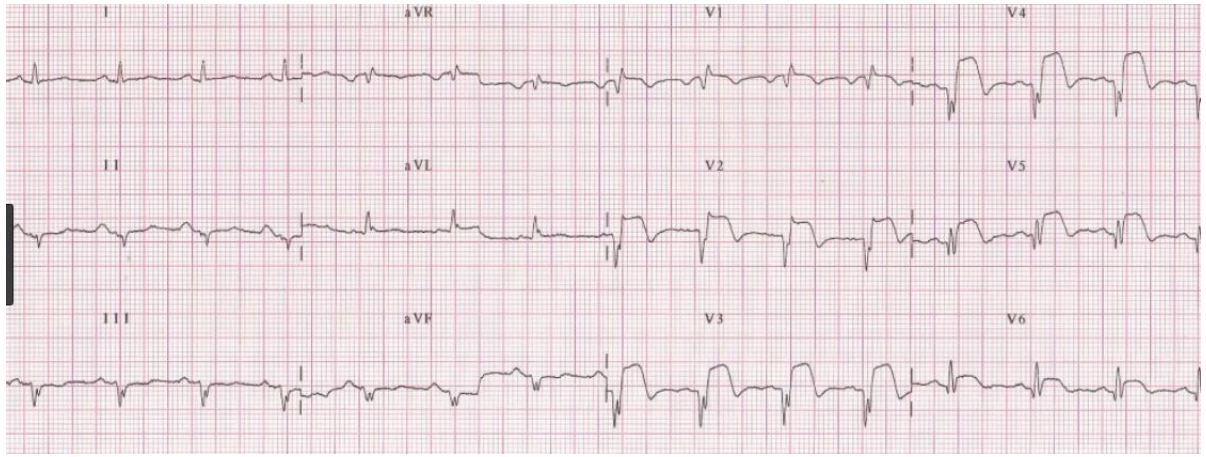
- A 3 anni Infarto acuto miocardico

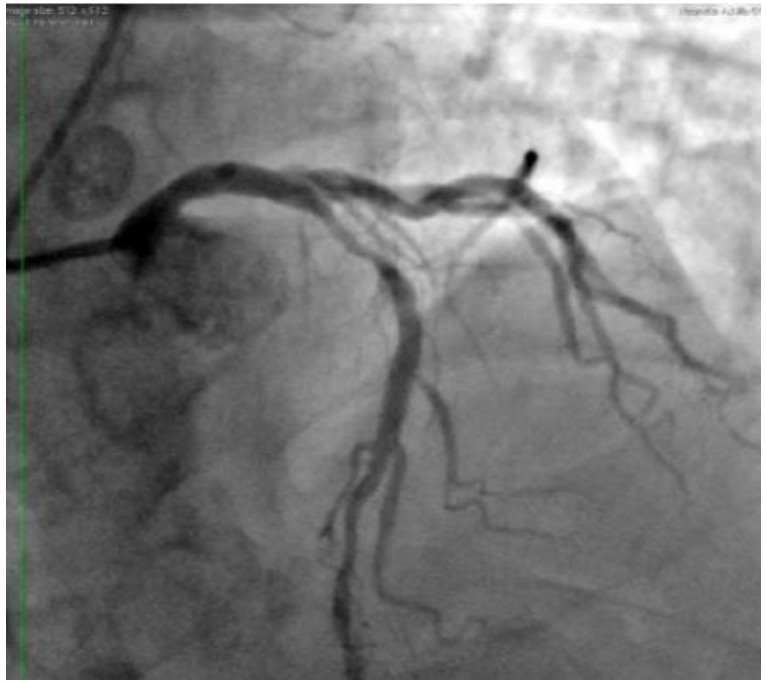


L’esame coronarografico evidenza di

malattia ostruttiva significativa IVA ,che viene trattata

Con **impianto di 2 DES** , con buon risultato angiografico finale.





Il problema:

The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

The current understanding is that DAPT is necessary to prevent stent thrombosis but not sufficient for stroke prevention,[307] and vice versa, that (N)OAC are essential for stroke prevention but on their own not suitable for preventing new coronary events, especially in the acute/subacute setting.[3] A combination of at least one antiplatelet agent in addition to (N)OAC is recommended for up to 12 months after an ACS event and/or stenting procedure according to the most recent ESC guidelines on AF,[3] ST-elevation myocardial infarction (STEMI),[33] and the use of antiplatelet agents.[32]

LE LINEE GUIDA

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

2018 ESC/EACTS Guidelines on myocardial revascularization

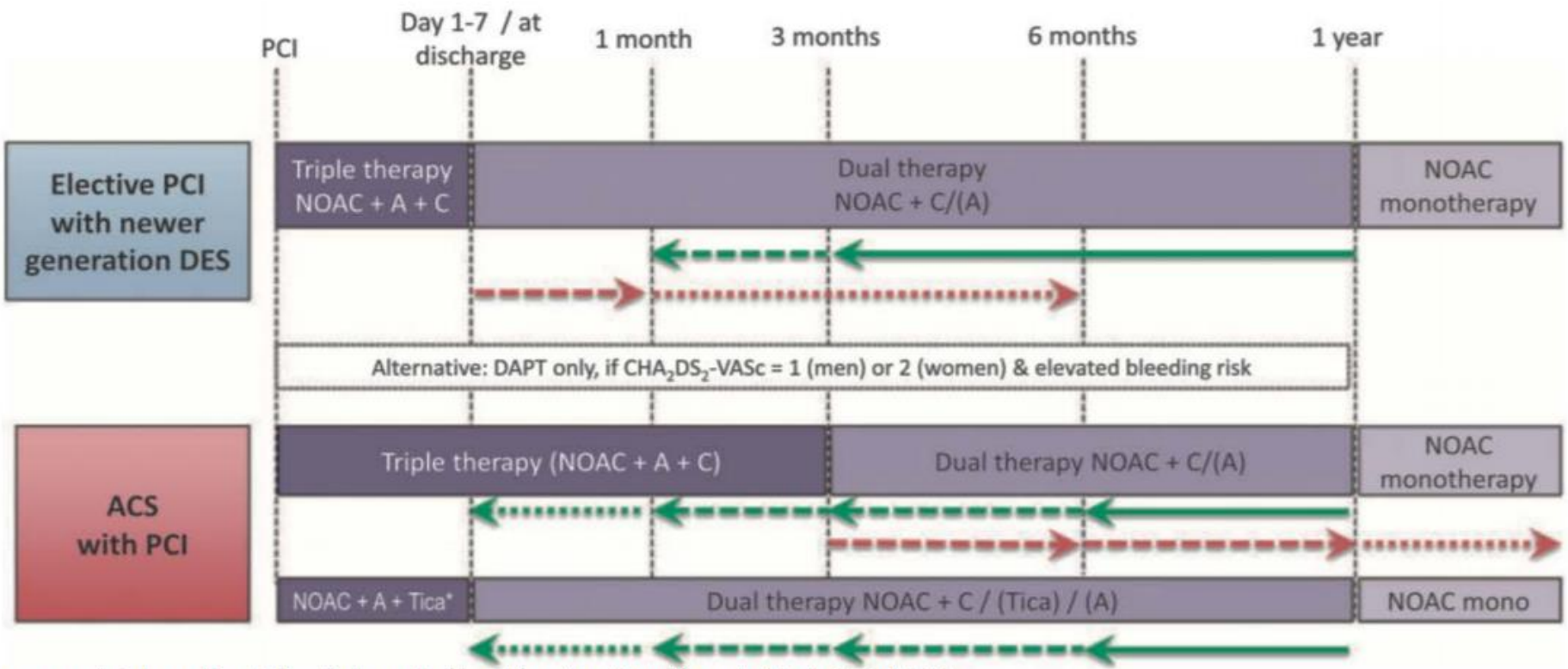
rancesco Messina, San Carlo Borromeo e i deputati ospedalieri

DAPT E NOAC , CHE FARE?

