4° CONGRESSO NAZIONALE FRAGILITY FRACTURE NETWORK - ITALIA

Appropriatezza, Qualità e Sostenibilità delle Cure nel Percorso Ortogeriatrico

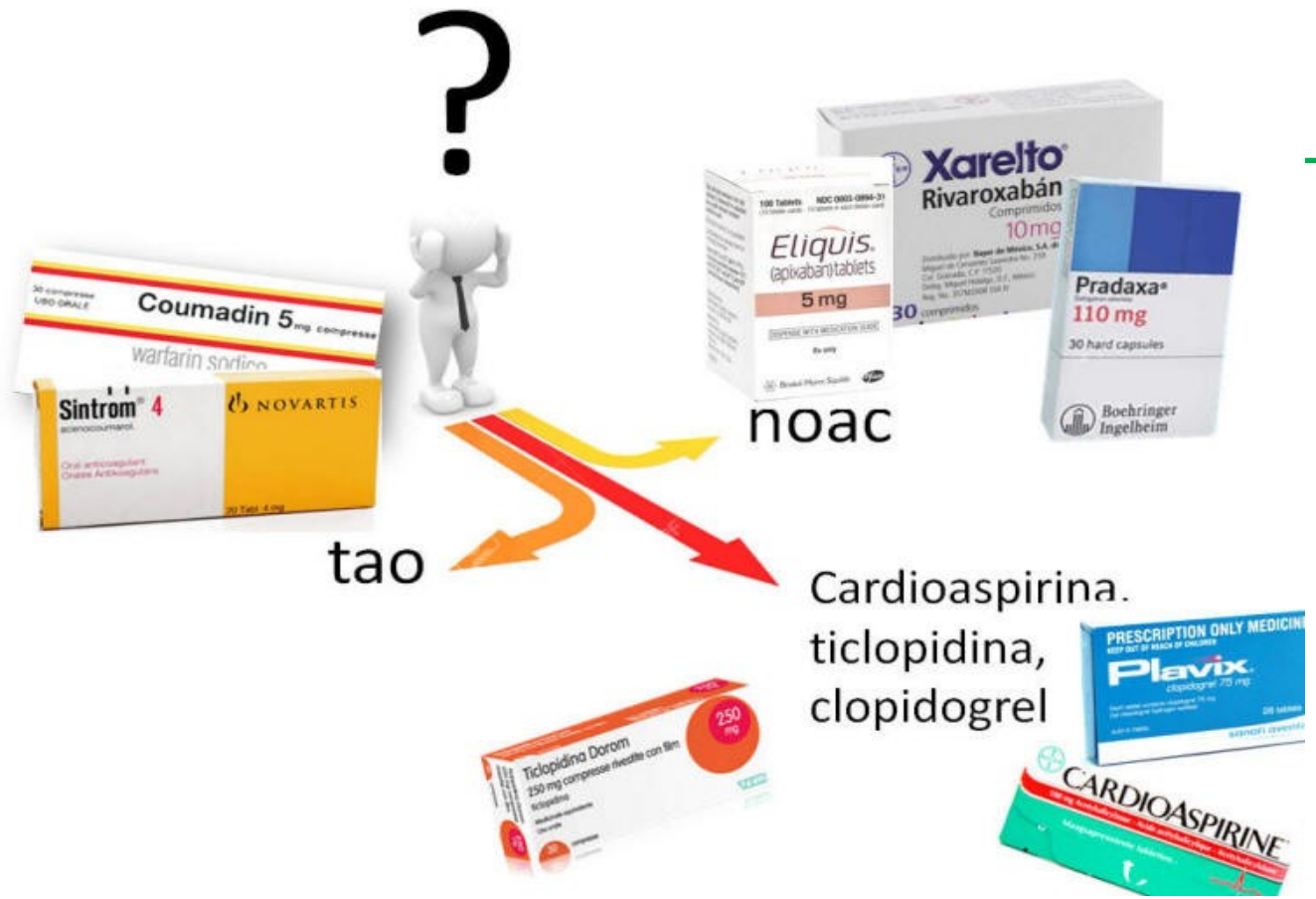
Aspetti cruciali del paziente ortogeriatrico in fase acuta

Anticoagulanti ed Antiaggreganti come ottimizzare il timing

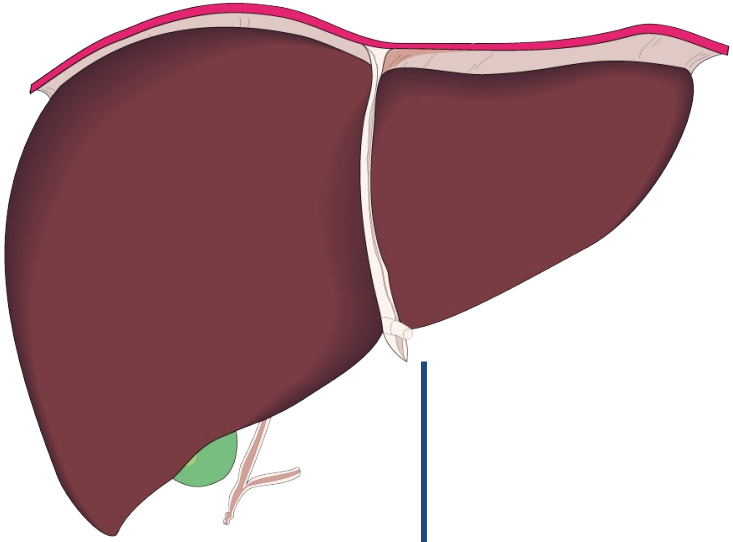
Eugenio Giuseppe Vadalà

U.O.C. Terapia Intensiva e Anestesia

GOM Reggio Calabria


?
Coumadin 5mg compresse
warfarin sodico
Sintrom 4
NOVARTIS
tao
Xarelto
Rivaroxabán
Comprimidos
10mg
Eliquis
(apixaban)tablets
5 mg
Pradaxa
110 mg
30 hard capsules
Boehringer Ingelheim
noac
Cardioaspirina.
ticlopidina,
clopidogrel
Ticlopidina Dorom
250 mg compresse rivestite con film
250
PRESCRIPTION ONLY MEDICINE
Plavix
CARDIOASPIRINE

