Quando, come e perché esaminare i pazienti con TEV per trombofilia e anticoagulante lupico (LAC)

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15'

Caso

- Donna di 34 anni si presenta al PS con dolore toracico pleurico e dispnea. Non è in terapia e non ha una storia medica nota.
- HR 115 BP 123/78 O2 sat 92%
- EO: Appare ansiosa; polmoni niente di rilevante; tachicardia, ritmo regolare, addome trattabile, estremità no edemi, no varicosità, livedo reticularis.
- LAB: Bianchi 4900 mcl, Hgb 13 g /dL, PLT 115 K / mcl 0,8.
- Angio TAC PE: emboli polmonari lobari bilaterali multipli; Rapporto RV / LV normale
- La paziente viene trattata con rivaroxaban 15 mg BID e ricoverato.

Perché sospettare APS

- Giovane
- Embolia Polmonare idiopatica
- Livedo reticularis

Patient selection for lupus anticoagulant (LA) testing

Patient selection
LA testing should be performed in the following situations: - asymptomatic patients (usually children) with unexplained **prolonged aPTT** as an incidental finding due to transient aPL triggered by infection - **younger patients (usually < 50 years) with unprovoked venous thromboembolism** - LA testing should be considered following provoked VTE in young patients - venous thromboembolism at unusual sites - younger patients (usually <50 years) with ischaemic stroke, transient ischaemic attack or other evidence of brain ischaemia - arterial thrombosis in other sites in young patients - microvascular thrombosis - recurrent thrombosis - pregnancy morbidity: fetal loss after 10 weeks, recurrent early (first trimester) miscarriages, prematurity (<34 weeks' gestation) associated with severe (pre)eclampsia, HELLP syndrome, placental insufficiency (fetal growth restriction), stillbirth - systemic lupus erythematosus: testing for LA is part of the diagnostic criteria and contributes to risk assessment - immune thrombocytopenia - **livedo reticularis**, particularly with presence of symptoms of other systemic autoimmune diseases or mild thrombocytopenia - LA testing should be considered in young patients with neurological/neurocognitive disorders (e.g. dementia, epilepsy, movement disorders), valvular heart disease, nephropathy

Devreese et al. In preparation

CASO A

- Il giorno successivo il team nota che i dati di laboratorio all'ingresso sono significativi per PTT prolungato 45,1 sec. PT 11,1 sec e INR è 1.0. Il team è preoccupato per la possibile sindrome antifosfolipidica (APS).
- Richiesta urgente di Lupus Anticoagulant, aCL e aβ2GPI IgG e IgM.

CASO A

- LAC: dRVVT + SCT +
- aCL: IgG 59 GPL
- aβGPI: IgG 75 GPL

- Tripla positività con isotipo IgG
- Embolia Polmnare
- Livedo reticularis

- APS apparentemente primitiva con tripla positività

blood

Plenary Paper

CLINICAL TRIALS AND OBSERVATIONS

Rivaroxaban vs warfarin in high-risk patients with antiphospholipid syndrome

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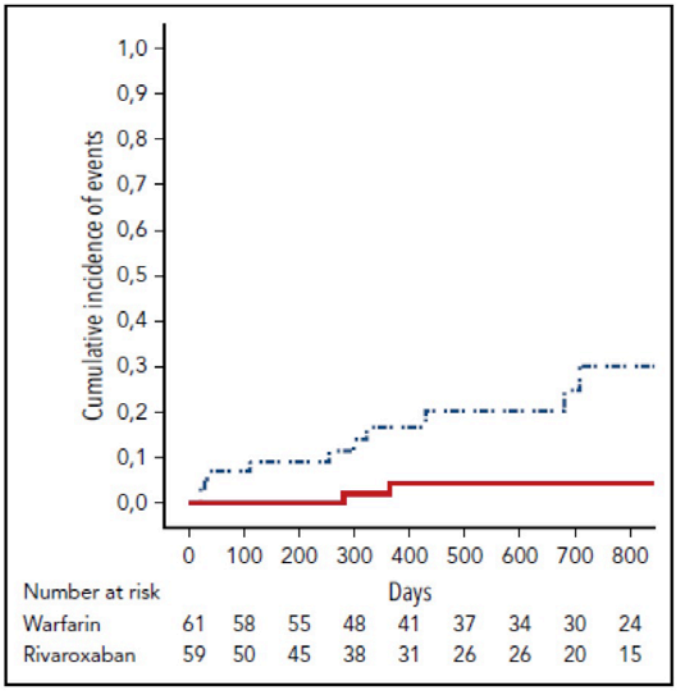
Pengo et al. Blood. 2018;132(13):1365-1371

