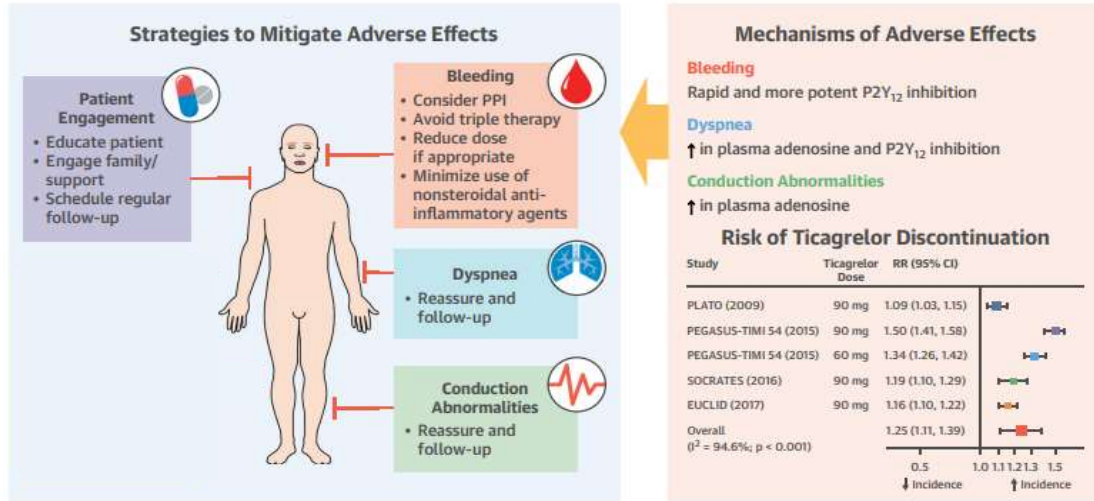


Practical Concerns of Prescribing Ticagrelor

- ✓ Switching
- ✓ Dyspnea
- ✓ Bleeding
 - intracranial Hemorrhage
 - Gastrointestinal bleeding
- ✓ Inconvenience (twice-daily dosing)

Ticagrelor's Adverse Effects and the Risk of Premature Discontinuation



J Am Coll Cardiol. 2019;73(19):2454-64



IR-0952-BRL-7080-SP



2017 DAPT Guidelines


Switching between oral P2Y12 inhibitors

RECOMMENDATION	COR	LOE
In patients with ACS who were previously exposed to clopidogrel, switching from clopidogrel to ticagrelor is recommended early after hospital admission at a loading dose of 180 mg irrespective of timing and loading dose of clopidogrel, unless contraindications* to ticagrelor exist.	I	B
Additional switching between oral P2Y12 inhibitors may be considered in cases of side effects/drug intolerance according to the proposed algorithms.	IIb	C

* Contraindications for ticagrelor: previous intracranial hemorrhage or ongoing bleeds.

European Heart Journal (2018) 39, 213-254







Switching Therapy

Switching therapy^{2,5}

Reasons for escalating from Clopidogrel to Ticagrelor	Reasons for de-escalation from Ticagrelor to Clopidogrel
<ul style="list-style-type: none"> ➤ ACS patients, who are initially treated with Clopidogrel at presentation: <ul style="list-style-type: none"> ■ Patients with either moderate- to high-risk non-ST elevation ACS (NSTEMI-ACS) (planned for either conservative or invasive management) ■ STEMI planned for primary PCI ➤ Admitted with thrombotic event (e.g., stent thrombosis or ACS), who have been treated with Clopidogrel ➤ Who are known poor metabolizer of Clopidogrel (e.g., CYP2C19 loss-of-function) 	<ul style="list-style-type: none"> ➤ Need for Oral Anticoagulant (OAC) ➤ Bleeding, intolerance ➤ Dyspnea, intolerance ➤ Triple therapy : OAC + DAPT ➤ Intolerable side effects

European Heart Journal (2018) 39, 213–254

Switching Between Oral P2Y12 Inhibitors

Acute setting:

Clopidogrel

Ticagrelor LD(180mg)
 Irrespective of prior clopidogrel timing & dosing

Clopidogrel LD(600mg)
 24h after last ticagrelor dose

Ticagrelor

Chronic setting:


Clopidogrel

Ticagrelor MD(90mg bd)
 24h after last clopidogrel dose

Clopidogrel LD(600mg)
 24h after last ticagrelor dose

Ticagrelor

10.1016/j.ahj.2014.05.001





Dyspnea in ACS patients

The most common causes are:

- Heart failure exacerbation
- Pneumonia or acute bronchitis
- Worsening of pre-existing chronic pulmonary disease
- Recurrent ischemia
- Pulmonary thromboembolism
- Anemia
- Side effects of beta-blockers or ticagrelor

✓ Ticagrelor-related dyspnea diagnosis is based on exclusion



ClinicalTrials.gov Identifier: NCT01073847/2012026649

16-0120-1001-0004-000




Dyspnea in PLATO study

	Ticagrelor 90mg + Aspirin (N=9235)	Clopidogrel + Aspirin (N=9186)
➔ Overall rate of dyspnea	14%	8%
Mild dyspnea	9.6%	5.5%
Moderate dyspnea	4.5%	2.4%
Severe dyspnea	0.4%	0.2%
➔ Discontinuation of dyspnea	0.9%	0.1%




HIGHLY PROBABLY NOT RELEVANT


16-0120-1001-0004-000




Dyspnea in PLATO sub-study



199 subjects
in a substudy of PLATO




After 1 month/ at least 6
months of chronic treatment




Pulmonary function testing
irrespective of reported
dyspnea

No indication of an adverse effect on pulmonary function



HIGH QUALITY EVIDENCE - INFORMATION Reference ID: 3677813




Management Of Ticagrelor-related Dyspnea

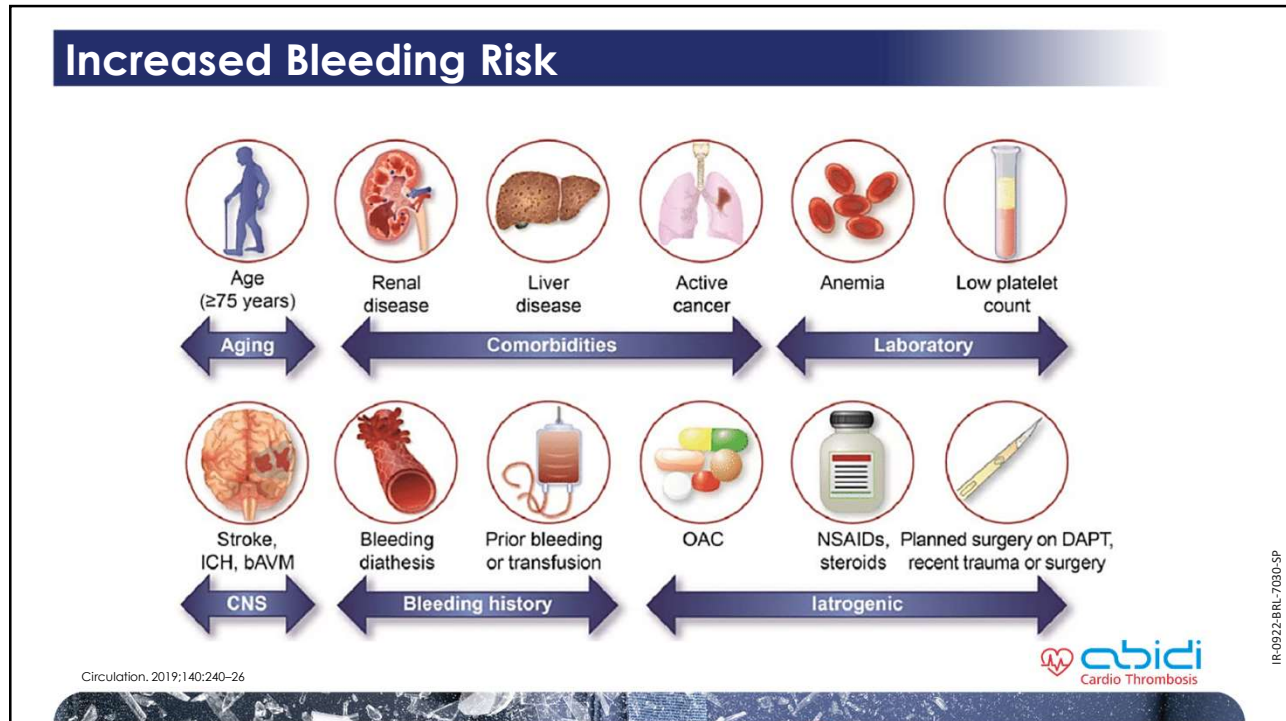
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    graph TD
      A[Evaluation for the most common causes+] --> B[Symptoms like wheezing*, orthopnea**, paroxysmal nocturnal dyspnea***, or chest tightness or pain****]
      A --> C[No]
      B --> D[Yes: Treatment of the main reason]
      C --> E[If usually occurs at rest, and is typically not related to exertion and does not limit exercise capacity]
      E --> F[Watch and wait for 3-4 Days]
      F --> G[Self limited]
      F --> H[If does not resolve spontaneously]
      G --> I[Continue Ticagrelor and follow up]
      H --> J[It is tolerable for the patient in the context of the benefit>risk profile of Ticagrelor treatment]
      H --> K[Persistent and intolerable]