Fattori coagulazione vitamina K-dipendenti



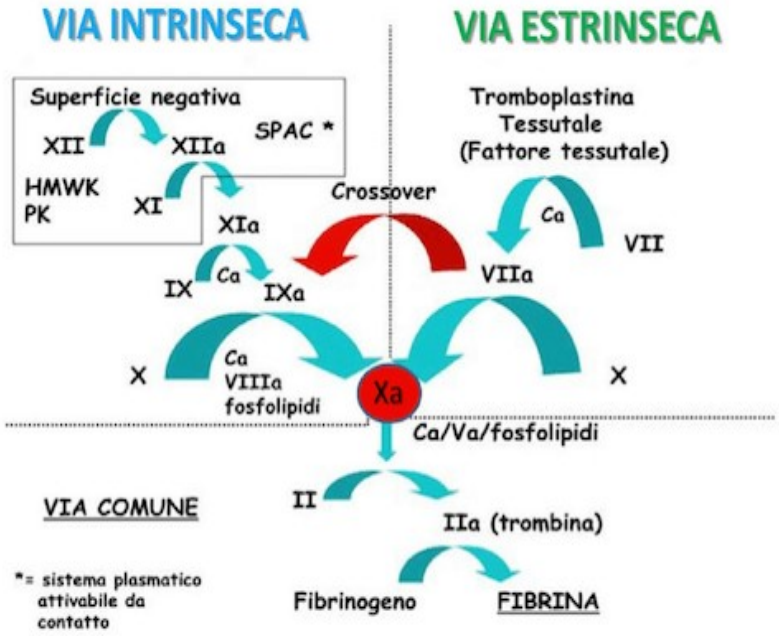
VII

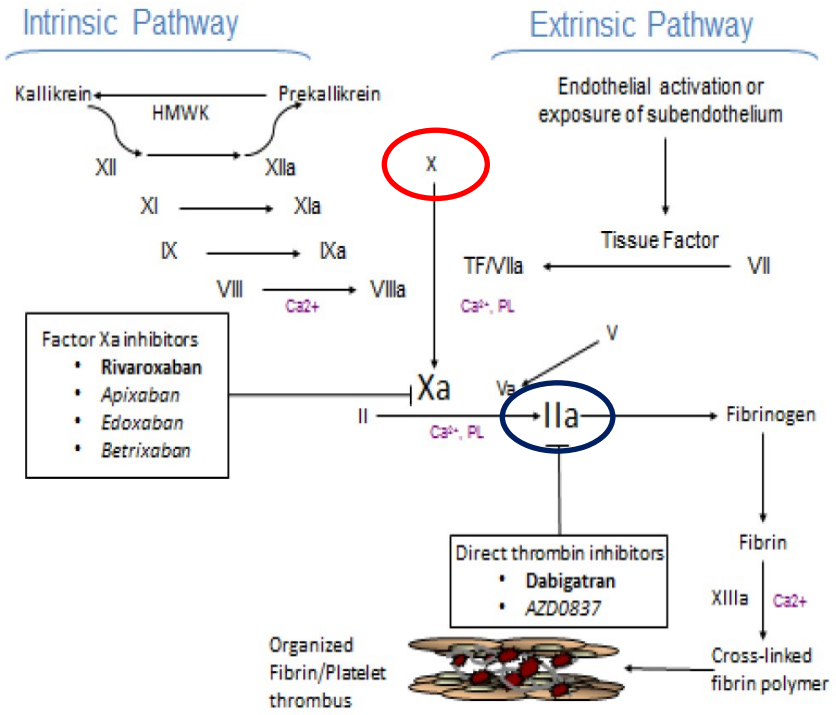
IX

X

II

Vitamina K





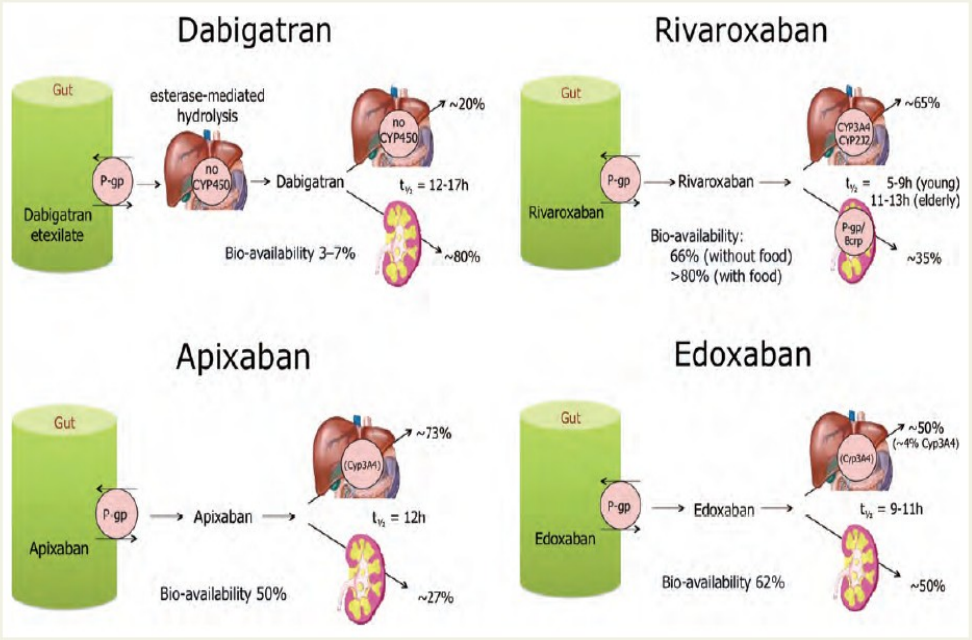


Figure 5 Absorption and metabolism of the different new anticoagulant drugs. There are interaction possibilities at the level of absorption or first transformation, and at the level of metabilisation and excretion. The brackets around (Cyp3A4) in the apixaban graph indicate a minor contribution of this pathway to hepatic clearance, the majority of the drug being excreted as unchanged parent. See also *Table 4* for the size of the interactions based on these schemes.

Gonsalves WI. Mayo Clin Proc 2013;88(5):495-511

Heidbuchel H et al. Europace 2013; 15: 625–51

NICE guideline

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Giornale Italiano di Ortopedia e Traumatologia
2021;47:101-123; doi: 10.32050/0390-0134-329

NICE National Institute for Health and Care Excellence

Hip fracture: management

Linea Guida SIOT
Fratture del femore prossimale nell'anziano

immobilità. Il tempo di attesa preoperatorio rappresenta la sfida principale per le strutture sanitarie, poiché implica il coordinamento tra più reparti e funzioni, dall'arrivo del paziente in PS al suo accesso alla sala operatoria (SO). La valutazione preoperatoria richiede capacità e tempistiche adeguate, in un'ottica multidisciplinare finalizzata alla rapida stabilizzazione del paziente riguardo comorbilità e squilibri comuni, come anemia, deficit della coagulazione, ipovolemia e disordini elettrolitici, per la maggior parte cor-

e di complicanze lievi e gravi. Esplorando l'associazione tra tempo di attesa preoperatorio e mortalità, la RS arriva a conclusioni coerenti con quanto emerso dagli studi osservazionali, riportando una riduzione della mortalità (OR 0,74, 95% CI 0,67 to 0,81, I2 = 85%).
La LG SIOT [1] ha incluso un'ulteriore RS [32] di 27 studi osservazionali (n = 33727), che evidenzia una possibile riduzione del rischio di mortalità associata all'intervento entro 48 ore 12 studi osservazionali n = 12780, RR = 0,72;

THE LANCET

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Accelerated surgery versus standard care in hip fracture (HIP ATTACK): an international, randomised, controlled trial

The HIP ATTACK Investigators † • Show footnotes