TRAPS-Results



Cumulative incidence of death, thromboembolism, major bleeding

rivaroxaban

warfarin

CASO A

- Il rivaroxaban viene sostituito da dosi terapeutiche di LMWH e viene iniziato warfarin 5mg/die.
- Non va sospeso rivaroxaban e iniziato warfarin senza bridging con LMWH

CASO B

- Donna giovane con EP: Il giorno successivo quando la paziente ha già assunto rivaroxaban 15mg/bid il team nota che i dati di laboratorio all'ingresso sono significativi per PTT prolungato 40,5 sec. e INR è 1.5. Il team è preoccupato per la possibile sindrome antifosfolipidica (APS).
- Richiesta urgente di Lupus Anticoagulant, aCL e aβ2GPI IgG e IgM.

CASO B

- LAC falsamente positivo in caso di terapia con DOACs che fare:
  - ❖ Prelievo per LAC a valle…ma non abbiamo certezze
  - ❖aCL e aβGPI a medio alto titolo stesso isotipo
  - ❖Sospendo rivaroxaban, somministro LMWH a dosi terapeutiche e chiedo di determinare il LAC a valle (I reagenti di solito contengono un inibitore della eparina) e contemporanea determinazione della attività anti Xa.

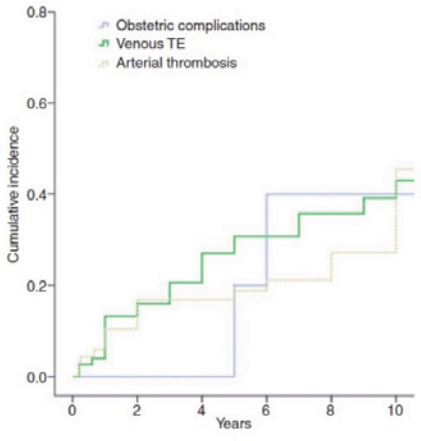
Caso B determinazione del LAC (alternative)

- Uso di test basati su estratti di veleno di serpente (Taipan e l'ecarina) che convergono protrombina in trombina ma uno richiede la presenza di PL mentre l'altro no.
  - Non esistono kit commerciali standardizzati ed uno studio è in corso per valutare l'attendibilità del metodo
- Uso di antidoti specifici per i DOAC (costi!)
- Utilizzo di resine che assorbono I DOAC disponibili in commercio (DOAC-StopTM, Haematex Research, Sydney, Australia e DOAC-RemoveTM, 5-Diagnostics, Quadratech, Switzerland), da validare

Perché devo sostituire il DOAC

- Nello studio TRAPS ho avuto solo eventi arteriosi e non venosi al follow-up

Eventi tromboembolici nel follow up in APS con tripla positività in base all'evento iniziale (stesso rate di recidiva)



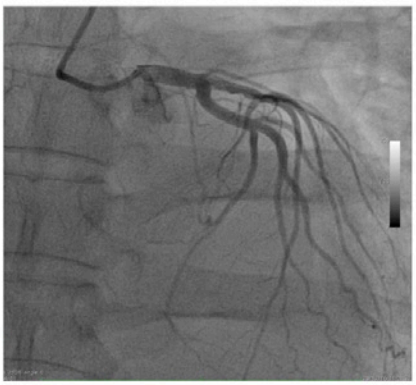
Recidive di VTE in chi aveva avuto VTE come primo episodio 16/27 (59%)
Recidiva di ATE in chi aveva avuto ATE come primo episodio 15/22 (68%)
CAPS come primo episodio: tutte 4 hanno avuto eventi nel fup (2 Venosi e 2 Arteriosi)

Pengo V, 2010

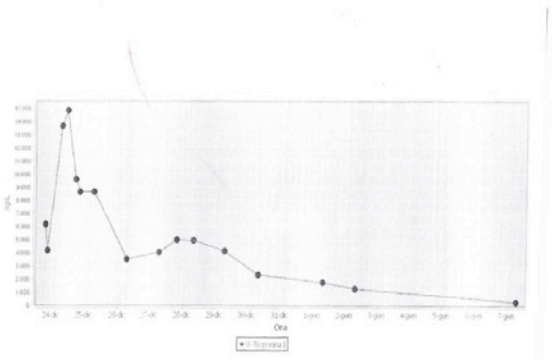
Case 1

- Young man 38 years of age, BMI=25, no smoking, no risk facors
- Previous pulmonary embolism at 18 years of age. Primary APS
- Days from randomization: 709
- ACUTE MYOCARDIAL INFARCTION

