CONTROINDICAZIONI ALLA TERAPIA ANTICOAGULANTE ORALE: IL PUNTO DI VISTA DELL'EMATOLOGO

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Guidance for prescribing of Dabigatran (Pradaxa▼) Rivaroxaban (Xarelto▼) and Apixaban (Eliquis▼) in Patients with Non-Valvular AF

NICE TAGs 249, 256 and 275 recommends dabigatran*, rivaroxaban and apixaban♦ respectively, as an option for prevention of stroke with non valvular AF if they have one or more of the following risk factors: Previous stroke or TIA, Age 75 Years or older, congestive heart failure, hypertension or diabetes.

The clinician should discuss the risks and benefits of dabigatran, rivaroxaban or apixaban compared to warfarin or other coumarin before considering initiating or switching.

NB. For patients with stable INR already on warfarin or coumarin it may be appropriate to remain on warfarin.

*For Dabigatran, NICE and SPC stipulates: heart failure of NYHA class 2 or above and age of over 65 **with** diabetes, CAD or hypertension.

♦For Apixaban, NICE and SPC stipulates:heart failure of NYHA class 2 or above

Recommendations for stroke prevention in patients with atrial fibrillation

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

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

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

prevalenza della FA in Italia dell'1,85%

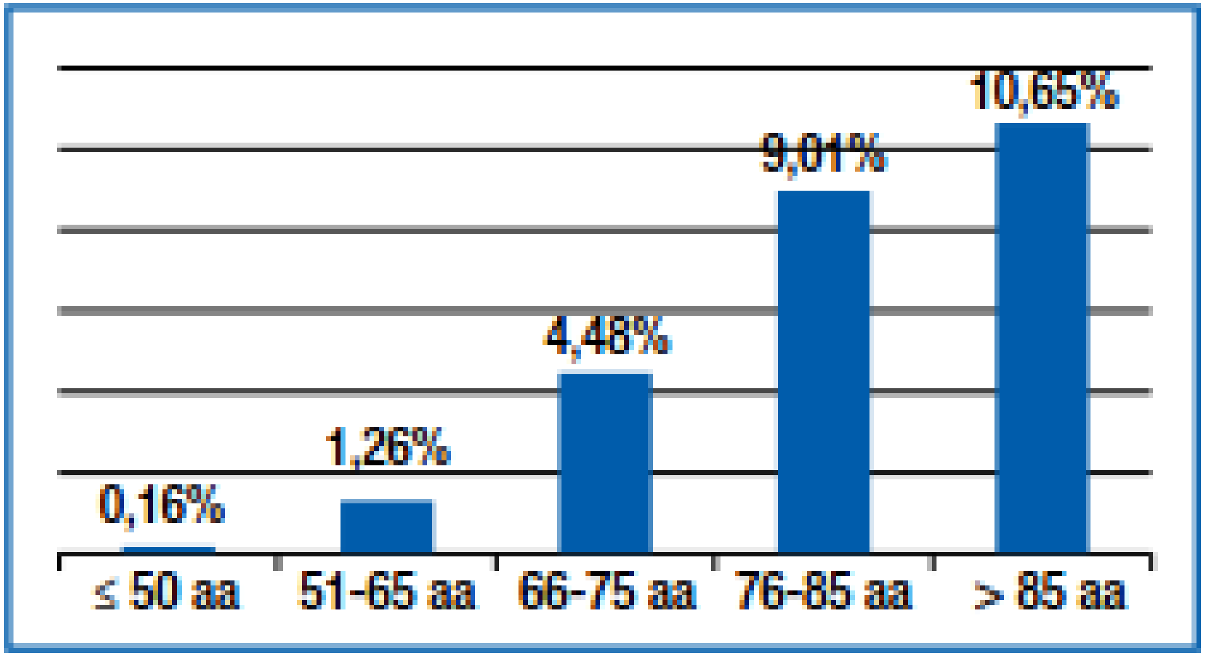

FIGURA 1.

Prevalenza della FA secondo le fasce di età considerate.

Cardiovasc Ther. 2015 August ; 33(4): 177–183. doi:10.1111/1755-5922.12129.

