Interruption of antiplatelet therapy: benefits and risks

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Case #1

- A 75-year-old patient with **high risk NSTEMI** is pretreated with ticagrelor or clopidogrel in addition to aspirin and UFH. ECG shows no ST deviation and no Q waves. Coronary angiography shows advanced 3vessel CAD including a critical LM stenosis, with a high SYNTAX score (34).
- Heart Team decision is to perform CABG
- The patient is stable, has been free of chest pain for 48 hours and troponin is falling. The LV ejection fraction is 40% in the presence of diffuse hypokinesia.
- How do you manage perioperative antithrombotic therapy and the timing of CABG?

Continue | **Stop**

JPh Collet et al. Eur Heart J. 2015 Aug 29. pii: ehv407

Case #1

- **Ticagrelor or clopidogrel should be stopped**.
- parenteral anticoagulation maintained and CABG delayed for **5 days**, if possible.
- **Platelet function testing prior to CABG may be considered** to shorten the time delay to surgery.
- It should be noted that CABG performed on DAPT treatment is associated with a two fold increase in major bleeding and in reoperation due to bleeding.
- If the patient was on clopidogrel instead of ticagrelor, the same time delay to C ABG would have applied, while a 7-day drug-free window prior to CABG is recommended in prasugrel-treated patients

Continue | **Stop**

JPh Collet et al. Eur Heart J. 2015 Aug 29. pii: ehv407

Case #2

- Your expertise is requested for a 62-year old man with no prior history of cardiovascular disease who underwent open surgical cure of an abdominal aortic aneurism 48 h earlier.
- An increase in highsensitivity troponin from 100 to 200 ng/L (ULN <14 ng/L) was observed within 24 h of surgery.
- The patient did not have chest pain but is receiving morphine and ECG is normal.
- His hemoglobin level is 9.5 g/dL. Echocardiography shows normal LV function in the absence of RWMA.
- Should aspirin and/or therapeutic doses of parenteral anticoagulation be started? Is any further investigation needed?

Continue | **Stop**

JPh Collet et al. Eur Heart J. 2015 Aug 29. pii: ehv407

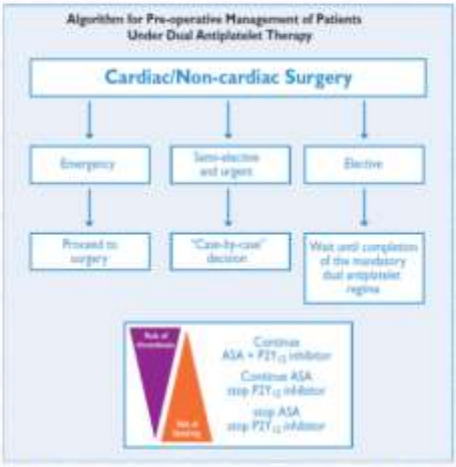
Case #2

- This patient suffered a perioperative MI.Additional information regarding intraoperative course (e.g. hypotension, major bleeding, arrhythmias) is necessary to **differentiate MI (i.e. due to a coronary atherosclerotic plaque rupture) from MI (e.g. due to intraoperative hypotension**).
- The patient qualifies for **aspirin administration and therapeutic parenteral anticoagulation**[e.g., with unfractionated heparin (UFH), because it is easy to titrate and re verse].
- However, a Heart Team discussion with the anesthesiologist and the surgeon is needed to assess the risks and benefits of early antithrombotic therapy in this patient. Subsequently, non-invasive testing should be performed to document myocardial ischaemia

