### **Case Report**



# **Ticagrelor Induced Upper Gastrointestinal Bleeding: A Case Report**

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#### **ABSTRACT**

Upper gastrointestinal bleeding is a common reason for hospitalisation in the elderly, and it has a high morbidity and mortality rate if not managed properly. Upper GI bleeding is caused by variables such as advanced age, H. pylori infection, drug use, cigarette smoking, and liver disease. Lowering the usage of aspirin and NSAIDs, as well as co-prescribing PPIs in patients initiating long-term NSAID therapy, are all controllable risk factors for upper GI bleeding. Upper GI bleeding is frequently caused by peptic ulcer disease, which is followed by erosive gastroesophagitis, gastroesophageal varices, Mallory-Weiss tears, Dieulafoy's lesions, gastric antral vascular ectasia (GAVE), and portal hypertensive gastropathy. The ESC advises stopping DAPT and continuing with SAPT, preferably with P2Y12 inhibitors, especially in GI bleeding. A 60-year-old male patient with intermittent melena and widespread weakness was diagnosed with antral and gastroduodenal ulcers, which caused upper GI hemorrhage. The guidelines suggest starting OAC again after a week, using the lowest acceptable target INR or the lowest effective dose. Aspirin should be continued until the P2Y12 inhibitor is discontinued for a maximum of 7 days in patients receiving DAPT.

**Keywords:** Upper GI Bleeding, DAPT, Ticagrelor, H. pylori Infection, NSAIDs.

### **INTRODUCTION**

pper gastrointestinal bleeding is a prevalent cause for hospitalization in older adults and has a high morbidity and death rate if not treated adequately. Advanced age, H pylori infection, drug usage (NSAIDs, Aspirin, P2Y12 inhibitors, anticoagulants, and steroids), cigarette smoking, and a history of liver disease are all risk factors for developing upper GI bleeding. Providers caring for older persons should aim to reduce any modifiable risk factors for upper GI bleeding, including lowering the use of aspirin and NSAIDs (where possible) and co-prescribing PPIs in patients who will be starting long-term NSAID therapy. Peptic ulcer disease is the most prevalent cause upper GI bleeding, followed by gastroesophagitis, gastroesophageal varices, Mallory-Weiss tears, Dieulafoy's lesions, gastric antral vascular ectasia (GAVE), portal hypertensive gastropathy (PHG). <sup>2</sup>

Both patients on oral anticoagulation (OAC) and those receiving antiplatelet therapy frequently experience bleeding complications, with significant bleeding happening in about 5% of cases in each group within a year.<sup>3</sup> Ticagrelor and Prasugrel, two P2Y12 inhibitors that are more potent than clopidogrel, are favoured, which further raises the risk of bleeding.<sup>4</sup> Major bleeding increases the risk of death (11 percent), myocardial infarction, and stroke significantly, presumably because the predictors of bleeding and those of ischemic events overlap so much and because effective antithrombotic medications are often stopped when bleeding begins.<sup>5,6</sup>

The European Society of Cardiology (ESC) advises to stop DAPT and continue with SAPT, preferably with P2Y12 inhibitors, especially in GI bleeding. A moderate bleeding

is significant blood loss (2mmol/L haemoglobin) or requires hospitalisation, but the patient is hemodynamically stable.<sup>7</sup> Restarting DAPT as soon as it is judged secure, ideally within three days.<sup>8,9</sup> Major bleeding increases the risk of death (11 percent), myocardial infarction, and stroke significantly. This association may be due to the high overlap between the predictors of bleeding and ischaemic events, as well as the fact that effective antithrombotic medications are often stopped when bleeding occurs.<sup>10</sup>

### **CASE PRESENTATION**

A 60-year-old male patient was brought with a 2-month history of intermittent melena and widespread weakness. Fever, jaundice, or weight loss were not present in the past. was diagnosed with antral and gastroduodenal ulcers, both of which caused upper GI haemorrhage. severe CKD. His co-morbidities were CAD, CKD (IgA Nephropathy), and hypertension. His vital signs were stable upon examination, including PR: 88bpm, BP: 120/68 mmHg, CVS: S1+S2+, RS:B/L clear, P/A was soft, and BS+. He seemed alert and well-focused.

He received IV fluids, antibiotics, and other supportive care at first. Investigations revealed that 2 units of PRBC were transfused by Hb-6.9, RBS-94, BU-147, Creat-4.35, Na-143, and K-4.14. On the day of admission, his treatment regimen included injections of Pan 80 mg, Emeset 4 mg, Ecosprin 150 mg, Prolomet am(5/50), Roxaver 20 mg, Revlamev 400 mg, and Felintaz 40 mg.

He complained of generalised weakness on the second day of admission, and an endoscopy reveals an impression of upper GI bleeding—antral ulcer, gastroduodenal ulcer. In



light of the aforementioned endoscopic result, Tab. AXCER was discontinued and replaced with Tab. Plavix 75mg OD.

He was advised to restart the older medications after 1 week. At discharge his Hb-8.9, TC-9780, Plc-189000, BU-132, Creat-4.60, Na-143, K-4.22. He was observed to stable and there were no further episodes of Melena.