Contraindications to Anticoagulation Therapy and Eligibility for Novel Anticoagulants in Older Patients With Atrial Fibrillation

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Table 2

Among Patients Without Absolute Contraindications, Proportion With Conditions That Place Them at Relatively High Risk of Adverse Events With Anticoagulation

Condition[a]	Patients, No. (%) (N = 84,799)
High risk for anticoagulation	39,592 (47.0)
Age > 85 years	22,451 (26.5)
Anemia	13,527 (16.0)
Prior gastrointestinal bleed	7973 (9.4)
Dementia	7102 (8.4)
Thrombocytopenia	2568 (3.0)
Hematological malignancy	1791 (2.1)
Traumatic intracranial hemorrhage	170 (0.2)

[a]Conditions are not mutually exclusive, and patients may be represented in more than 1 group.

Controindicazioni "ematologiche" all'anticoagulazione

CONTRA-INDICATIONS AND INTERACTIONS - Dabigatran

- Hypersensitivity to the active substance
- Patients with less severe renal impairment, eGFR < 30
- Clinically significant active bleeding
- Organic lesion at risk of bleeding
- Spontaneous or pharmacological impairment of haemostasis
- Hepatic impairment or liver disease expected to have any impact on survival
- Concomitant treatment with systemic ketoconazole, ciclosporin, itraconazole, tacrolimus and dronedarone **List not exhaustive - refer to SPC for full list**

CONTRA-INDICATIONS AND INTERACTIONS - Rivaroxaban

- Hypersensitivity to the active substance
- Patients with severe renal impairment eGFR < 15
- Clinically significant active bleeding
- Organic lesion at risk of bleeding
- Hepatic disease associated with coagulopathy and clinically relevant bleeding risk
- Pregnancy and breast feeding
- Concomitant treatment with systemic: ketoconazole, voriconazole, itraconazole and dronedarone **List not exhaustive - refer to SPC for full list**

CONTRA-INDICATIONS AND INTERACTIONS – Apixaban

- Hypersensitivity to the active substance
- Patients with severe renal failure eGFR < 15
- Clinically significant active bleeding
- Organic lesion at risk of bleeding
- Hepatic disease associated with coagulopathy and clinically relevant bleeding risk
- Concomitant treatment with systemic: ketoconazole, itraconazole and voriconazole
  List not exhaustive - refer to SPC for full list

WARNING : aVK = DOACs !!!

HAS-BLED score for bleeding risk on oral anticoagulation in atrial fibrillation

Letter	Clinical Characteristic	Score (if present)
H	Hypertension (systolic ≥ 160 mmHg) – on treatment	1
A	Abnormal renal function (Dialysis, transplant, Cr > 2.6 mg/dL or > 200 µmol/L)	1
A	Abnormal liver function (Cirrhosis or bilirubin >2xNormal or AST/ALT/AP >3xNormal)	1
S	Stroke in past	1
B	Prior major bleeding or predisposition to bleeding	1
L	Labile INRs (Unstable/high INRs, time in therapeutic range <60%)	1
E	Elderly – age ≥ 65 years	1
D	Drugs: Medication usage predisposing to bleeding (antiplatelet agents, NSAIDs)	1
D	Drugs: Concomitant alcohol intake (≥8 drinks/week)	1

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DOI 10.1007/s11739-017-1628-6

CE - ORIGINAL

Italian intersociety consensus on DOAC use in internal medicine

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Abstract The direct oral anticoagulants (DOACs) are drugs used in clinical practice since 2009 for the prevention of stroke or systemic embolism in non-valvular atrial fibrillation, and for the treatment and secondary prevention of venous thromboembolism. The four DOACs, including the three factor Xa inhibitors (rivaroxaban, apixaban and edoxaban) and one direct thrombin inhibitor (dabigatran) provide oral anticoagulation therapy alternatives to Vitamin K antagonists (VKAs). Despite their clear advantages, the DOACs require on the part of the internist a thorough knowledge of their pharmacokinetic and pharmacodynamic characteristics to ensure their correct use, laboratory monitoring and the appropriate management of adverse events. This document represents a consensus paper on the use of DOACs by representatives of three Italian scientific societies: the Italian Society of Internal Medicine (SIMI), the Federation of the Associations of Hospital Managers (FADOI), and the Society for the Study of Haemostasis and Thrombosis (SISET). This document formulates expert opinion guidance for pragmatic managing, monitoring and reversing the anticoagulant effect of DOACs in both chronic and emergency settings. This practical guidance

Members of SIMI (Italian Society of Internal Medicine), FADOI (Federation of Associations of Hospital Doctors on Internal Medicine) and SISET (Italian Society for the Study of Haemostasis and Thrombosis) are listed in Acknowledgement.