JPh Collet et al. Eur Heart J. 2015 Aug 29. pii: ehv407

GUIDELINES

Perioperative management on DAPT



Windecker S, Kolh P, Alfonso F, Collet JP, Eur Heart J. 2014 Oct 1;35(37):2541-619

www.escardio.org/guidelines

Surgery on Dual Antiplatelet Therapy

Recommendations	Class[a]	Level[b]
Surgery on DAPT		
It is recommended not to interrupt antiplatelet therapy within the recommended duration of treatment.	I	C
In patients on $P2Y_{12}$ inhibitors who need to undergo nonemergency major surgery (including CABG), it should be considered to postpone surgery for at least 5 days after cessation of ticagrelor or clopidogrel, and for 7 days for prasugrel, if clinically feasible and unless the patient is at high risk of ischaemic events should be considered.	IIa	C
It should be considered to resume clopidogrel, ticagrelor or prasugrel after CABG surgery as soon as considered safe.	IIa	C
Platelet function testing should be used to guide antiplatelet therapy interruption rather than arbitrary use of a specified period of delay in patients undergoing CABG surgery.	IIa	C

Windecker S, Kolh P, Alfonso F, Collet JP, Eur Heart J. 2014 Oct 1;35(37):2541-619

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NSTE-ACS Guidelines

Perioperative management of antiplatelet therapy in non-ST-elevation acute coronary syndrome patients requiring coronary artery bypass surgery		
Aspirin is recommended 6–24 h post-CABG in the absence of ongoing bleeding events.	I	A
It is recommended to continue low-dose aspirin until CABG.	I	A
In stabilised patients requiring CABG on DAPT, discontinuation of ticagrelor and clopidogrel 5 days before and prasugrel 7 days prior to surgery should be considered.	IIb	A
After CABG, resuming $P2Y_{12}$ inhibitor therapy should be considered as soon as deemed safe.	IIa	C
Platelet function testing may be considered in shortening the time window to CABG following $P2Y_{12}$ inhibitor discontinuation.	IIb	B

Authors/Task Force Members, Roffi M, Patrono C, Collet JP, Eur Heart J. 2015 Aug 29. pii: ehv320.

www.escardio.org/guidelines

ACC/AHA Update : perioperative management

I	B-NR	**Elective noncardiac surgery should be delayed 30 days after BMS implantation and optimally 6 months after DES implantation** (101-103,143-146).
I	C-EO	In patients on DAPT after coronary stent implantation who must undergo surgical procedures that mandate the discontinuation of $P2Y_{12}$ inhibitor therapy, **it is recommended that aspirin be continued if possible** and the $P2Y_{12}$ platelet receptor inhibitor be restarted as soon as possible after surgery.
IIa	C-EO	When noncardiac surgery is required in patients currently taking a $P2Y_{12}$ inhibitor, a consensus decision among treating clinicians as to the relative risks of surgery and discontinuation or continuation of antiplatelet therapy can be useful.
IIb	C-EO	Elective noncardiac surgery after **DES implantation** in patients for whom $P2Y_{12}$ inhibitor therapy will need to be discontinued may be considered **after 3 months** if the risk of further delay of surgery is greater than the expected risks of stent thrombosis.
III Harm	B-NR	**Elective noncardiac surgery should not be performed within 30 days after BMS implantation or within 3 months after DES implantation in patients in whom DAPT will need to be discontinued perioperatively** (101-103,143-146).