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

Table 4 Strategies to avoid bleeding complications in patients treated with oral anticoagulant

• Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA_2DS_2-VASc, ABC, HAS-BLED) with a focus on modifiable risk factors.
• Keep triple therapy duration as short as possible; dual therapy after PCI (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.
• Consider the use of NOACs instead of VKA.
• Consider a target INR in the lower part of the recommended target range and maximize time in therapeutic range (i.e. > 65–70%) when VKA is used.
• Consider the lower NOAC regimen tested in approval studies and apply other NOAC regimens based on drug-specific criteria for drug accumulation.[a]
• Clopidogrel is the $P2Y_{12}$ inhibitor of choice.
• Use low-dose (≤ 100 mg daily) aspirin.
• Routine use of PPIs.



If triple therapy needs to be continued after discharge clopidogrel is preferred over ticagrelor (due to lack of data).

Factors to shorten combination therapy

- (Uncorrectable) high bleeding risk
- Low atherothrombotic risk (by REACH or SYNTAX score if elective; GRACE ≥140 if ACS)

Factors to lengthen combination therapy

- First-generation DES
- High atherothrombotic risk (scores as above ; stenting of the left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk

The 2018 European Heart Rhythm Associatio Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

EHRA Guidelines 2018

Randomized clinical trial evidence for non-vitamin K antagonist oral anticoagulants post-percutaneous coronary intervention

agents.[141,308] In essence, these trials focus on bleeding as the primary endpoint, and are underpowered to address relatively rare ischaemic/thromboembolic events including stroke, re-infarction and stent thrombosis. A meta-analysis combining WOEST, PIONEER AF-PCI, and RE-DUAL PCI suggests that the likelihood of an excess of thromboembolic events during dual therapy vs. triple therapy is low.[309] The two ongoing NOAC in AF trials, AUGUSTUS (NCT02415400) and ENTRUST-AF PCI (NCT02866175)[310] will add further information on how and how long (if at all) triple anticoagulation should be administered.

The NEW ENGLAND JOURNAL of MEDICINE

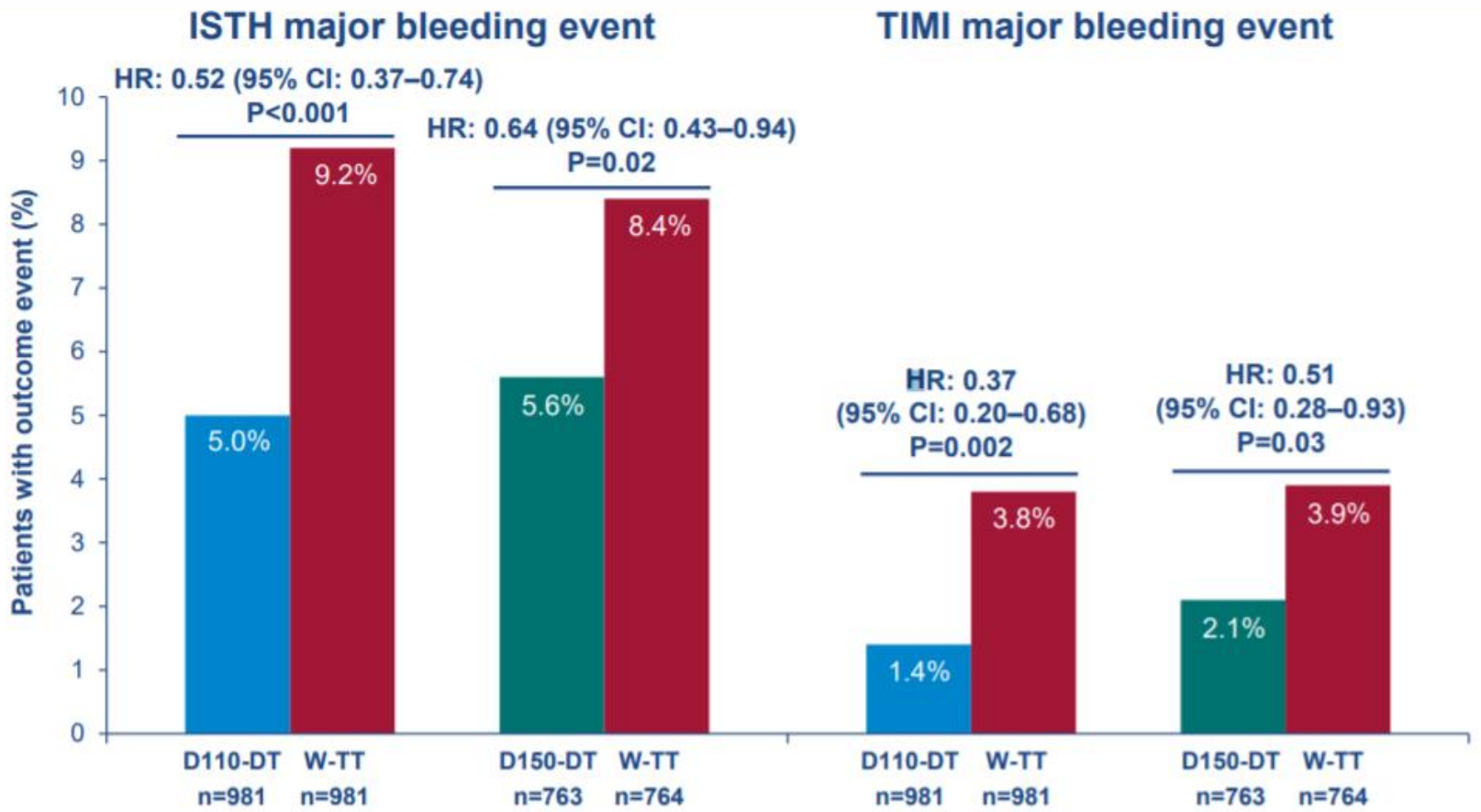
ESTABLISHED IN 1812 OCTOBER 19, 2017 VOL. 377 NO. 16

Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation

RE-DUAL

- Studio multicentrico di confronto fra triplice terapia con wafarin o duplice con dabigatran (110x2 o 150x2) + P2Y12 (no ASA)
- End poit primario = major o non major bleeding
- Confronto di non inferiorita' per eventri tromboembolici compositi (IMA, stroke, embolie sistemiche). Sottodimensionato per valutare trombosi stent
- Risultati:
- - Gruppo duplice ha meno beeding e non inferiorita' per eventi trombotici compositi