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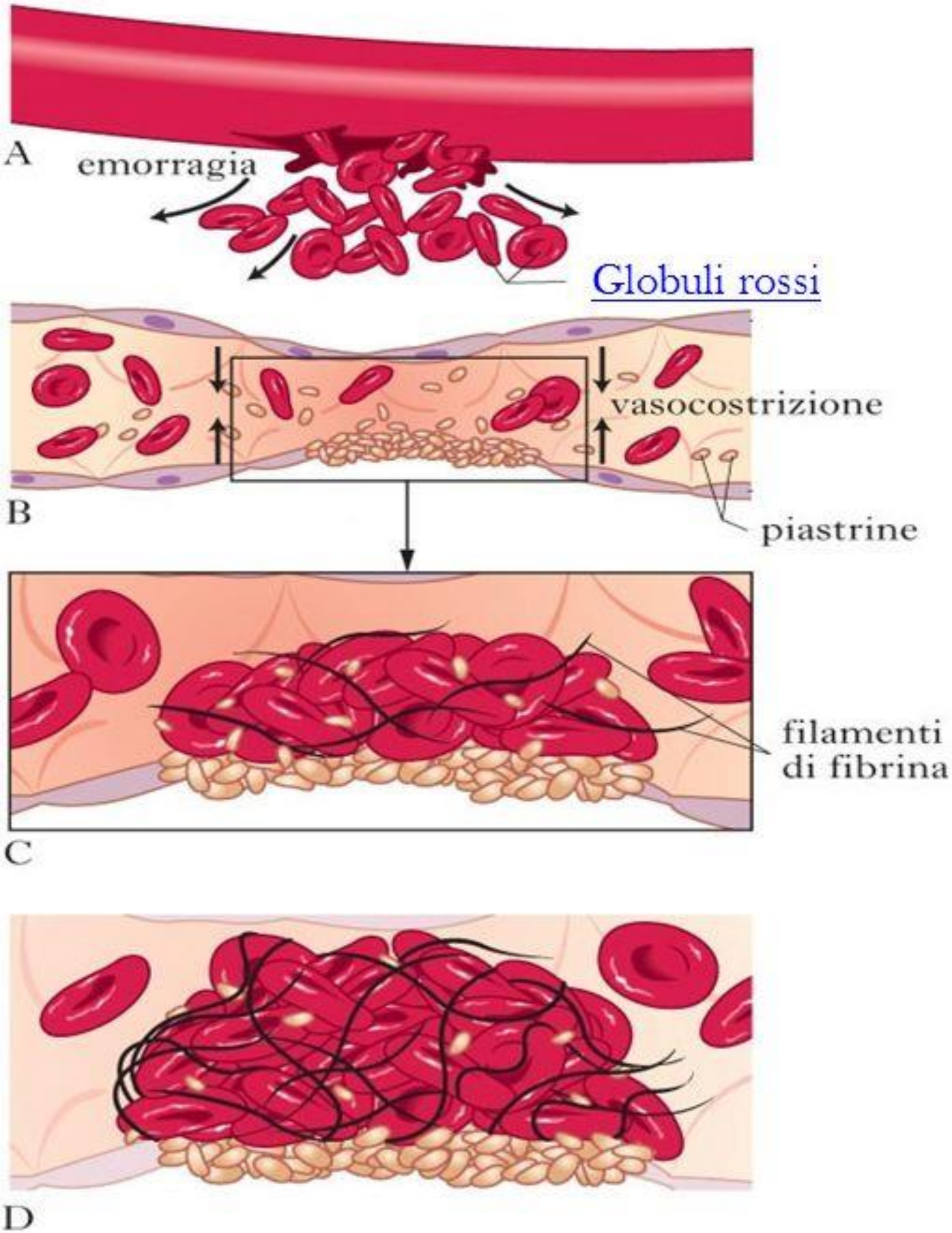
Table 7 Individual characteristics at high bleeding risk

o ClCr <50 ml/min
o Inherited or acquired coagulation defects
o Liver diseases with coagulopathy or history of previous bleedings
o Thrombocytopenia (platelets count <75.000 mm^3)
o Trauma
o Previous bleedings
o Treatment with concomitant drugs able to increase the bleeding risk such as antiplatelets, FANS, corticosteroids, drugs giving interference with P-gp or CYP3A4)