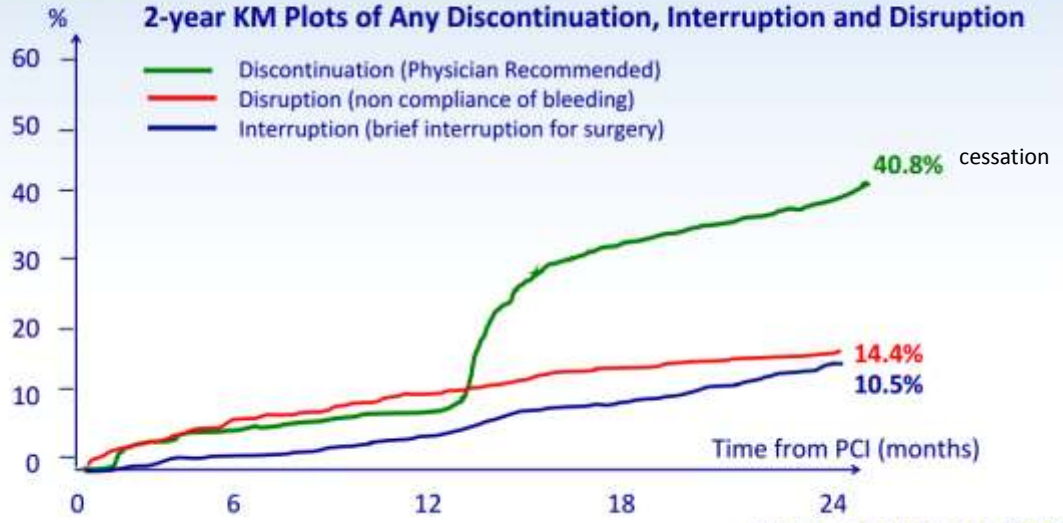
J Am Coll Cardiol. 2016 Mar 23. pii: S0735-1097(16)01699-5. doi: 10.1016/j.jacc.2016.03.513. [Epub ahead of print] No abstract available.

Limitations of the guidelines

- Do not stratify bleeding risk for individual intervention
- Do not stratify the risk of thrombosis according to coronary and clinical characteris tics
- Only refer to an individual assessment of the risk/benefit ratio
- Do not provide precise management of patients at high thrombotic risk candidate for a surgery not to be postponed
- Do not precise APT recovery after cessation

Risks of DAPT cessation

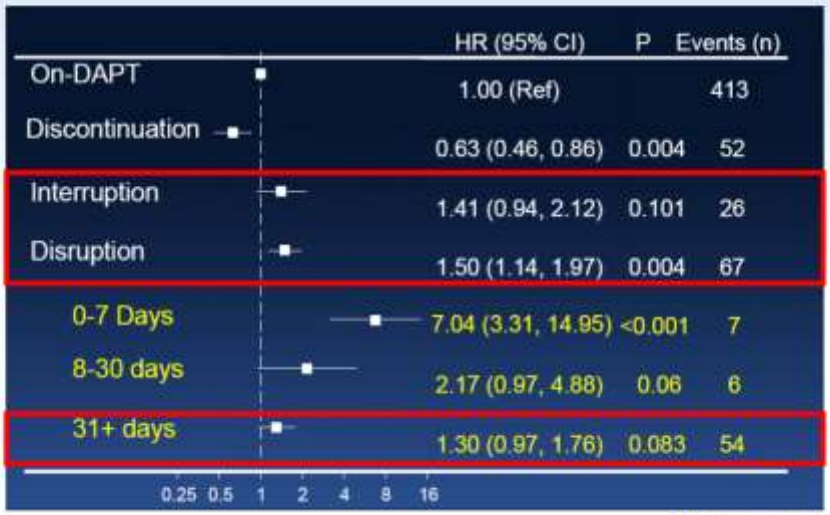
DAPT Cessation and MACE: The PARIS Registry 5031 pts



Merhan et al. *Lancet* 2013

DAPT Cessation and MACE: The PARIS Registry

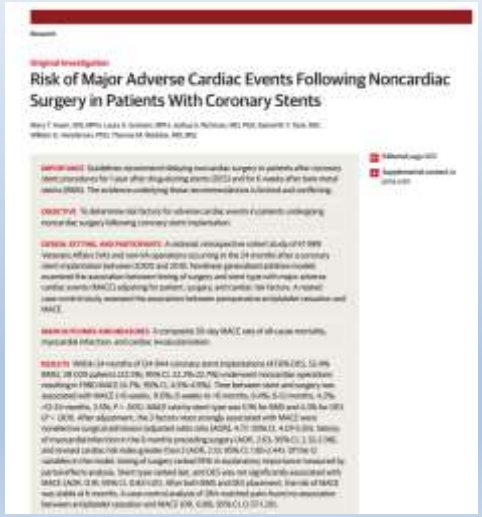
(Death, ST, MI and Clinically Driven TLR) 11.5% MACE rate over 2Y