Published: February 09, 2020 • DOI: https://doi.org/10.1016/S0140-6736(20)30058-1 • Check for updates

PlumX Metrics

dell'indipendenza, minor incidenza di ulcere da pressione

ni meno comuni, che richiedono una valutazione individua-

EFORT open reviews

HIP | 8:7 | 561–571

Review of perioperative outcomes and management of hip fracture patients on direct oral anticoagulants

Pelle V Wall[1], Brendon C Mitchell[2], Canhnghi N Ta[2] and William T Kent[2]

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[2]Department of Orthopaedic Surgery, University of California San Diego, West Arbor Drive, California, United States of America

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Study	Study type	Inclusion criteria	*n*	Hip fracture patients DOAC	Hip fracture patients VKA
Tran et al. (16)	CCS*	Operative, isolated hip fracture	2258	1.2%	10.3%
Lott et al. (43)	RCS	Isolated hip fracture, ≥60 years	479	0.8%	7.7%
Sabo et al. (31)	PCS	Low-energy, operative hip fracture	55	9.1%	14.5%
Taranu et al. (17)	PCS	Hip fracture, >60 years	1965	4.5%	7.1%
Bruckbauer et al. (35)	RCS	Isolated hip fracture, ≥65 years	320	16.9%	18.4%
Cafaro et al. (42)	RCS	Acute operative hip fracture, ≥18 years	472	6.6%	5.9%
Daugaard et al. (36)	RCS	First time hip fracture, ≥65 years	74791	1.4%	5.6%
Hourston et al. (32)	RCS	Surgically treated femoral neck fracture	844	3.8%	9.8%
Schermann et al. (40)	RCS	Operative (CRIF or HA only) intertrochanteric and femoral neck fracture, ≥65 years	1714	5.2%	9.3%
Schuetze et al. (47)	RCS	Operative, isolated per- or subtrochanteric fracture	327	15.9%	7.6%
Viktil et al. (23)	PCS	Operative acute hip fracture, ≥65 years	167	6.6%	8.4%
Creeper et al. (56)	RCS	Acute hip fracture	1240	6.6%	5.4%
Hoerlyck et al. (61)	RCS	Hip fracture, ≥50 years	2307	1.4%	8.7%
Meinig et al. (51)	RCS	Isolated operative fragility hip fracture, ≥65 years	459	19.8%	39.0%
Saliba et al. (39)	RCS	Operative hip fracture, ≥65 years	3418	7.2%	4.8%
Tarrant et al. (28)	RCS	Hip fracture, ≥65 years	3264	3.4%†	

*Overall percentage, however, rates increased annually and were 9% in 2018; †Percentages for DOAC and VKA patients calculated from a cohort of all hip fracture patients.
CCS, case–control study; CRIF, closed reduction internal fixation; DOAC, direct oral anticoagulation; HA, hemiarthroplasty; PCS, prospective cohort study; RCS, retrospective cohort study.