Coagulazione



Emostasi primaria
(tappo piastrinico)

Emostasi secondaria
(coagulazione)

Classificazione delle malattie dell'emostasi

A) Alterazione della fase vasale
1) porpora allergica o anafilattoide (m. di Schonlein-Henoch)
2) porpora non allergica
3) Teleangectasia ereditaria emorragica (m. di Rendu-Osler)

B) Alterazione della fase piastrinica
1) da modificazioni del numero
   a) trombocitopenie da difetto di produzione
   b) trombocitopenie da eccesso di distruzione (PTI)
   c) trombocitopenie da ipersequestro
2) da anomalie qualitative
   a) congenite (Bernard-Soulier e Glanzmann)
   b) acquisite (farmaci, ecc.)

C) Alterazioni della fase plasmatica
a) congenite (Emofilia, ecc)
b) acquisite

D) Sindrome da coagulazione intravascolare disseminata (CID)

E) Alterazioni della fibrinolisi

Alterazioni della fase plasmatica

Acquisite	***Congenite***
• Da difetto di sintesi fattori – ***epatopatie*** – ***farmaci anti-vit.K*** • Da attivazione e/o consumo dei fattori – ***C.I.D*** – ***anticoagulanti circolanti*** • Da diluizione dei fattori – trasfusioni massive	• ***Emofilia A e B*** • Malattia di von Willebrand • Deficit fattore VII • Deficit fattore II • Deficit fattore X • Deficit fattore XI • Deficit fattore XIII • Ipo-disfibrinogenemia

Controindicazioni ematologiche agli anticoagulanti

1. Storia di bleeding significativi (angiodisplasie ecc)
2. Piastrinopenie e –patie congenite ed acquisite (piastrinopenie autoimmuni, epatopatia, ecc)
3. Alterazioni congenite ed acquisite dell’emostasi plasmatica (es epatopatia, emofilia e Willebrand, ecc.)