Merhan et al. *Lancet* 2013

Risk of MACE following noncardiac surgery in patients with coronary stents

- National, Retrospective Cohort Study of 41,989 Operations Occurring in the 24 months After Coronary Stent Implantation (2000-2009)
- 1980 MACE (death/MI/cardiac revasc) within 30 days (5.1% after BMS vs. 4.3% after DES, (p<0.001)


Risk of Major Adverse Cardiac Events Following Noncardiac Surgery in Patients With Coronary Stents

Hawn et al. JAMA 2013;310:1462-72

Risk of MACE following noncardiac surgery in patients with coronary stents

- **Factors associated with MACE**
  - Non-elective surgery HR 4.8 [4.1-5.6]
  - Recent MI (< 6 months) HR 2.6 [2.3-3.0]
  - Revised cardiac index (Lee) >2 HR 2.1 [1.9-2.4]
- **No relationship between MACE and stent type**
- **DAPT continuation does not substantially mitigate risk**

Hawn et al. JAMA 2013;310:1462-72

Surgery and ischemia: summary

- **Predictors of thrombotic and ischemic events**
  - Individual risk of thrombosis (clinical, angiographic)
  - Specific risk of surgery (higher with vascular interventions)
  - Time from ACS/PCI to surgery (higher within 6 months)

- Interrupting DAPT in proximity to surgery is not free of harm (when aspirin is continued throughout and thienopyridine restarted asap after the procedure)
  - Whether this concept applies to all ACS/PCI undergoing surgery is unknown due to the complex interplay between the variables entered in the risk equation

Hawn et al. JAMA 2013;310:1462-72

Risks of DAPT continuation

Mechanisms linking bleeding to death

- **Fatal hemorrhage (e.g. intracranial bleeding)**
- **Vol. depletion hypotension, ischemia, arrhythmia**
- **Complications from procedures to manage bleeding**
- **Discontinuation of lifesaving medication**
- **Blood transfusion**
- **Unmeasured confounders**

Surgery and bleedings: summary

• Perioperative bleeding may occur as a consequence of the surgical procedure with hazards varying according to the type of intervention, and just in some cases as a consequence of the APT.

→Discriminating between different causes of bleeding is difficult

• Guidelines to identify a group of surgeries&procedures that appear to be associated with a high risk for bleeding in the context of APT use

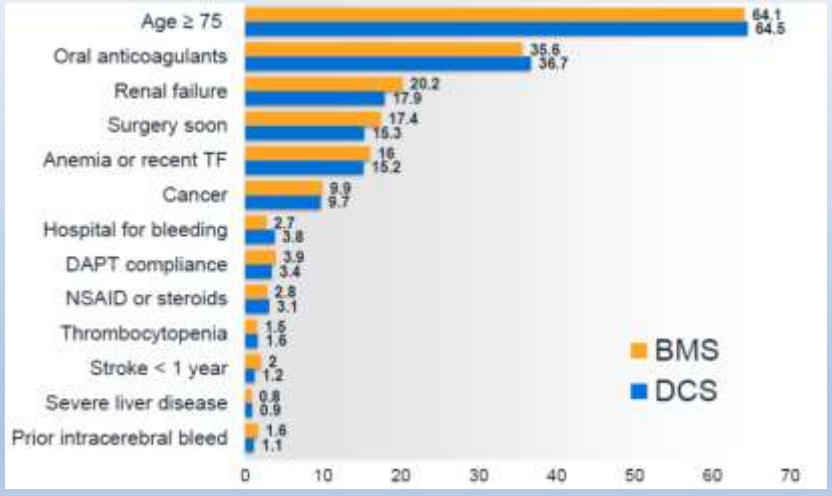
→ Cardiac surgery should be regarded as a special category and distinguished for non cardiac surgery due to incorporation of additional risk factors for bleeding

• Despite the potential of increasing bleeding risk, APT most importantly exerts a protective effect.