Table 3 Time to surgery in hip fracture patients on DOAC vs VKA and no oral anticoagulation. Data are presented as mean±S.D., median or as median (IQR).

Study	TTS	Major Findings	LOE
h) compared with non-anticoagulated controls (29). The amount of surgical delay DOAC patients faced compared with non-anticoagulated patients varies significantly between studies, ranging from no significant difference to 41 h longer (30, 31). However, these studies were limited	(26.6-46.4)	TTS: DOAC > VKA > No OAC TTS: DOAC > No OAC TTS >48h: DOAC > No OAC	III III III
	± 45; 59% <48h		
	± 21h	TTS: DOAC > VKA > No OAC	II
	h (median)	TTS: Anticoagulated > No OAC.	II
(35) >48h >48h >48h	% <24h; 8.4%	TTS: DOAC > No OAC. Greater proportion DOAC operated on >48h after hospitalization	III
33). You *et al.* found that anticoagulated patients had	-84)	TTS: DOAC and VKA > No OAC, DOAC = VKA	III
three-fold higher odds of receiving surgery >48 h from	<24 h; 21.3%	TTS > 36 h in twice as many DOAC, VKA patients vs No OAC	III
admission compared with non-anticoagulated controls,	; 40.7% >36 h % <36 h; 95%	DOAC use independently associated with increased TTS >36 h but not >48 h. TTS VKA = No OAC	III
		TTS: DOAC > No OAC in CRIF only. DOAC = No OAC in HA	III
et al., collecting data from 2010 to 2014, suspected the significant surgical delay they found in DOAC users was due to uncertainty surrounding perioperative management of DOACs (mean DOAC TTS of 66.9 h vs 26.2 h for non-anticoagulated patients) (16). A 2018 case–control study		TTS: DOAC > VKA TTS: DOAC > No OAC. No statistical comparison done for proportion of DOAC vs. *No-OAC receiving surgery <24 h, <4 8h	III III
of 796 hip fractures found waiting for a decrease in DOAC	h ± 15.1	TTS: OAC (DOAC + VKA) > No OAC	III
drug activity was responsible for surgical delay in 70%		TTS: DOAC > No OAC	III
of DOAC users (no DOAC patients were reversed), while		TTS: DOAC = No OAC	III
only 32% of patients on VKA (who were routinely reversed	h (22.5–55.3); % <48 h	TTS: DOAC, VKA > No OAC. Lower proportion of DOAC, VKA patients operated on <48h after hospitalization	III
with vitamin K) experienced a surgical delay due to INR levels (33). Bruckbauer *et al.* cite a lack of specific tests for rapid quantification of Xa and thrombin inhibitors, and no specific reversal agents for FXa inhibitors at the time, for the increased TTS and higher proportion of patients receiving surgery after 48 h observed in DOAC users compared with non-anticoagulated patients (35).		TTS: DOAC > No OAC TTS: DOAC > No OAC Mean difference for DOAC TTS vs no-OAC: +15.46 h (95% CI: 9.20–21.72 h). TTS: DOAC = VKA	III III III

parison specifically for patients on DOAC vs No OAC.
days; DOAC, direct oral anticoagulant; h, hours; HA, comparison group(s); No OAC, no oral anticoagulation; ime to surgery; RCS, retrospective cohort study; VKA,

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Tab. 4 ANTICOAGULANTI E ANTIAGGREGANTI: CONSIDERAZIONI PER L'OPERABILITÀ E PER L'ANESTESIA NEUROASSIALE [12, 22-27]

Farmaco	Considerazioni per l'operabilità	Considerazioni per l'anestesia neuroassiale	Test di laboratorio
Warfarin	operabile con INR <2. Se INR>1,5, consigliabile somministrazione di 1-3 mg di vitamina K ev PCC indicato nel caso non si riesca ad ottenere INR<1,5 dopo *reverse* con vitamina k	INR ≤ 1,5	INR
Xabani* dose profilattica Rivaroxaban (Xarelto) Apixaban (Eliquis) Edoxaban (Lixiana)	dopo 12-48h dall'ultima dose	dopo 24-72h, → attendere 40-75h, se dosaggi maggiori, creatinina > 1,5 mg/dl, età > 80 anni, peso <60 Kg	attività anti-Xa farmaco specifica
Dabigratan* (Pradaxa) a dose profilattica	dopo 24-48h dall'ultima dose considerare idarucizumab (Praxbind) 5 g ev come reverse rapido	incompatibile con chirurgia < 48h o solo dopo Praxbind; se CrCl ≥80 ml/min attendere 72h se 50 < CrCl<79 → 96h se 30 < CrCl<49 →120h se CrCl < 30 sconsigliato	TT, dTT (aPTT) Hemoclot thrombin inhibitor assay
[illegible]	[illegible] 2-4h prima dell'intervento	[illegible]	[illegible]
LMWH dose profilattica	ultima dose pre-operatoria 12h prima	dopo 12h	
LMWH dose terapeutica	ultima dose preoperatoria 24h prima (monitorare il sanguinamento)	dopo 24h	
Clopidogrel Ticlopidina Prasurgrel Ticagrelor	non ritardare l'intervento monitorare il sanguinamento	incompatibile con chirurgia < 48h considerare AG + blocco periferico (sempre in caso di DAPT)	aggregometria POC
Aspirina	non controindicato	non controindicata	