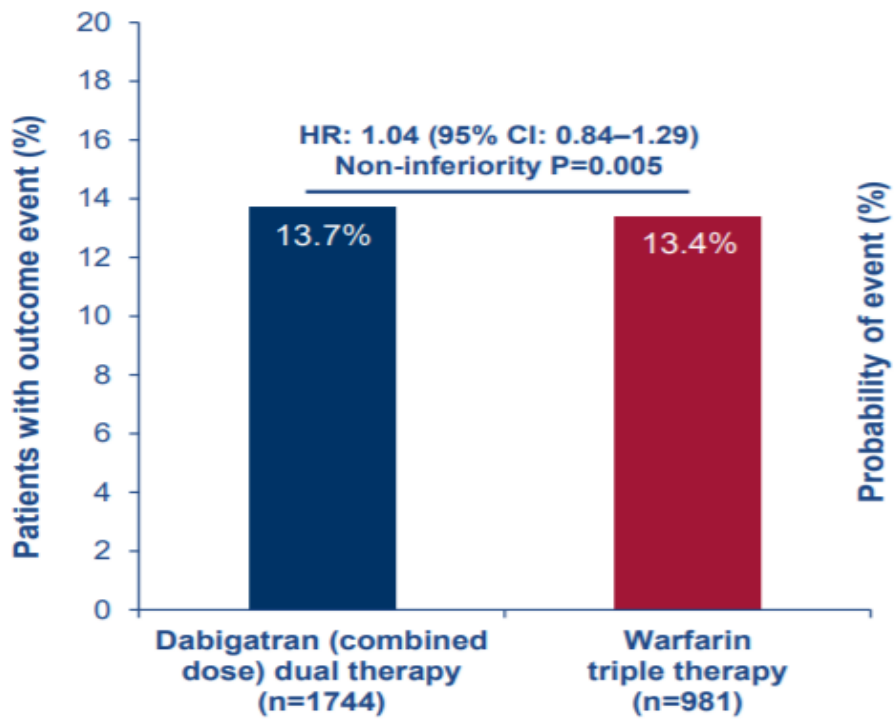
ISTH and TIMI major bleeding: significantly lower rates for dabigatran dual therapy

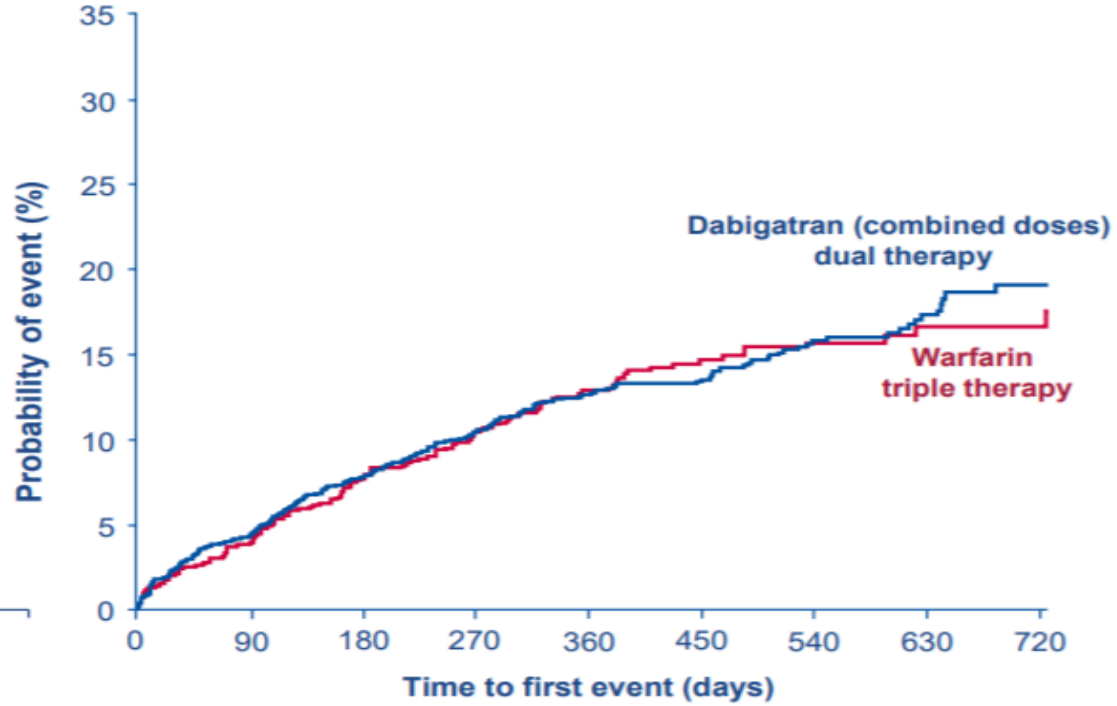


ISTH major bleeding definition: fatal, critical organ (including ICH), clinically overt bleeding with fall in Hb ≥2 g/dL; TIMI major bleeding definition: fatal, ICH, clinically overt bleeding with fall in Hb ≥5 g/dL. D110/150-DT, dabigatran 110 mg/150 mg dual therapy; ISTH, International Society on Thrombosis and Haemostasis; TIMI, Thrombolysis in Myocardial Infarction; W-TT, warfarin triple therapy; Cannon et al. N Engl J Med 2017

Dabigatran dual therapy was non-inferior to warfarin triple therapy

Composite endpoint of death or thromboembolic event (MI, stroke or systemic embolism) or unplanned revascularization (PCI/CABG)





CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; Cannon et al. N Engl J Med 2017;

- Ai controlli cardiologici , si evidenza un dilatazione ventricolare sinistra e riduzione della funzione contrattile – FE 25%

- Cardiopatia dilatativa post ischemica, dopo terapia medica ottimizzata

, si decide per impianto ICD

Pazinete in NAO che indicazione a chirurgia elettiva

Table 12 Classification of elective surgical interventions according to bleeding risk