What has changed?

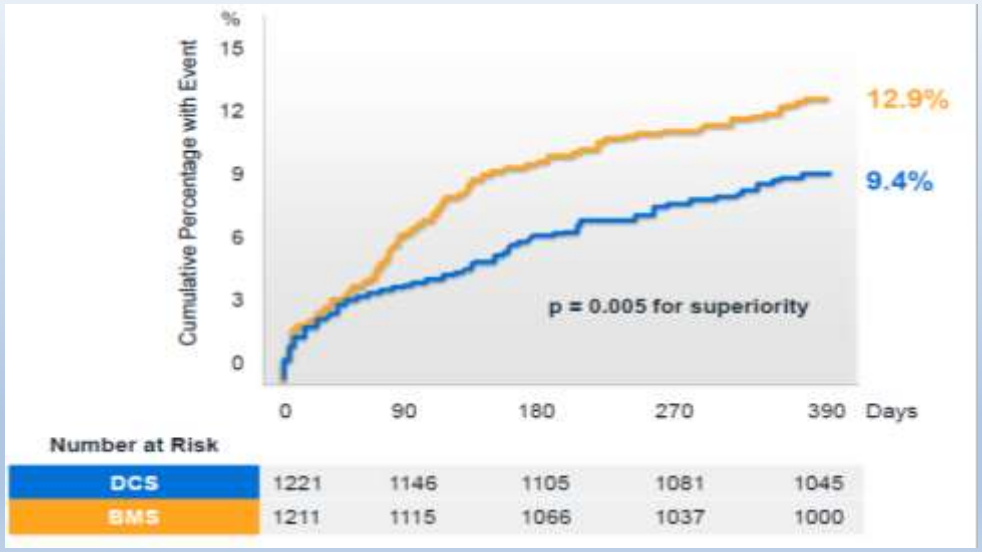
Leaders free

Biofreedm DCS in high bleeding risk patients



Urban Ph et al. NEJM 2015

Leaders free



Urban Ph et al. NEJM 2015

Drug Eluting Stent

Recommendations	Class[a]	Level[b]
In patients undergoing PCI, new generation DESs are recommended	I	A
In patients in whom a short DAPT duration (30 days) is planned because of an increased bledding risk, a new generation DES may be considered over BMS	IIb	B

Authors/Task Force Members, Roffi M, Patrono C, Collet JP, Eur Heart J. 2015 Aug 29. pii: ehv320.
Valgimigli M et al. J Am CollCardiol2015;65: 805–15

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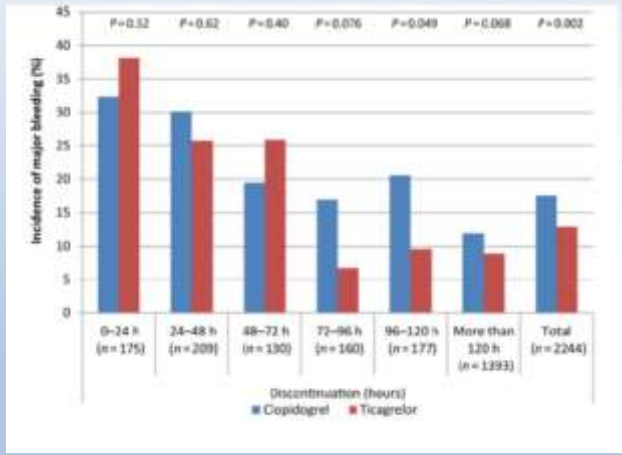
What could change?