PCC complesso protrombinico concentrato; CrCl *clearence* della creatinina; TT tempo di trombina; dTT tempo di trombina diluito; aPTT tempo di tromboplastina parziale attivata; UFHs eparina non frazionata; LMWH eparina a basso peso molecolare; AG anestesia generale; DAPT doppia terapia antiaggregante; POC, *point of care*.
*L'Esperienza sui blocchi neuroassiali in pazienti in terapia con i nuovi anticoagulanti è ancora molto limitata. Le raccomandazioni sono basate sull'opinione di esperti e sulle proprietà farmacocinetiche del farmaco. INR International Normalised Ratio;

Tabella V. Considerazioni per l'operabilità e l'esecuzione di anestesia locoregionale nei pazienti in trattamento con anticoagulanti e antiaggreganti [43].

Farmaco	Emivita di eliminazione	Gestione	Accettabile per anestesia spinale
Warfarin	4-5 giorni	1-3 mg vitamina K ev, INR dopo 4-6 h, può essere ripetuto o considerare PPC per reversal	INR < 1.5
Clopidogrel	effetto irreversibile sulle PLT	procedere con la chirurgia, monitorizzare perdite, se sanguinamento importante considerare trasfusione di PLT	in monoterapia: valutare rischio/beneficio in DAPT: AG + BP
Aspirina	effetto irreversibile sulle PLT	procedere con la chirurgia, continuare la terapia	in monoterapia
Ticagrelor	8-12h	procedere con chirurgia in AG + BP, monitorizzare le perdite, se importante sanguinamento considerare trasfusione di PLT	dopo 5 giorni dopo trasfusione PLT almeno 6h dall'ultima dose
Eparina non frazionata	1-2 h	2-4 h pre op stop eparina ev	4h
EBPM sc dose profilattica	3-7h	ultima dose 12h preop	12h
EBPM sc dose terapeutica	3-7h	ultima dose 12-24h preop monitorare perdite ematiche	24h
Xabani: Rivaroxaban Apixaban Edoxaban	 7-10h 12h 10-14h	chirurgia/anestesia dopo 24h se funzionalità renale ok	se funzionalità renale ok 2 emivite/24 h dopo l'ultima dose
Dabigatran	12-24h	procedere se TT normale, se TT allungato considerare reversal con idarucizumab	con TT normale 30' dopo reversal con idarucizumab

AG = anestesia generale, BP = blocco periferico, DAPT = doppia antiaggregazione, INR = international normalised ratio, EBPM = eparina a basso peso molecolare, ev = endovena, PCC = complesso protrombinico concentrato, PLT = piastrine, sc = sottocute, TT = tempo di trombina.

Review

Yasmin Youssef*, Anna K. I. M. Dietrich and Annika Hätt

Anticoagulation manager elderly patients with proximal femur f verview of current concepts

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Instructional Lecture: Trauma

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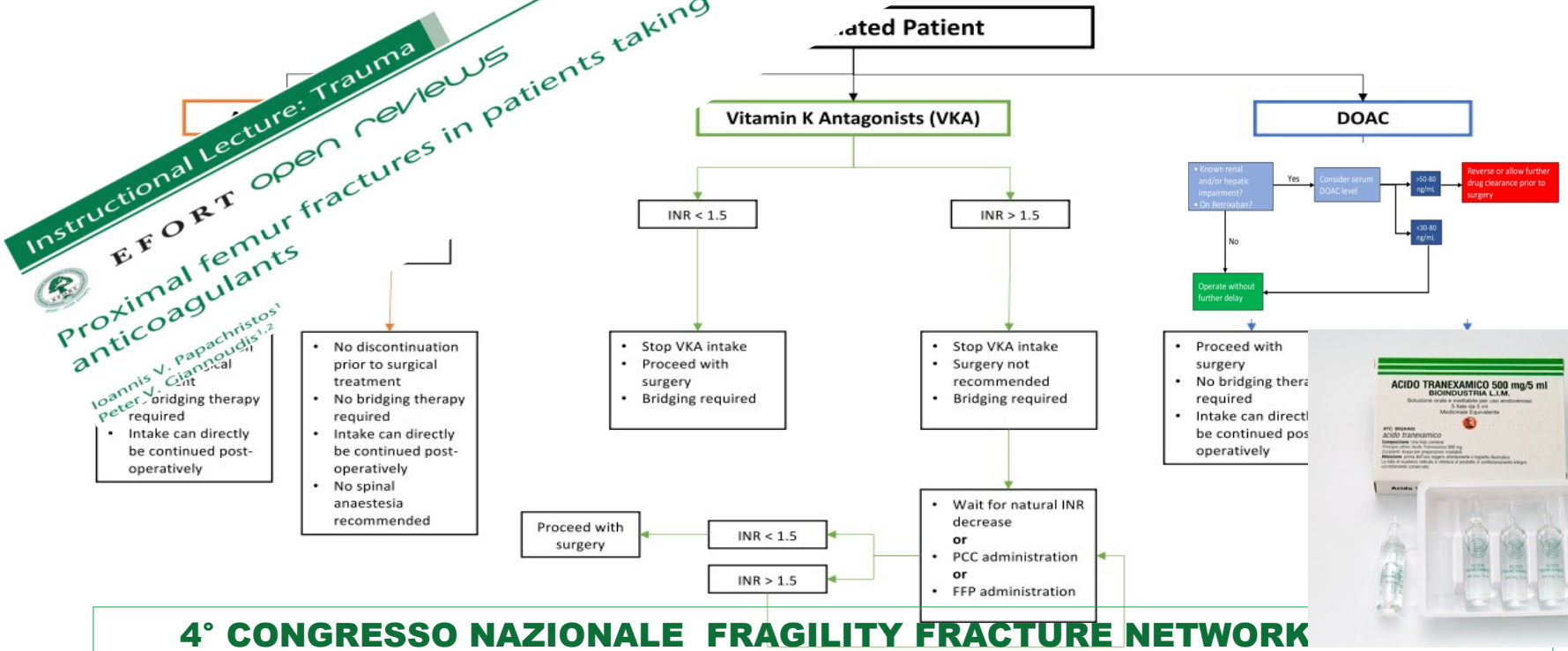
Proximal femur fractures in patients taking anticoagulants