Case 1



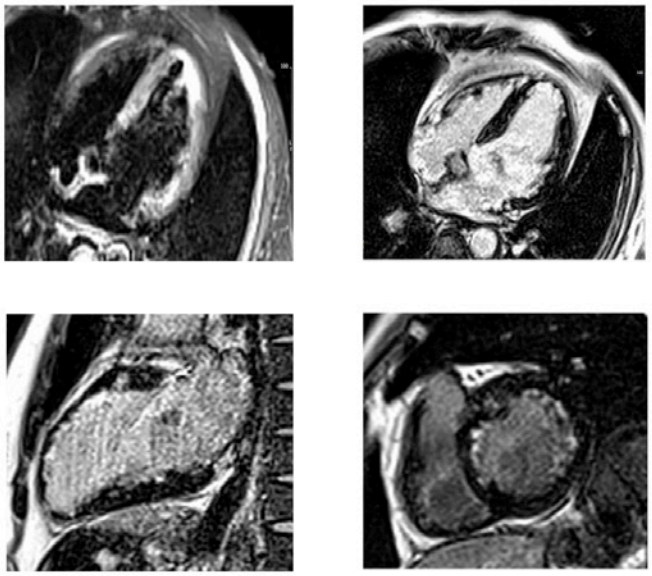
Angiography showing sub-acute thrombosis of the proximal tract of anterior descendent coronary artery without atherosclerotic plaques.



Troponin-I levels after myocardial infarction and arise after a new episode

Case 1

M.C.



Conclusion
Coronary thrombosis (embolism) with subsequent distal embolization

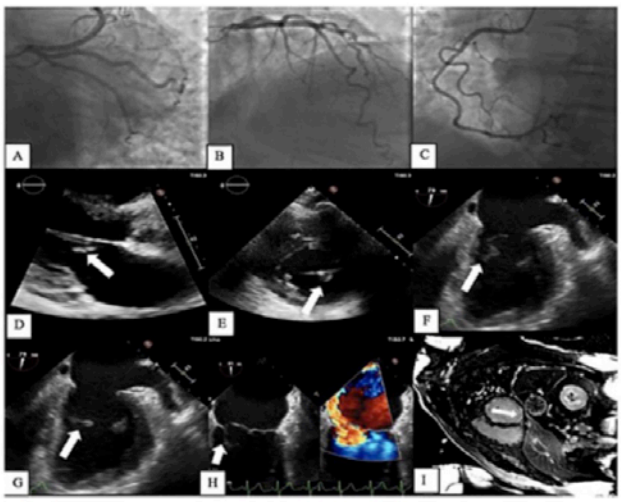
(A) Cardiac MRI showing in turbo inversion recovery magnitude (TIRM) sequence a large amount of patchy, subendocardial edema in interventricular septum and apex. (B-C-D) Late gadolinium enhancement revealing trans mural myocardial scarring lesion in the apex and subendocardial scars in the anterior wall and IVS, suggesting infarcts due to distal multifocal embolism in the LAD territory.

Case 2 TI.LO.

- Male 47 years of age, no smoking
- Recurrent deep vein thrombosis, primary APS
- Days from randomization: 20
- Chest pain, dyspnea, syncope and elevated troponin I level.
- Shock: Vasoactive Medications, VV ECMO, negative coronary angiography
- TEE ECHO: massive mitral regurgitation due to rupture of ischemic papillary muscle: urgent mitral valve substitution patient survived.
- Conclusion: coronary embolism

Case 2 (same as that recently described)

A Coronary Conundrum: Papillary Muscle Rupture and Ischemic Mitral Regurgitation Secondary to Coronary Thromboembolism in Antiphospholipid Syndrome . *Journal of investigative Medicine High Impact Case Report 2019;7:1-4.*



(A-C) Cardiac catheterization displaying nonobstructive coronary artery disease. (D) TTE parasternal long axis (PLAX) view of mitral value displaying flail A2/A3 segment (arrow). (E) Parasternal short axis (PSAX) view displaying ruptured posteromedial papillary muscles (PMPM; arrow). (F and G) TEE displaying ruptured PMPM (arrow). (H) TEE displaying severe mitral regurgitation with a posterior medially directed jet due to ruptured PMPM (arrow). (I) CMR short axis view demonstrating subendocardial late gadolinium enhancement involving basal to mid-inferolateral wall (arrow).

Case 6 PA.MU.

- Female, 57 years, smoking, no other risk factors, primary APS
- Days since randomization: 299
- Previuos DVT and PE
- At hospitalization: Slurred speech that deteriorated in the following days
- Imaging: Cerebral CT was negative
- MRN was positive: Recent ischemic areas in the parietal lobe (disseminated embolization?)

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