### **DISCUSSION**

The guidelines state that OAC should be started again after a week, using the lowest acceptable target INR or, in the case of NOAC, the lowest effective dose. OAC and clopidogrel dual therapy for patients receiving triple therapy should be taken into consideration<sup>7</sup> 156 individuals with upper gastrointestinal bleeding who were taking aspirin for secondary prevention were enrolled in a double-blinded, randomised controlled trial (RCT) and assigned to continue taking aspirin or receive a placebo. 10.3 percent vs. 5.4 percent (HR 1.9; 95 percent CI 0.6-6.0)

more people in the aspirin-treated group experienced recurrent upper gastrointestinal haemorrhage. However, the frequency of blood transfusions was the same in both groups, suggesting very minor recurrent bleeding episodes. However, aspirin-treated patients had a considerably decreased mortality rate at 8 weeks: 1.3% vs. 12.9% (HR 0.2; 95 percent CI 0.06-0.60). In cases of DAPT, continue the P2Y12 inhibitor and consider a three-day aspirin break in patients who have active bleeding upon endoscopy (strong recommendation, moderate quality evidence). Section 2.5%

Aspirin should be continued until the P2Y12 inhibitor is discontinued for a maximum of 7 days in patients receiving DAPT. However, DAPT should continue if the patient experienced an ACS within 90 days or had a coronary stent placed within 30 days (strong recommendation, low quality evidence). <sup>12</sup>

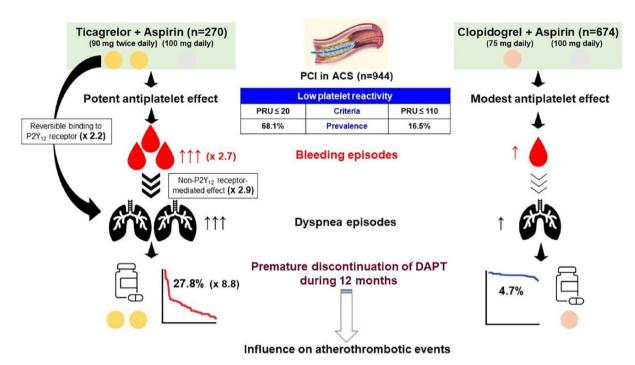


Figure 1: Association between type of P2Y12 inhibitor, adverse events and premature discontinuation of DAPT

### **CONCLUSION**

The optimum length of time for antiplatelet therapy is 12 months, however patients with a high risk of bleeding may be evaluated for shorter treatments, which should last at least 1 month and 6 months in patients who have had PCI. We thought about stopping DAPT and continuing SAPT instead, preferably with P2Y12 inhibitors, especially in GI bleeding, because the patient was experiencing moderate bleeding.

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## **REFERENCES**

- Costable NJ, Greenwald DA. Upper gastrointestinal bleeding. Clin Geriatr Med. 2021;37(1):155-72. doi: 10.1016/j.cger.2020.09.001, PMID 33213769.
- Al-Mallah M, Bazari RN, Jankowski M, Hudson MP. Predictors and outcomes associated with gastrointestinal bleeding in patients with acute coronary syndromes. J Thromb Thrombolysis. 2007 Feb 12;23(1):51-5. doi: 10.1007/s11239-006-9005-8, PMID 17186397.
- Gimbel ME, Minderhoud SCS, ten Berg JM. A practical guide on how to handle patients with bleeding events while on oral antithrombotic treatment. Neth Heart J. 2018 Jun 8;26(6):341-51. doi: <a href="https://doi.org/10.1007/s12471-018-1117-1">10.1007/s12471-018-1117-1</a>, PMID 29740754.
- Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. ESC Guidelines for the management of



- acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J Jan 14;37(3):267–315 2016;37(3):267-315. doi: 10.1093/eurhearti/ehv320, PMID 26320110.
- Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KAA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. Circulation. 2006 Aug 22;114(8):774-82. doi: 10.1161/CIRCULATIONAHA.106.612812, PMID 16908769.
- Steg PG, Huber K, Andreotti F, Arnesen H, Atar D, Badimon L, et al. Bleeding in acute coronary syndromes and percutaneous coronary interventions: position paper by the Working Group on Thrombosis of the European Society of Cardiology. Eur Heart J. 2011 Aug 1;32(15):1854-64. doi: 10.1093/eurheartj/ehr204, PMID 21715717.
- 7. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, et al. ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS. Eur Heart J Jan 14;39(3):213–60 2018;39(3):213-60. doi: 10.1093/eurheartj/ehx419, PMID 28886622.
- Halvorsen S, Storey RF, Rocca B, Sibbing D, ten Berg J, Grove EL, et al. Management of antithrombotic therapy after bleeding in patients with coronary artery disease and/or atrial fibrillation: expert consensus paper of the European Society of Cardiology Working Group on Thrombosis. Eur Heart J. 2016 Oct 27:ehw454.
- Gralnek IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, Kurien M, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy.

- 2015 Sep 29;47(10):a1-46. doi: <u>10.1055/s-0034-1393172</u>, PMID 26417980.
- Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KAA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. Circulation. 2006 Aug 22;114(8):774-82. doi: 10.1161/CIRCULATIONAHA.106.612812, PMID 16908769.
- Sung JJY, Lau JY, Ching JY, Wu JC, Lee YT, Chiu PW et al. Continuation of low-dose Aspirin therapy in peptic ulcer bleeding: a randomized trial. Ann Intern Med. 2010 Jan 5;152(1):1-9. doi: 10.7326/0003-4819-152-1-201001050-00179, PMID 19949136.
- 12. Abraham NS, Hlatky MA, Antman EM, Bhatt DL, Bjorkman DJ, Clark CB, et al. ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitors and thienopyridines: A focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. Circulation. 2010 Dec 14;122(24):2619-33. doi: 10.1161/CIR.0b013e318202f701, PMID 21060077.
- 13. Kang MG, Ahn JH, Kim K, Koh JS, Park JR, Hwang SJ et al. Prevalence of adverse events during ticagrelor versus clopidogrel treatment and its association with premature discontinuation of dual antiplatelet therapy in East Asian patients with acute coronary syndrome. Front Cardiovasc Med. 2022;9:1053867. doi: 10.3389/fcvm.2022.1053867, PMID 36578832.

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