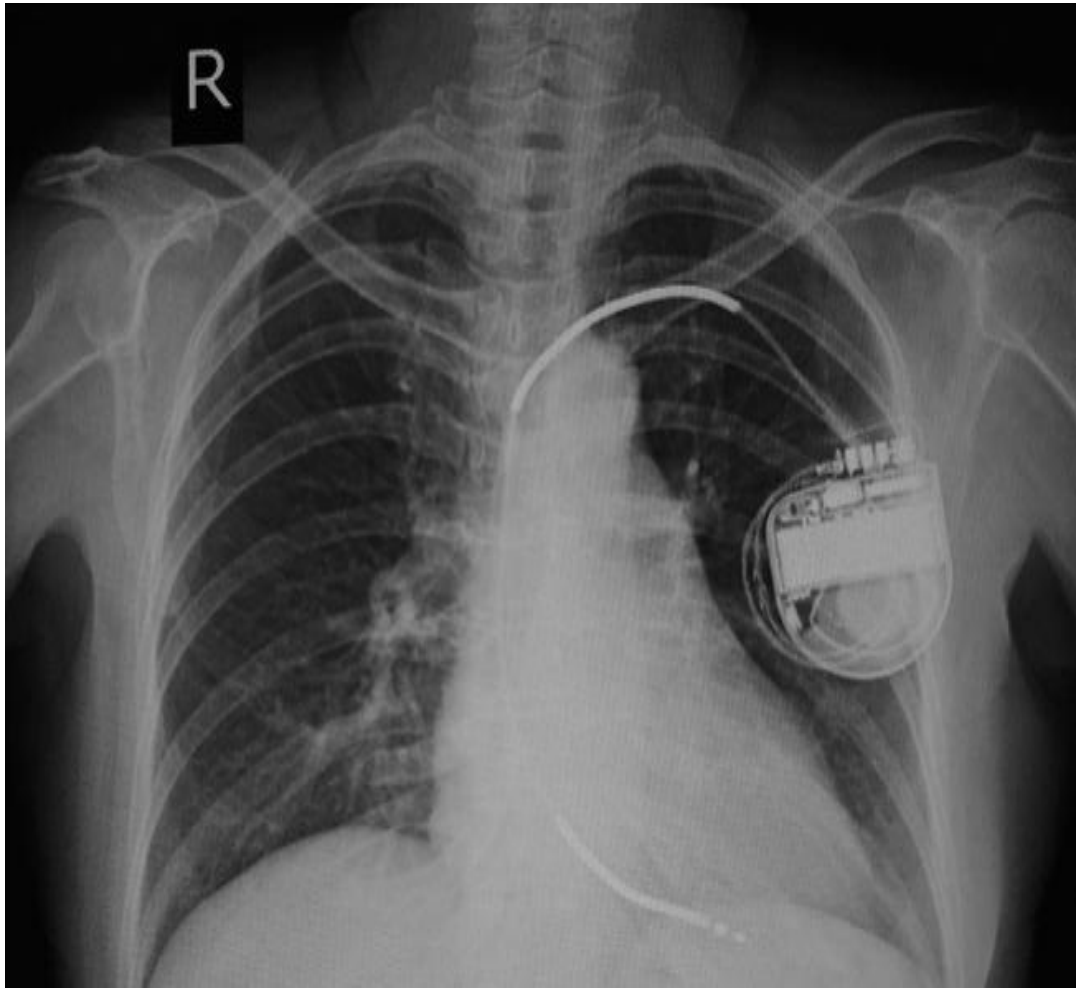
Interventions with minor bleeding risk
Dental interventions
Extraction of 1–3 teeth
Paradontal surgery
Incision of abscess
Implant positioning
Cataract or glaucoma intervention
Endoscopy without biopsy or resection
Superficial surgery (e.g. abscess incision; small dermatologic excisions; . . .)
Interventions with low bleeding risk (i.e. infrequent or with low clinical impact)
Endoscopy with biopsy
Prostate or bladder biopsy
Electrophysiological study or catheter ablation (except complex procedures, see below)
Non-coronary angiography (for coronary angiography and ACS: see Patients undergoing a planned invasive procedure, surgery or ablation section)
Pacemaker or ICD implantation (unless complex anatomical setting, e.g. congenital heart disease)
Interventions with high bleeding risk (i.e. frequent and/or with high impact)
Complex endoscopy (e.g. polypectomy, ERCP with sphincterotomy etc.)
Spinal or epidural anaesthesia; lumbar diagnostic puncture
Thoracic surgery
Abdominal surgery
Major orthopaedic surgery
Liver biopsy
Transurethral prostate resection

Table 11 Timing of last non-vitamin K antagonist oral anticoagulant intake before start of an elective intervention

	Dabigatran		Apixaban – Edoxaban – Rivaroxaban	
	No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. 12 h or 24 h after last intake)			
	Low risk	**High risk**	**Low risk**	**High risk**
CrCl ≥80 mL/min	≥24 h	≥48 h	≥24 h	≥48 h
CrCl 50–79 mL/min	≥36 h	≥72 h	≥24 h	≥48 h
CrCl 30–49 mL/min	≥48 h	≥96 h	≥24 h	≥48 h
CrCl 15–29 mL/min	Not indicated	Not indicated	≥36 h	≥48 h
CrCl <15 mL/min	No official indication for use			
No bridging with LMWH/UFH				
Resume full dose of NOAC ≥24 h post-low bleeding risk interventions and 48 (–72) h post-high-bleeding risk interventions (see also *Figure 8*)				
Patients undergoing a planned intervention should receive a written note indicating the anticipated date and time of their intervention, and the date and time of the last intake of their NOAC (and any other medication)				

Low risk: with a low frequency of bleeding and/or minor impact of a bleeding; high risk: with a high frequency of bleeding and/or important clinical impact. See also *Table 12*.
CrCl, creatinine clearance; LMWH, low molecular weight heparin; UFH, unfractionated heparin.

- Si ricovera presso una Clinica in cui si effettua impianto di ICD e inzia terapia riabilitativa



Terapia alla dimissione :

Bisoprololo 2,5 mg, Lasix 25 mg , Luvion 50 mg , Torvast 80 mg 1cp, **Dabigatran 150mg x2 /die**

Dopo la procedura……

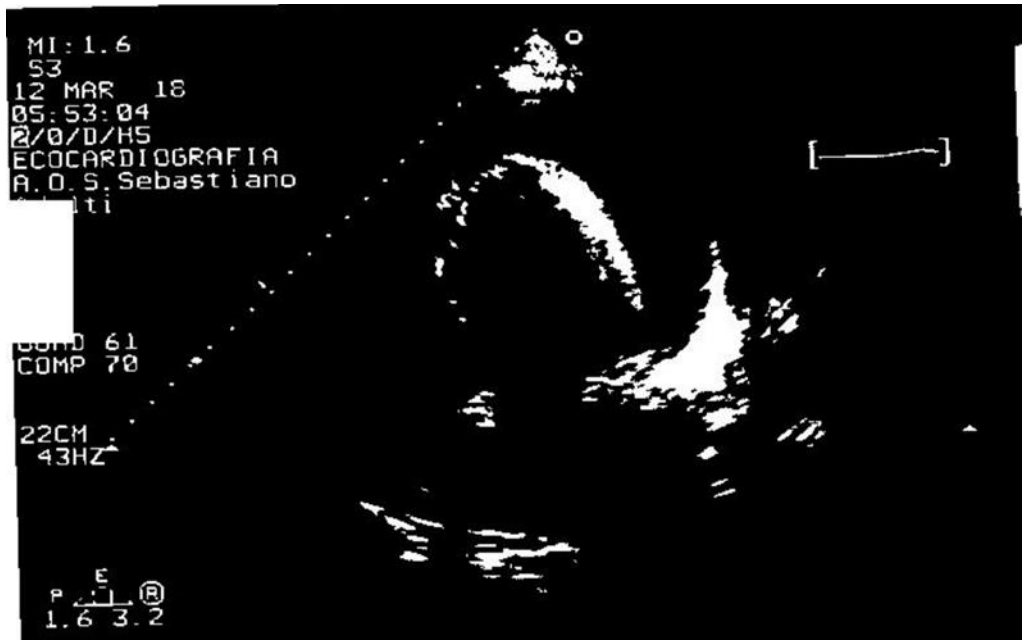
10 giorni dopo l’impianto, riferisce malessere , sudorazione , episodio sincopale nel tentativo di alzarsi dal letto