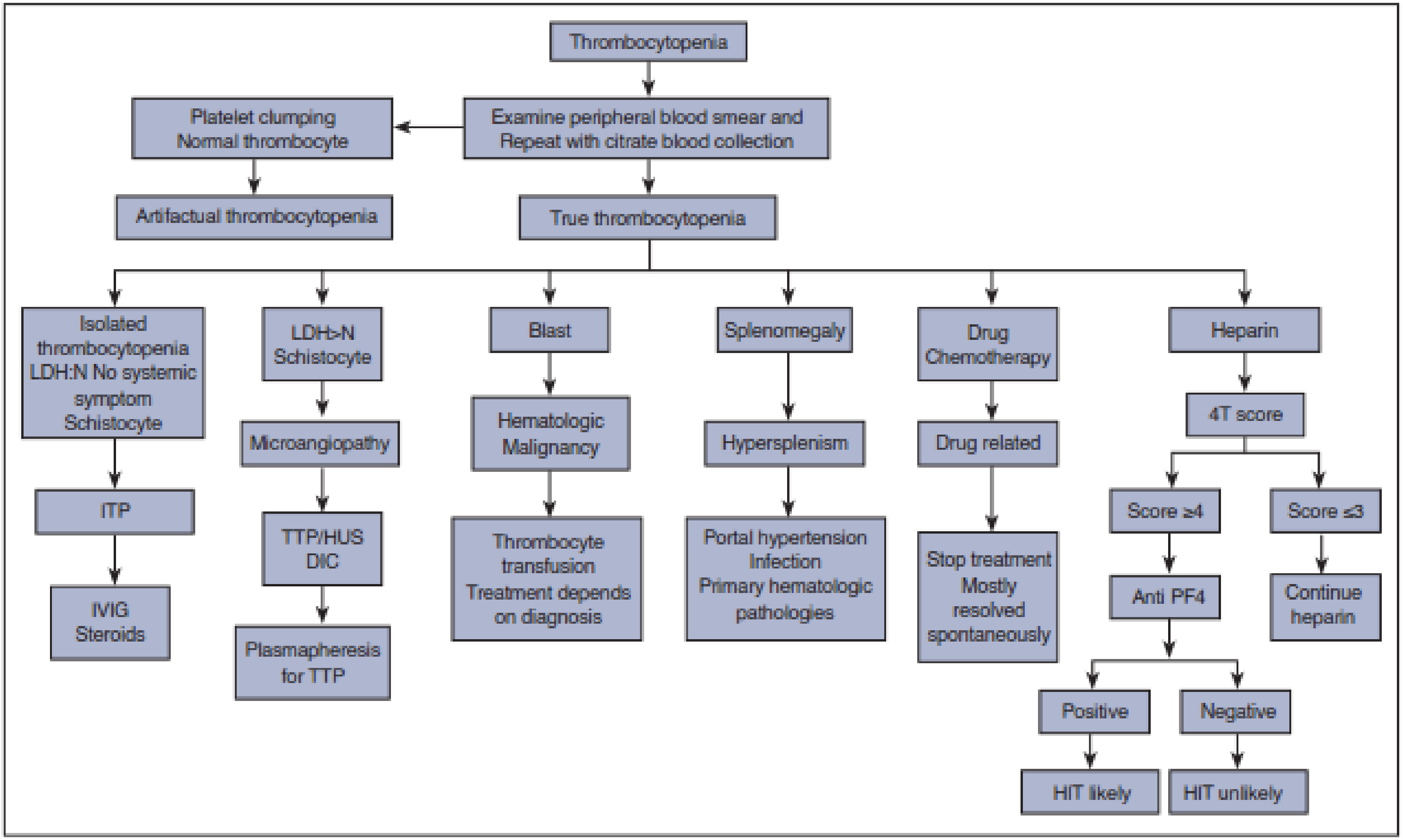


Figure 1. Approach to thrombocytopenia (DIC: Disseminated intravascular coagulation; HIT: Heparin-induced thrombocytopenia; ITP: Immune thrombocytopenia; IVIG: Intravenous immunoglobulin; LDH: Lactate dehydrogenase; TTP: Thrombotic thrombocytopenic purpura).

Feasible concomitant tre... ×

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Platelets. 2014;25(4):309-10. doi: 10.3109/09537104.2013.770137. Epub 2013 Feb 27.

Feasible concomitant treatment with eltrombopag and oral anticoagulation in a patient with chronic immune thrombocytopenia and severe cardiac comorbidities.

Sanchez-Gonzalez B[1], Ancochea A, Garcia-Pallarols F, Jimenez C, Pedro C, Besses C.

⊕ Author information

Comment on

Long-term follow-up of concomitant treatment with romiplostim and warfarin in a patient with immune thrombocytopenia and severe cardiac comorbidities. [Platelets. 2013]

Immune thrombocytopenia and anticoagulation: the role of romiplostim in the early treatment. [Br J Haematol. 2012]

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Platelets. 2013;24(3):242-3. doi: 10.3109/09537104.2012.686074. Epub 2012 May 30.

Long-term follow-up of concomitant treatment with romiplostim and warfarin in a patient with immune thrombocytopenia and severe cardiac comorbidities.

Baldini S, Rigacci L, Carrai V, Fjerza R, Alterini R, Bosi A.

Comment in

Feasible concomitant treatment with eltrombopag and oral anticoagulation in a patient with chronic immune thrombocytopenia and severe cardiac comorbidities. [Platelets. 2014]

PMID: 22646237 DOI: 10.3109/09537104.2012.686074

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How I treat patients with inherited bleeding disorders who need anticoagulant therapy

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Situations that ordinarily necessitate consideration of anticoagulation, such as arterial and venous thrombotic events and prevention of stroke in atrial fibrillation, become challenging in patients with inherited bleeding disorders such as hemophilia A, hemophilia B, and von Willebrand disease. There are no evidence-based guidelines to direct therapy in these patients, and management strategies that incorporate anticoagulation must weigh a treatment that carries a risk of hemorrhage in a patient who is already at heightened risk against the potential consequences of not treating the thrombotic event. In this paper, we

How I treat patients with inherited bleeding disorders who need anticoagulant therapy

Possibile indicazione a chiusura auricola ?