      J --> I
      K --> L[Drug discontinuation : when dyspnea is persistent & cannot be tolerated]
  
```

*Heart failure exacerbation, Pneumonia or acute bronchitis, Worsening of pre-existing chronic pulmonary disease, Recurrent ischemia, Pulmonary thromboembolism, Anemia



IR-0122-8RL-6365-5P
Eur Heart J Acute Cardiovasc Care 2015; 4(6): 555-560.



DAPT & Bleeding

- **GI hemorrhage** is the **most common** serious bleeding complication from the use of **long-term antiplatelet therapy**
- Omeprazole & esomeprazole have the highest propensity for **clinically relevant interactions** with **clopidogrel** & lansoprazole an intermediate probability
- **No interaction** between concomitant **use of PPIs** and **prasugrel** or **ticagrelor**

Logo: abidi Cardio Thrombosis

Reference: IR-0120-BRL-0044-SP

Management GI bleeding in DAPT therapy

Measures to minimize bleeding while on dual antiplatelet therapy

Recommendations	Class ^a	Level ^b
Radial over femoral access is recommended for coronary angiography and PCI if performed by an expert radial operator. ^{43,44}	I	A
In patients treated with DAPT, a daily aspirin dose of 75 - 100 mg is recommended. ^{45-47,51,52}	I	A
A PPI in combination with DAPT ^c is recommended. ^{70,79,80,86,87}	I	B
Routine platelet function testing to adjust antiplatelet therapy before or after elective stenting is not recommended. ⁵⁸⁻⁶⁰	III	A

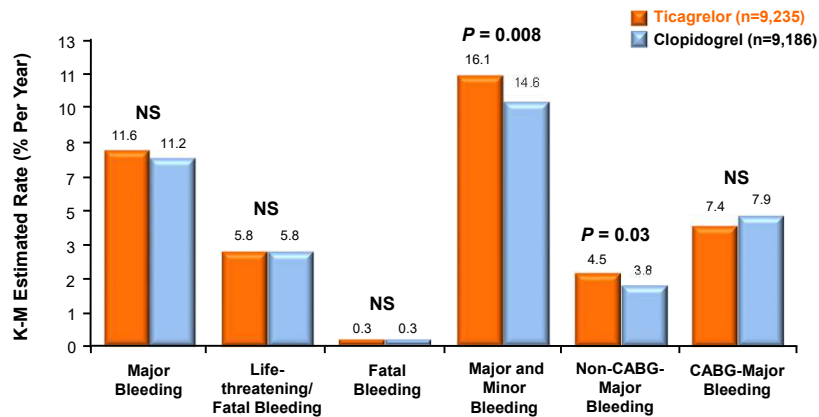
- PPIs have been recommended for reducing the risk of GI bleeding associated with DAPT.
- Aspirin plus Clopidogrel However, studies have found **decreased efficacy of clopidogrel** when concurrently administered with a PPI.
- Ticagrelor **does not have** drug interactions with PPIs.

European Heart Journal (2018) 39, 213-254



No significant difference in major fatal/life-threatening **bleeding** with Ticagrelor vs. Clopidogrel

PLATO Study



All values presented by PLATO criteria. Both groups included aspirin.

N Engl J Med. 2009;361:1045-1057.