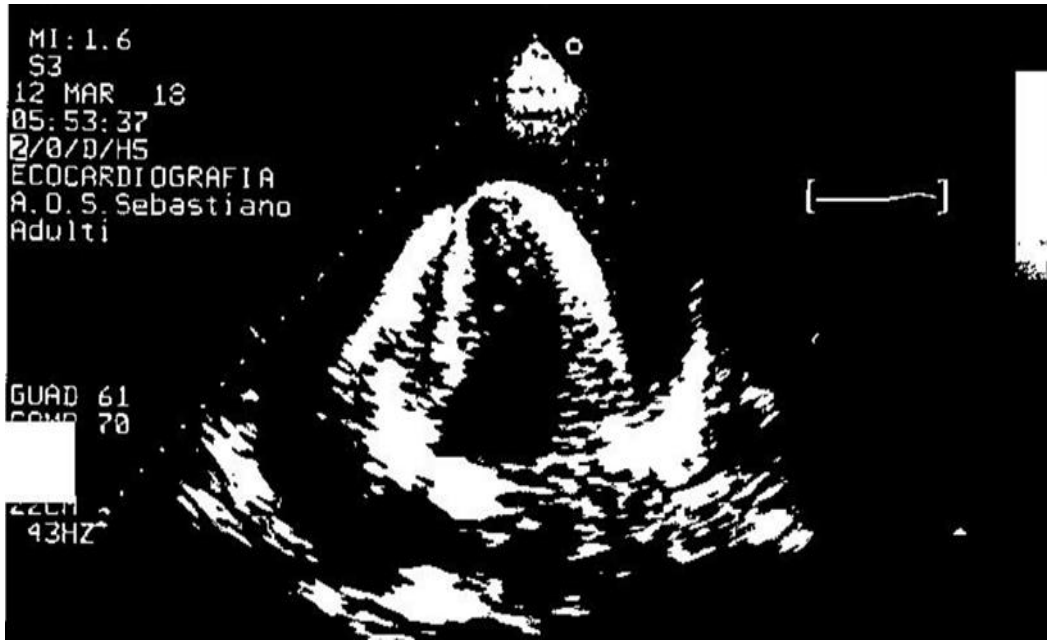
Il Paziente giunge alla nostra osservazione

- Sensorio obnubilato , Ipoteso,
- Cute fredda e pallida
- Polsi periferici non palpabili

SHOCK cardiogeno

All’ Ecocardiogramma…..





……**Tamponamento cardiaco**

Cosa fare ?

- Infusione Liquidi
- Trasfusione emazie concentrate
- Complesso protrombinico CCP/ Complesso protrombinico attivato
- Pericardiocentesi d’emergenza
- Intervento CCH
- **Idarucizumab**

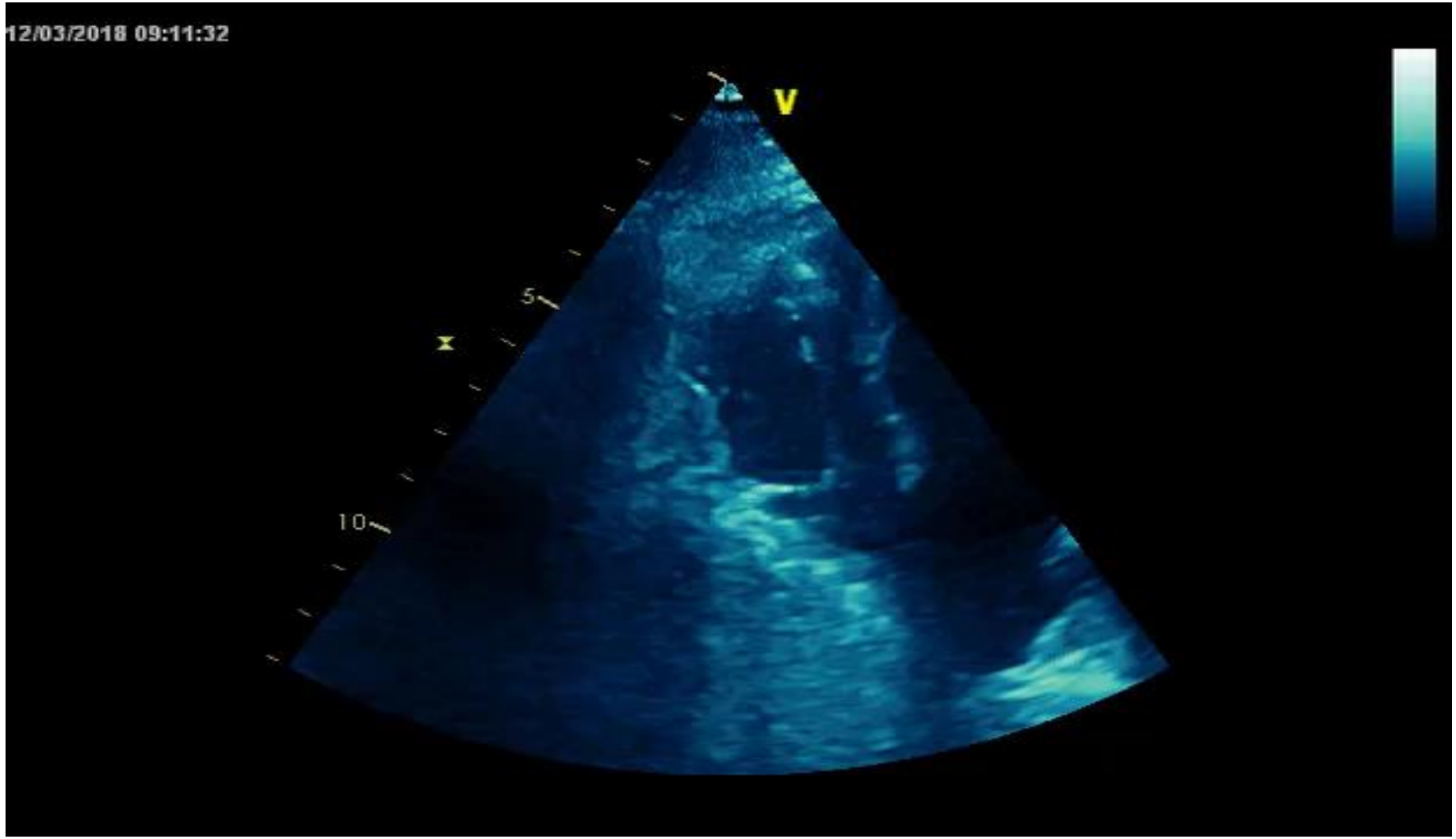
Idarucizumab was Designed as a Specific Reversal Agent for the Anticoagulant Activity of Dabigatran