Karlyn Martin and Nigel S. Key

Division of Hematology/Oncology, Department of Medicine, University of North Carolina, Chapel Hill, NC

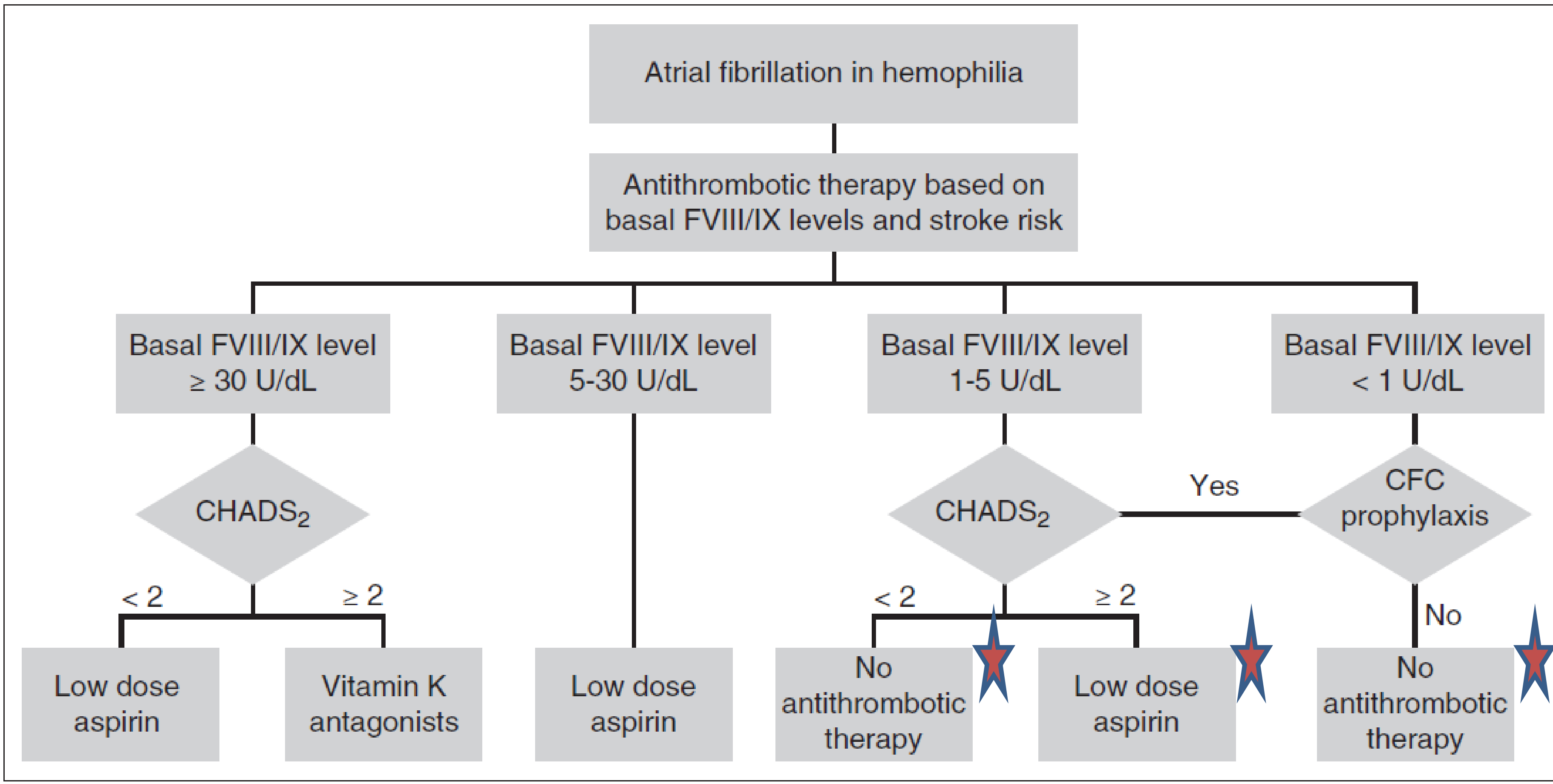

Figure 1. Recommended management algorithm for AF in hemophilia. CFC, clotting factor concentrate; CHADS$_2$, congestive heart failure, hypertension, age ≥75, diabetes, stroke/transient cerebral ischemia (doubled) score. Reprinted with permission from Mannucci et al.[34]