Ioannis V. Papachristos[1]
Peter V. Giannoudis[1,2]



SIAARTI
PRO VITA CONTRA DOLOREM SEMPER

BUONE PRATICHE CLINICHE

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2021;47:101-123; doi: 10.32050/0390-0134-329

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UFHs ev	sospendere infusione 2-4h prima dell'intervento	dopo 4h	aPTT
LMWH dose profilattica	ultima dose pre-operatoria 12h prima	dopo 12h	
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REVIEW

Perioperative management of antiplatelet therapy in noncardiac surgery

Daniela C. Filipescu[a,b], *Mihai G. Stefan*[b], *Liana Valeanu*[a,c], *and Wanda M. Popescu*[d]

KEY POINTS

- Surgery should be delayed at least for 1 month and ideally for 3–6 months from a cardiac event.
- Aspirin indicated for secondary prevention of ischemic events should be continued perioperatively, except in high bleeding risk procedures (neurosurgery).
- DAPT could be continued perioperatively in patients with high risk of thrombosis and low bleeding risk but de-escalating from ticagrelor or prasugrel to clopidogrel can further decrease the bleeding risk.
- In case of surgery with intermediate or high bleeding risk, APAs should be discontinued for as short as possible (i.e., aspirin and ticagrelor 3–5 days, clopidogrel 5 days, and prasugrel 7 days) and be resumed postoperatively as soon as hemostasis is controlled.
- Individualized APT, using a web-based tool providing real-time personalized risk prediction of thrombotic risk or bleeding risk at 5 years with and without DAPT, is more appropriate than a 'one-size-fits all' approach.

Purpose of review
Perioperative management of antiplatelet agents (APAs) in the setting of noncardiac surgery is a controversial topic of balancing bleeding versus thrombotic risks.

Recent findings
Recent data do not support a clear association between continuation or discontinuation of APAs and rates of ischemic events, bleeding complications, and mortality up to 6 months after surgery. Clinical factors, such as indication and urgency of the operation, time since stent placement, invasiveness of the procedure, preoperative cardiac optimization, underlying functional status, as well as perioperative control of supply–demand mismatch and bleeding may be more responsible for adverse outcome than antiplatelet management.

Summary
Perioperative management of antiplatelet therapy (APT) should be individually tailored based on consensus among the anesthesiologist, cardiologist, surgeon, and patient to minimize both ischemic/thrombotic and bleeding risks. Where possible, surgery should be delayed for a minimum of 1 month but ideally for 3–6 months from the index cardiac event. If bleeding risk is acceptable, dual APT (DAPT) should be continued perioperatively; otherwise $P2Y_{12}$ inhibitor therapy should be discontinued for the minimum amount of time possible and aspirin monotherapy continued. If bleeding risk is prohibitive, both aspirin and $P2Y_{12}$ inhibitor therapy should be interrupted and bridging therapy may be considered in patients with high thrombotic risk.

Keywords
antiplatelet therapy, bleeding, major adverse cardiovascular events

Stratification Risk

Perioperative management of antiplatelet therapy in noncardiac surgery

Daniela C. Filipescu[a,b], Mihai G. Stefan[b], Liana Valeanu[a,c], and Wanda M. Popescu[d]