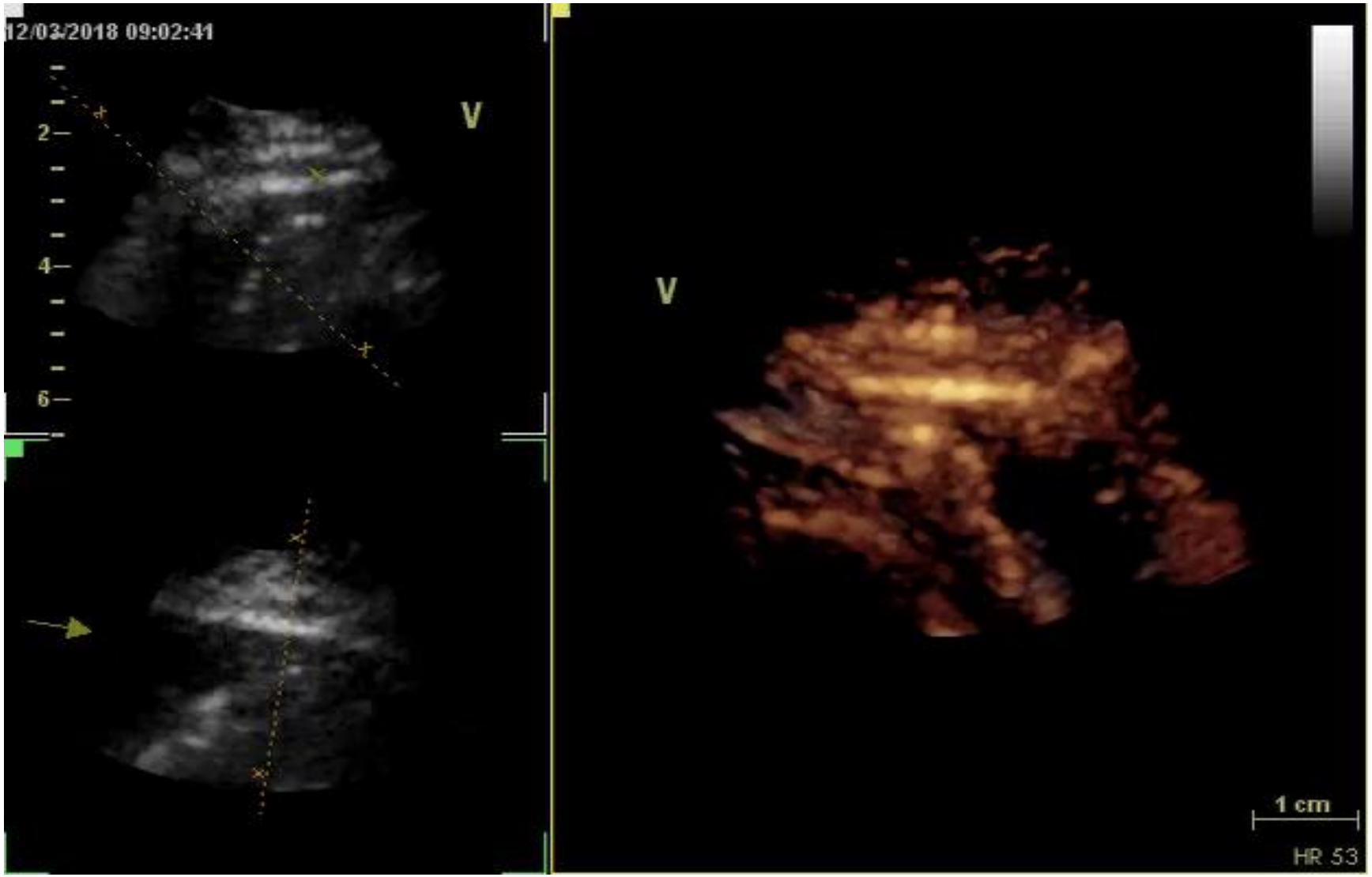
- Humanized Fab fragment
- IV administration, immediate onset of action
- Binding affinity for dabigatran ~350× higher than dabigatran to thrombin
- No intrinsic procoagulant or anticoagulant activity
- Short half-life

- Dose di 5 g **Idarucizumab** è sommistrata in due boli di 2.5 g in 15 min

- Si procede quindi a **pericardiocentesi d'emergenza** , sotto guida ecocardiografica , sono drenati 1500 cc di liquido ematico

- Rapido miglioramento clinico, con ripresa del sensorio e PA


12/03/2018 09:11:32
V
5
10


12/03/2018 09:02:41
V
2
4
6
V
1 cm
HR 53

Indicazioni cliniche

CHD trivasale. Recente impianto di ICD.
In NAO+ASA.
Tamponamento cardiaco ematico drenato stanotte.

[MISURE BIDIMENSIONALI]

Ventricolo sinistro: **LVEVd** 180 cm3 **LVEVs** 137 cm3 **LVEF** 23,8%

[CINETICA SEGMENTARIA]

	Setto I-V		Pareti			
	Ant.	Post.	Inf.	P.lat.	Lat.	Ant.
Livello basale	2	2	3	2	2	2
Livello intermedio	2	2	2	2	2	2
Livello apicale	3		3		3	3

1	Normocinesia
2	Ipocinesia
3	Acinesia
4	Discinesia
5	Aneurisma
0	Non valutabile

Wall motion score index:2,31 Estensione % della acinesia:31,2

[MISURE DOPPLER]