Bleeding phenotype and anti-thrombotic treatment

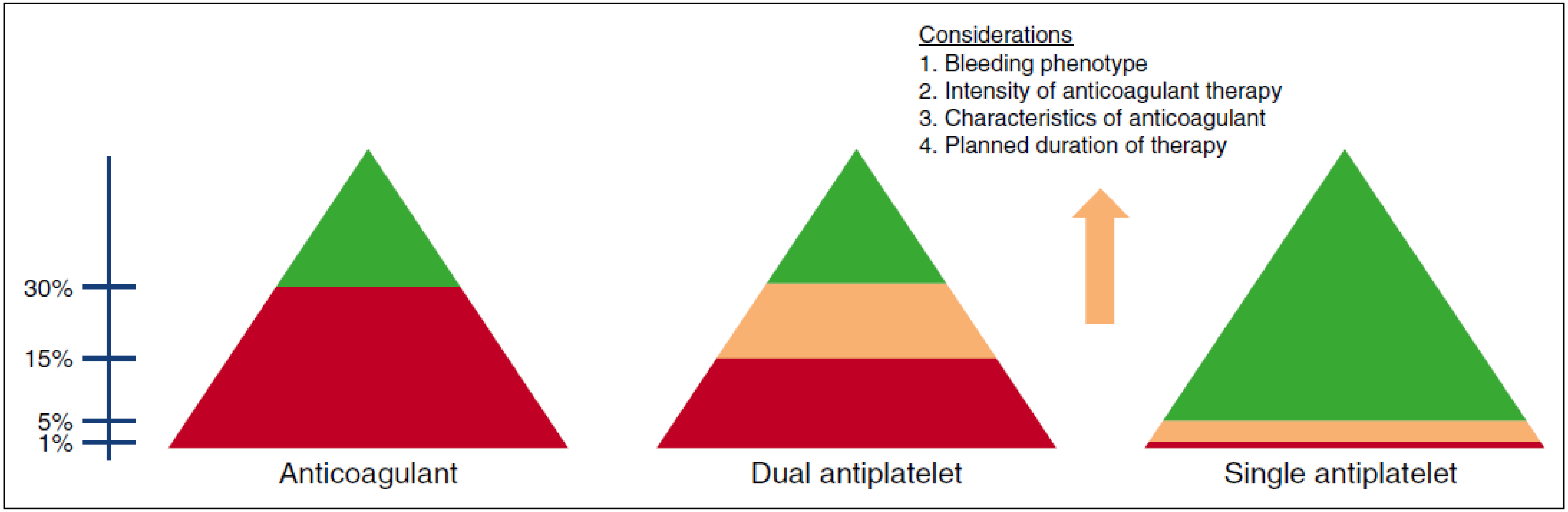

Figure 2. Approach to FVIII or FIX goals for the use of anticoagulant and antiplatelet therapy in hemophilia. Red, avoid use; green, likely okay to use; peach, decisions on use made after considerations as outlined in the figure.

Controindicazioni ematologiche agli anticoagulanti

1. Generalmente note al paziente, esami coagulativi basali alterati (eccetto Willebrand* !)
2. Conta piastrinica all’emocromo (se < 75.000)
3. Anamnesi dettagliata !

↓

TERAPIA ANTICOAGULANTE CONTROINDICATA

* Solo il tempo di stillicido, il PFA100 ed il test di Born possono essere alterati

Patologie Oncoematologiche

1. Piastrinopenia:

- condizione transitoria legata a tossicità da terapia
- massiva infiltrazione midollare con malattia avanzata e scarsa aspettativa di vita

2. Leucemia Linfatica Cronica : trattamento con Ibrutinib (aumenta R FA e aumenta R Bleeding quando associata a terapia antitrombotica?)
3. ????

Proposta : possibile indicazione a chiusura auricola

- Bleeding (localizzazione, frequenza, grado di anemizzazione)
- Piastrinopenia cronica refrattaria (definire cut off)
- Piastrinopenia/patia congenita o acquisita
- Per deficit congenito o acquisito di fattori
- ?