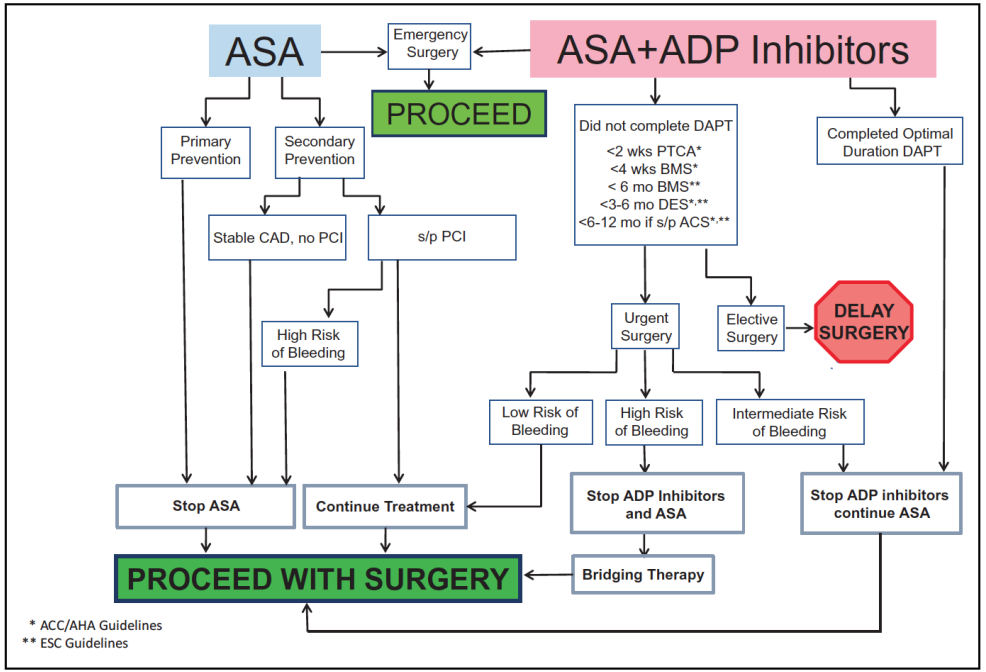

FIGURE 1. Algorithm for perioperative management of antiplatelet therapy in patients with coronary artery disease. ACS, acute coronary syndrome; ADP, adenosine diphosphate; ASA, aspirin; BMS, bare-metal stents; CAD, coronary artery disease; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty. Adapted with permission [9].

Table 1. Perioperative management of a

Type of surgery	Thrombotic risk	Aspir
	Low	Continu
Elective surgery	Intermediate and high	Postpor surge
Nondeferrable surgery	Intermediate	Continu
	High	Continu

[a]Discontinue $P2Y_{12}$ inhibitors as per guideline recomm
[b]Postpone surgery until full dual antiplatelet therapy cc
[c]Discontinue oral $P2Y_{12}$ inhibitors and consider bridgi

KEY POINTS

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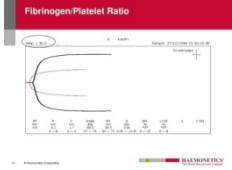
Urological surgery
Reconstructive surgery
ed
Intracranial neurosurgery
Extensive thoracoabdominal dissection



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ORIGINAL RESEARCH

Platelet aggregometry for hip fracture surgery in patients treated with clopidogrel: a pilot study

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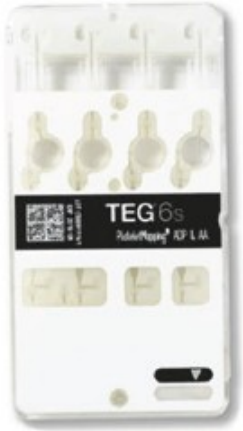
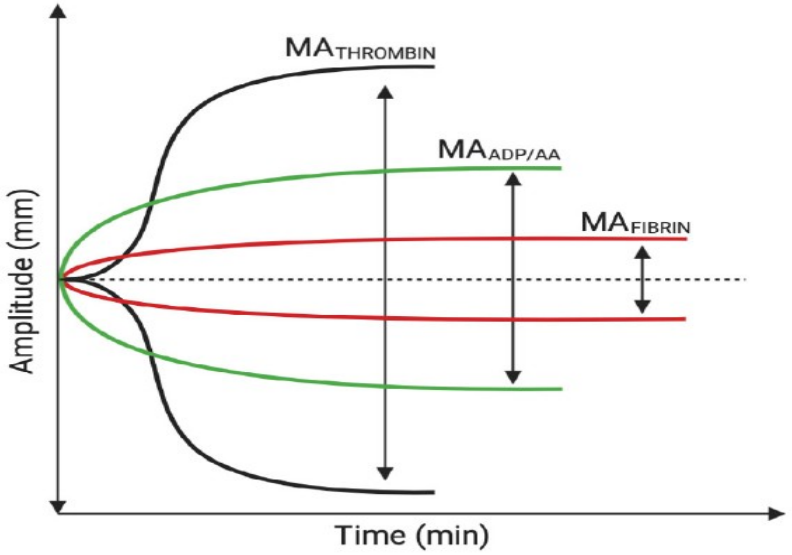
Abstract
Surgery for hip fractures should be performed within 48 h from patient's admission. However, several factors including chronic antiplatelet therapy could delay operation. Among the totality of patients taking clopidogrel, up to 30% are resistant to the drug and have a normal platelets reactivity. We propose thromboelastography (TEG) with an ADP Platelet Mapping assay kit to assess platelet aggregation, a safe tool that could help to avoid surgery delay in those patients treated with antiplatelet therapy. A patient's blood sample was collected for aggregometry. If MA-ADP and platelets aggregation (%) were within normal values, the patient was fit for immediate surgery with neuraxial anesthesia and ultrasound-guided nerve block. If one of the two parameters or both were deranged, a mortality risk assessment was estimated. In the low risk category, the patients waited till normalization of the parameters, whereas in the high-risk group a general anesthesia and peripheral antalgic block was carried out. Nine patients were enrolled. Four of them showed normal aggregometry and surgery was performed within 24 h from admission. Two patients were classified as high mortality risk and surgery was carried out under general anesthesia. Three patients awaited operation till normalization of parameters. No peri or post-operative complications were reported. An aggregometry-guided protocol can safely expedite hip fracture surgery in patients taking clopidogrel. Nonetheless, in presence of a normal platelets function, clinician can opt for a neuraxial instead of general anesthesia reducing the incidence of postoperative delirium and cognitive dysfunction.
Trial registration: prospectively registered at clinicaltrials.gov (NCT04642209; date of registration: 23rd November 2020)