Tricuspide **Valutazione dell' insufficienza:** Lieve

RVPs 40 mmHg

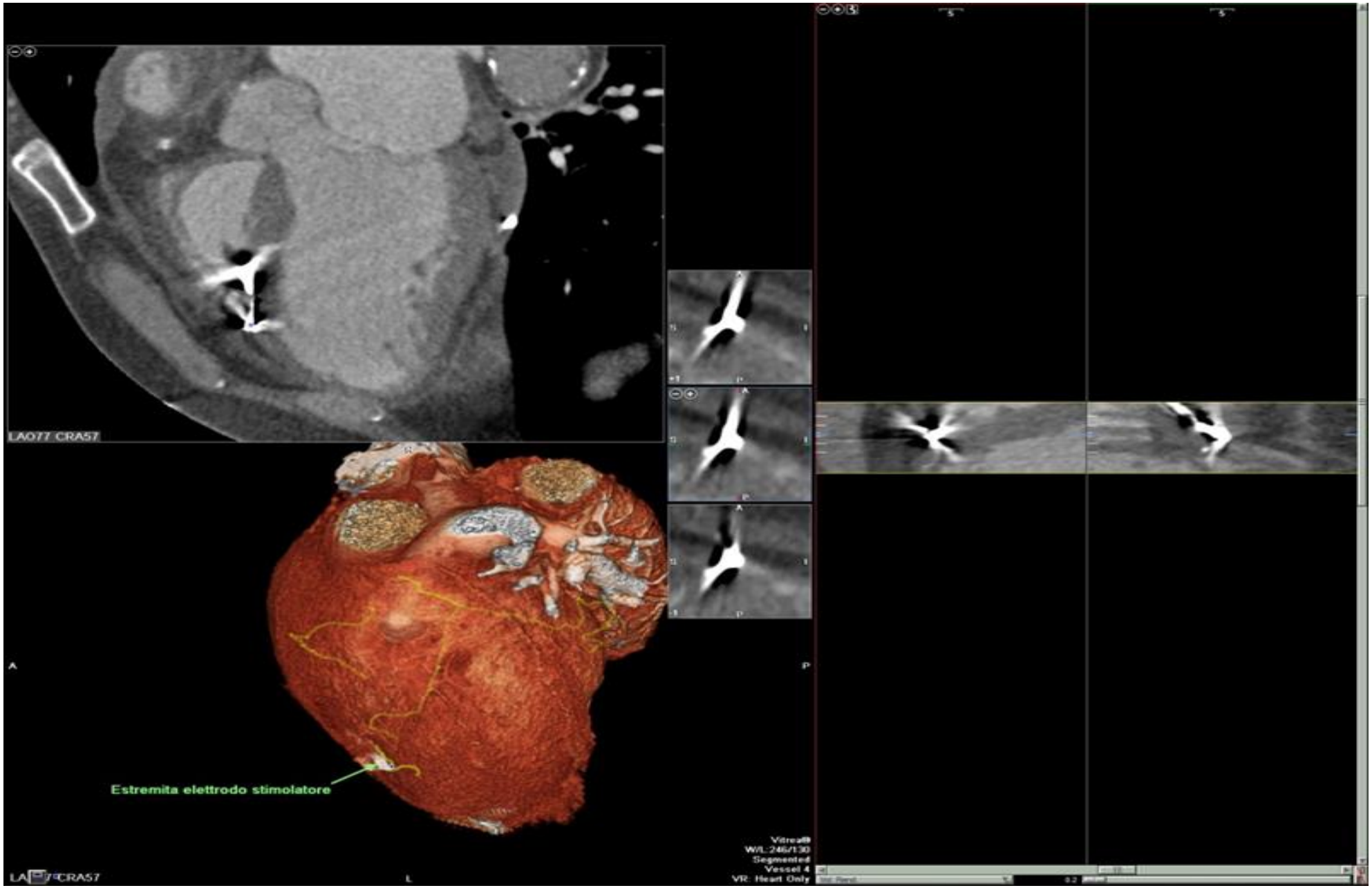
Descrizione

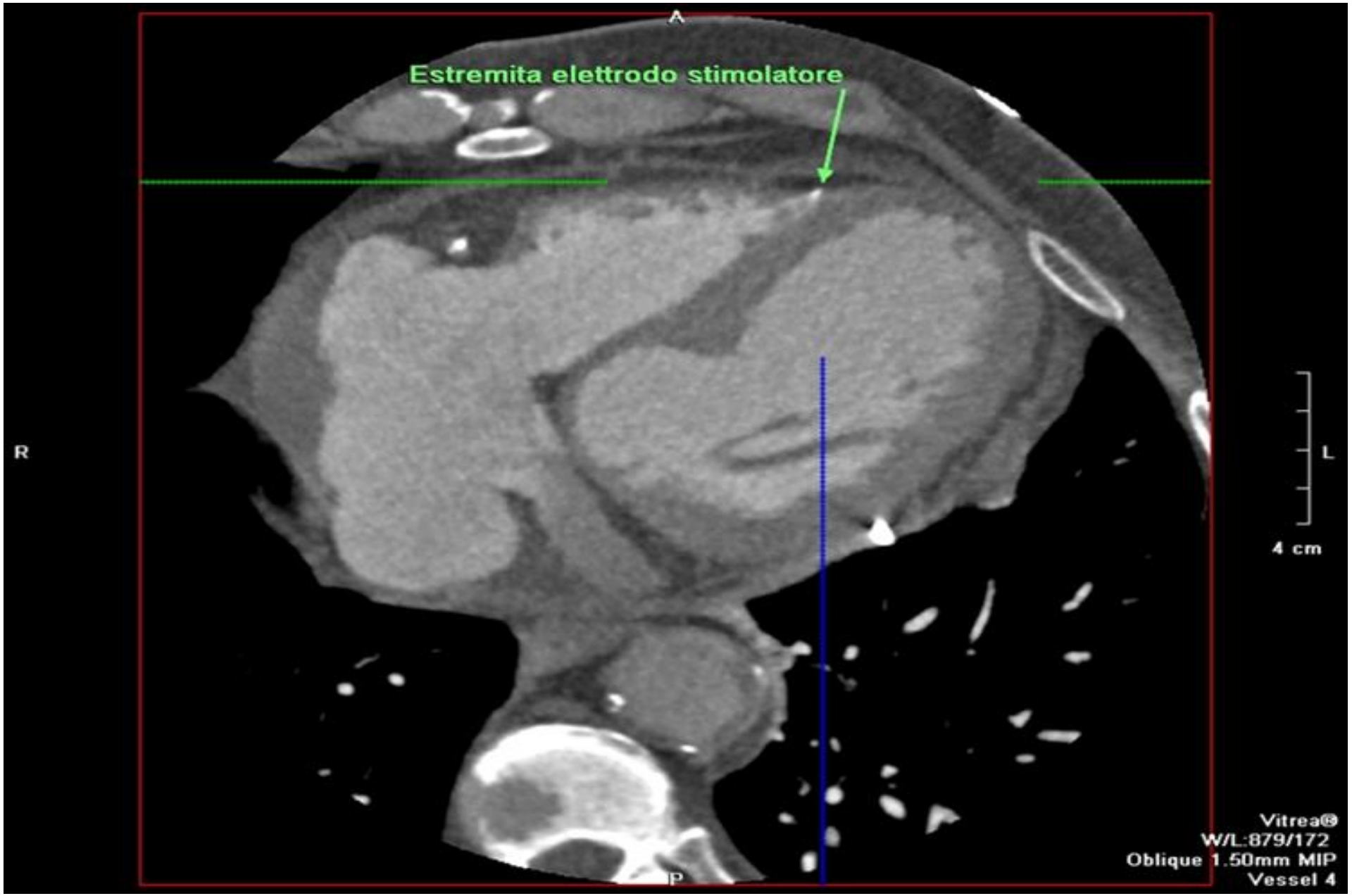
Ventricolo sinistro dilatato, globalmente ipocinetico. FE 25%.
Pattern transmitralico da alterato rilasciamento.
Atrio sinistro di dimensioni lievemente aumentate.
Insufficienza mitralica eccentrica di grado severo.
Radice ed aorta ascendente nei limiti.
Sezioni destre nella norma.
Presenza di catetere elettrostimolatore in ventricolo destro, impuntato a livello del tratto distale della parete libera con estremità apicale verosimilmente transparietale. Ventricolo destro ipocinetico (TAPSE 13 mm).
Non evidenza di versamento pericardico residuo.

Conclusioni

CMD.
Insufficienza mitralica severa
Catetere da shock in posizione verosimilmente transparitale a livello dell'estrmità distale della parete libera del ventricolo destro (NB utile integrazione con TC CARDIACA).