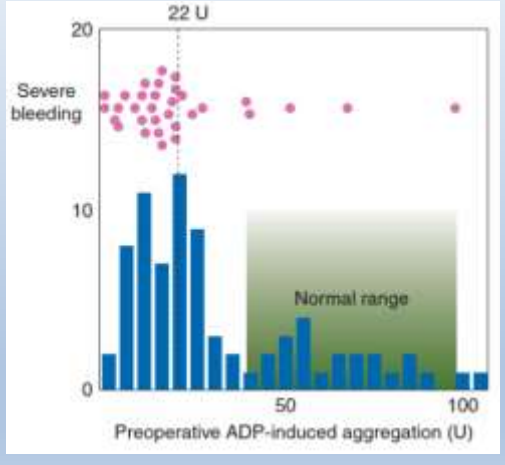
Major bleeding by day of discontinuation of clopidogrel/ticagrelor to surgery

- Major Bleedings : 12.9% vs. 17.6%, adjOR 0.72 (0.56 0.92), P=0.012 for ticagrelor & clopidogrel
- 72h-120h vs >120h waiting period:
  - OR= 0.93 (0.53-1.64), p=0.80 for ticagrelor
  - OR 1.71 (1.04-2.79), P = 0.033 for clopidogrel



European Heart Journal (2016) 37, 189–197

Major bleeding by day of discontinuation of clopidogrel/ticagrelor to surgery



- ADP-induced aggregation < 22, 24/38 (61%) developed severe bleeding compared with 8/52 (14%) when aggregation was at or above the cut-off value (P<0.001).
- The positive and negative predictive values for this cut-off value were 63% and 85%, respectively.

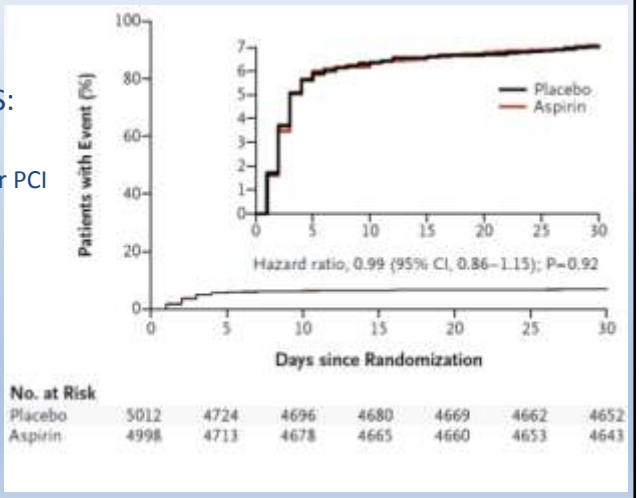
Br J Anaesth. 2016 Sep;117(3):309-15. doi: 10.1093/bja/aew189

Use of perioperative aspirin

Lessons of the POISE 2 trial

- Do not support routine use of aspirin in NCS:
  - Patients at low risk
  - 23% patients with known CAD and 5% with prior PCI

- Do not exclude a benefit of peri-operative aspirin continuation in patients at high risk



N Engl J Med 2014; 370:1494-1503

ESC recommendations on peri-operative aspirin use

Recommendations	Class	Level
Continuation of aspirin in patients previously treated with aspirin may be considered in the peri-operative period (based on risk of bleeding and thrombosis).	IIb	B
Discontinuation of aspirin in patients previously treated with that drug should be considered in patients in whom haemostasis is anticipated to be difficult to control during surgery.	IIa	B

European Heart Journal (2014) 35, 2383–2431

Peri-operative aspirin use after stenting

Recommendations	Class[a]	Level[b]	Ref.[c]
It is recommended that aspirin be continued for 4 weeks after BMS implantation and for 3–12 months after DES implantation, unless the risk of life-threatening surgical bleeding on aspirin is unacceptably high.	I	C	

« Importantly, whenever possible, aspirin should be continued throughout surgery »

European Heart Journal (2014) 35, 2383–2431

Conclusions

- Indications for peri-operative aspirin use have been downgraded
- This should not be applied straightforward to patients having undergone stent implantation
- Non-cardiac surgery should be performed after completion of DAPT and under
- aspirin if possible
- Non-cardiac surgery should be avoided in the first weeks (2-4) following stent implantation
- In other cases, timing of surgery and therapeutic modalities should rely on an individualized risk-benefit analysis

Thank You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