Keywords Thromboelastography · Aggregometry · Hip fracture · Clopidogrel · Anesthesia





$$\%\ \text{aggregation} = \frac{MA_{ADP/AA} - MA_{FIBRIN}}{MA_{THROMBIN} - MA_{FIBRIN}} \times 100$$

$$\%\ \text{inhibition} = 100 - \%\ \text{aggregation}$$

Platelet aggregometry for hip fracture surgery in patients treated with clopidogrel: a pilot study

5 Conclusions

As suggested by standard guidelines, the presence of antiaggregant therapy could postpone hip fracture surgery up to 5 days after diagnosis, further compromising the preservation of independence and activities of daily living and causing functional decline in elderly patients.

The implementation of an aggregometry-based protocol could help to avoid operation delay in a consistent group of geriatric patients taking clopidogrel. Nonetheless, in presence of a normal platelets function despite antiaggregant therapy, clinician could opt for a neuraxial instead of general anesthesia reducing the incidence of postoperative delirium and cognitive dysfunction.

Results from our pilot study are promising, however further research is required to assess if this management protocol would translate into a clinical benefit and mortality reduction.

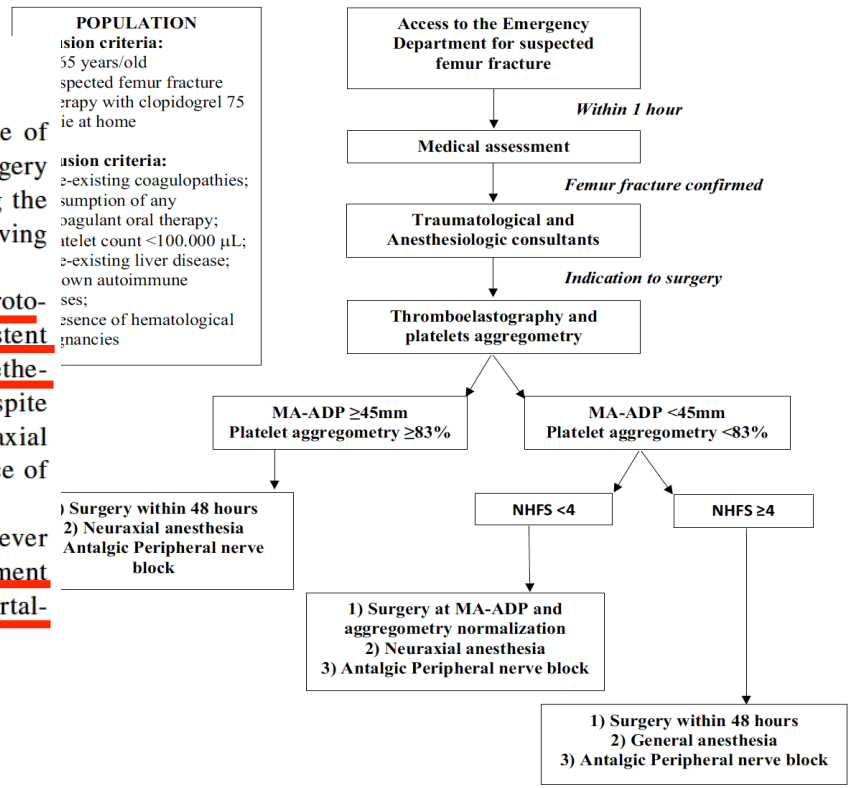


Fig. 1 Flowchart of the management protocol

SERVIZIO SANITARIO REGIONALE
Dipartimento Tutela della Salute e Politiche Sanitarie

GRANDE OSPEDALE METROPOLITANO
"Bianchi Melacrino Morelli"
Reggio Calabria

REGIONE CALABRIA

Protocollo Aziendale per la gestione perioperatoria del Paziente fragile

Rev n.0	
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Dipartimento Emergenza

REGIONE CALABRIA

Protocollo Per Il Percorso Intraospedaliero Di Gestione Del Paziente Con Frattura Di Femore

INTRODUZIONE

di femore sono diventate un
portante causa di malattia, di
e di femore sono rilevanti sia in

no al 15-25%. In circa il 20%
llow-up solo il 30-40% riprende

più appropriata ed efficiente
ata valutazione preoperatoria,

chirurgico entro le 48 ore
parte dei casi (National Health
può provocare complicanze,
paziente.

tivi e qualitativi dell'assistenza
venti chirurgici entro 48 ore su

Il programma nazionale valutazione esiti (PNE) affidato all'Age.Na.S. dal Ministero della Salute analizza le conoscenze disponibili sul tema della valutazione degli esiti, definendo ed elaborando indicatori di esito nell'ambito di disegni di studio osservazionali.

Gli indicatori selezionati (mortalità a 30 giorni dal ricovero; tempi di attesa per intervento chirurgico; intervento chirurgico entro le 48 ore) misurano la qualità delle prestazioni erogate dagli ospedali per identificare potenziali criticità che necessitano ulteriori approfondimenti analitici. Sono utili a promuovere una attività di auditing clinico e organizzativo per valorizzare l'eccellenza ed individuare le criticità promuovendo il miglioramento dell'efficacia e della equità dell'assistenza erogata e non producono nella loro versione ufficiale classifiche, graduatorie e giudizi.


Grazie per