TC Cardiaca

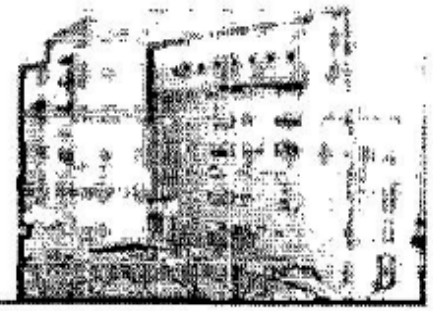



A
Estremita elettrodo stimolatore
R
L
4 cm
P
Vitrea®
W/L:879/172
Oblique 1.50mm MIP
Vessel 4

Azienda Ospedaliera di Caserta Sant'Anna e San Sebastiano di rilievo nazionale e di alta specializzazione

Azienda Ospedaliera di Caserta "Sant'Anna e San Sebastiano"

di rilievo nazionale e di alta specializzazione



Dipartimento di Diagnostica per Immagini

Paziente: 2010384987 -- **DAINO PASQUALE** nato/a il **06/06/1948**

Accettazione: **20180301512** data acc: 12/03/2018 11:43:57

Reparto Provenienza: **U.T.I.C.** Tecnico Esecutore: **MATERA PASQUALE**

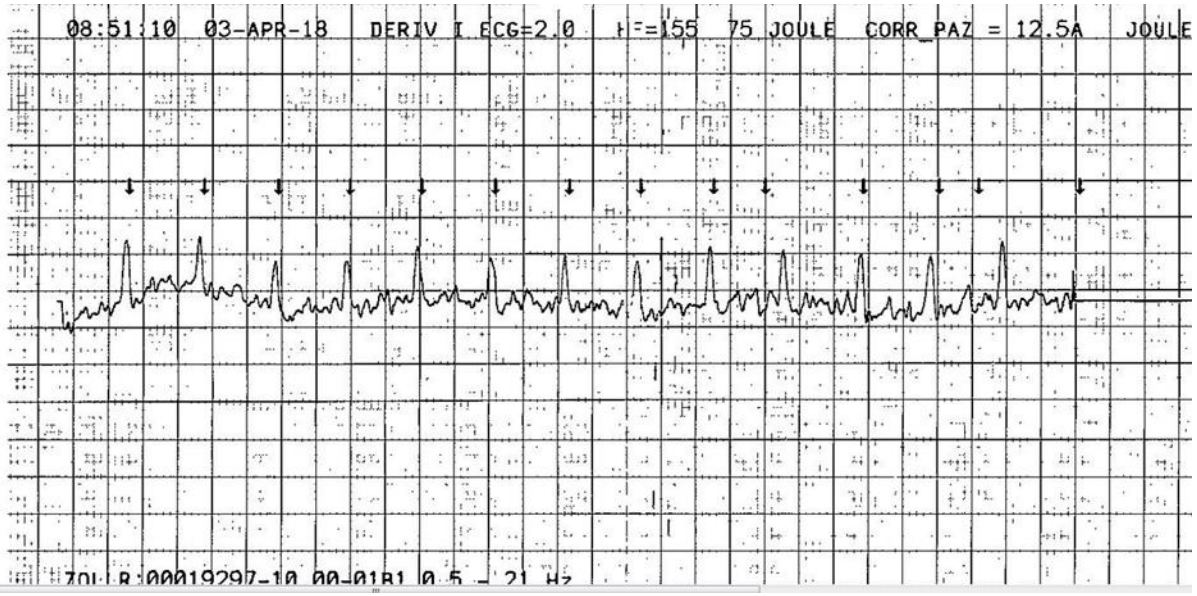
TC CUORE (SENZA E CON CONTRASTO)

Esame eseguito con TC 320 slice (AquilionONE Toshiba) ed acquisizioni ECG-Gated durante iniezione di 40 ml di m.d.c. iodato e.v. (350 mgI/ml) con ricostruzioni multiplanari e 3D. FC: 90 bpm

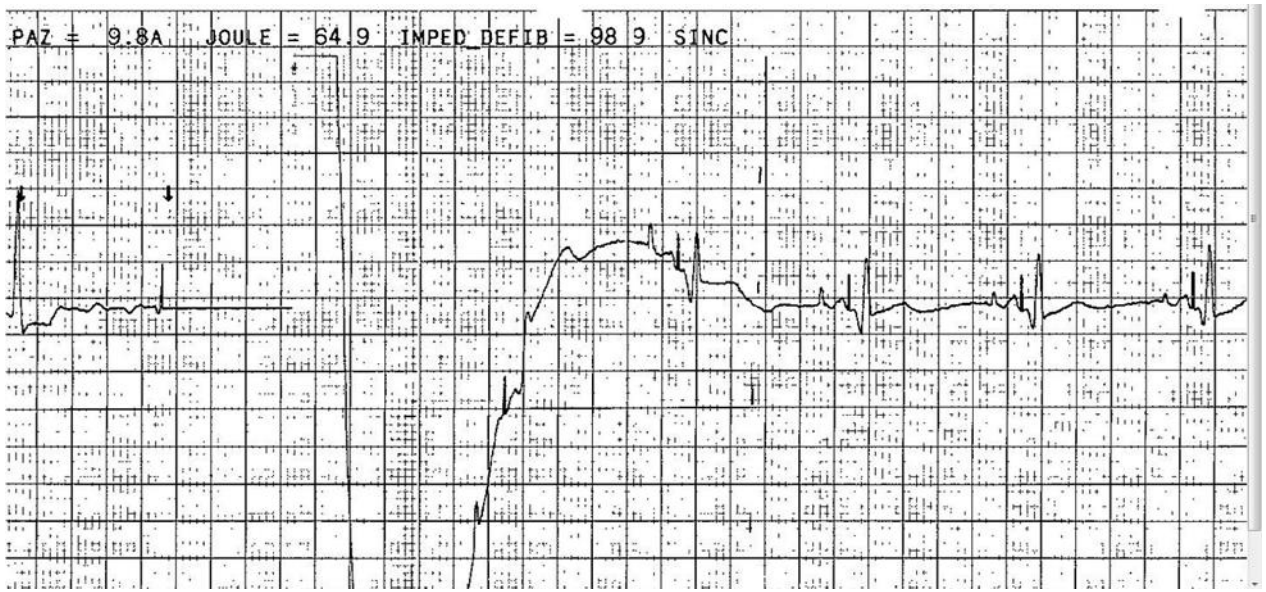
L'esame, eseguito in urgenza per lo studio del ventricolo destro in relazione al quesito clinico, evidenzia estremità apicale di catetere stimolatore di ICD posizionata verosimilmente in sede transparietale a livello della regione apicale del ventricolo destro (in contiguità con il tratto apicale del setto interventricolare) con scollamento del pericardio adiacente associato, allo stato, a modesta falda di versamento pericardico.

Caserta, 12/03/2018

Durante la degenza ….



Recidiva di Fibrillazione atriale



Cardioversione elettrica con ripristino RS

- Paziente in compenso emodinamico
- Dopo discussione collegiale si procede a intervento di estrazione e riposizionamento di di ICD , che si effettua in sala elettrofisiologia
- Buoni parametri elettrici post procedura

- Terapia alla dimissione:

Pantoprazolo 40mg, Sprionolattone 25 mg 1cp,Furosemide 25x 2cp, Bisoprololo 2,5 mg 1cp, Amlodipina 5 mg 1cp, Cardiosideral 1cp, Plavix 75 mg,

Dabigatran 150 mg x 2

Grazie per l'attenzione !