Peer Review File

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Reviewer A

Comment 1: P1 L29 I would state from the beginning that DOACs (in those with an indication) are now preferred by the guidelines
Reply 1: Text updated as recommended
Changes in the text:
Original Text:
Dual antiplatelet therapy (DAPT) is the standard of care for patients post PCI, and anticoagulation with vitamin K antagonists (VKA) or direct acting oral anticoagulants (DOAC) is the standard of care for patients with AF and elevated ischemic stroke risk.

Updated text: Dual antiplatelet therapy (DAPT) is the standard of care for patients post PCI, and anticoagulation with vitamin K antagonists (VKA) or direct acting oral anticoagulants (DOAC) is the standard of care, with DOACS being recommended by ACC/AHA and ESC as preferred, for patients with AF and elevated ischemic stroke risk.

Comment 2: P3 L74 makes no sense, this line does not run properly
Reply 2: The text has been updated as described below
Changes in the text:
Original text: Here, we review provide historical review of DAPT in PCI and anticoagulation in AF. In addition, we review the currently available contemporary primary literature regarding triple therapy involving DAPT plus warfarin and dual therapy with DOAC plus a P_2Y_{12}.

Updated text: Here, we provide a historical review of DAPT in PCI and anticoagulation in AF as well as provide a contemporary review of the currently available literature regarding triple therapy involving DAPT plus warfarin and dual therapy with DOAC plus a P_2Y_{12}.

Comment 3: P4 delete BMS unless in your country these are still used
Reply 3: On occasions, BMS stents are still used in the US, but very infrequently.
Changes in the text:
Original text: Percutaneous coronary intervention can be performed with bare metal stents (BMS), and now more commonly, drug eluting stents (DES).

Updated Text: Percutaneous coronary intervention is performed most commonly with drug eluting stents (DES) and less commonly with bare metal stents (BMS).

Comment 4: P4 L109 should be give (delete s)
Reply 4: Text will be updated as recommended
Changes in the text:

Original text: The 2014 ACC/AHA Guideline for the Management of Patients with Non ST Elevation Acute Coronary Syndromes (15) and the 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease (16) gives a Class I recommendation of at least 12 months of DAPT which includes a P_2Y_{12} inhibitor with clopidogrel, prasugrel or ticagrelor as options plus low dose aspirin after DES implantation for ACS (16).

Updated Text: The 2014 ACC/AHA Guideline for the Management of Patients with Non ST Elevation Acute Coronary Syndromes (15) and the 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease (16) give a Class I recommendation of at least 12 months of DAPT which includes a P_2Y_{12} inhibitor with clopidogrel, prasugrel or ticagrelor as options plus low dose aspirin after DES implantation for ACS (16).

Comment 5: Cure also included IAP patients
Reply 5: Indeed CURE included IAP patients. Is it necessary to specify that for the purposes of this paper?
Changes in the text: no changes at this time

Comment 6: state that patients over 75 and <60 kg can be treated with prasugrel 5 mg
Reply 6: Made updates to text to include language for ESC recommending a reduced dose and specified the dose when discussing the ISAR-REACT trial.
Changes in the text:
P8 line 161
Original text: prasugrel loading dose of 60mg followed by 10mg daily in (n=2,006)

Updated text: prasugrel loading dose of 60mg followed by 10mg daily in (n=2,006) or 5mg daily maintenance dose in patients who were $\geq$ 75 years of age or patients weighing <60 kilograms (26)

Comment 7: L177 Isar-react 5 was not a head-to-head comparison between prasugrel and ticagrelor, but rather between the strategy of pretreatment with ticagrelor vs. post PCI treatment with prasugrel
Reply 7: Deleted text stating head-to-head
Changes in the text:
Line 158
Original text: In 2019, the ISAR-REACT 5 (Ticagrelor or Prasugrel in Patients with Acute Coronary Syndrome) (26) compared ticagrelor to prasugrel head-to-head in a trial which randomized 4,018 patients with ACS to ticagrelor

Updated text: In 2019, the ISAR-REACT 5 (Ticagrelor or Prasugrel in Patients with Acute Coronary Syndrome) (26) compared ticagrelor to prasugrel in a trial which randomized 4,018 patients with ACS to ticagrelor

Comment 8: and further delete Chinese figures
Reply 8: The Chinese characters are not present in our version of the document. They seem to appear in spots where the figures are linked in the text. I will save the document differently. Hopefully that will fix this issue.
Changes in the text: No changes made

Reviewer B

Comment 1: Page 6, line 3. TRITON TIMI 28 should be revised to TIMI 38.
Reply 1: The text has been updated as recommended
Changes in the text:
Original text: TRITON TIMI 28
Updated Text: TRITON TIMI 38

Comment 2: Chinese characters are found in the manuscript. Please correct them.
Reply 2: The Chinese characters are not present in our version of the document. They seem to appear in spots where the figures are linked in the text. I will save the document differently. Hopefully that will fix this issue.
Changes in the text: No changes made

Reviewer C

Comment 1: Please review 2020 ESC guidelines for management of ACS and incorporate the recommendations in the text
Reply 1: Recommendations from the 2002 ESC guidelines were added to the text. See below regarding updates
Changes in the text:
Deleted text: although prasugrel is included in the 2014 ACC/AHA Non-ST-Elevation Acute Coronary Syndromes guidelines (15) and 2016 ACC/AHA focused updated on duration of DAPT after ACS guidelines for use in PCI after ACS (16), it is utilized less often in the US.

Added text: P4 line 142 Despite this, the 2020 ESC ACS in patients presenting without persistent ST-segment elevation guidelines recommend prasugrel over ticagrelor and clopidogrel in patients who will receive PCI in the setting of non-ST elevation (17) ACS partially based on the results of the ISAR-REACT 5 trial. Additionally, the 2020 ESC ACS NSTEMI guidelines recommend a reduced dose for patients who are ≥ 75 years of age and patients weighing <60 kilograms, which was the recommended dosing strategy in those patients in the ISAR-REACT trial. ACC/AHA guidelines have not been updated to include the ISAR-REACT 5 data.

Comment 2: The article is lengthy and can be rewritten in more concise fashion
The important findings of each trial could be highlighted briefly in the main text and leave

further details to be mentioned in tables.

Reply 2: We intended to provide a comprehensive review on this topic and we believe that the content is of relevance and interest to the wide readership of the journal.

Changes in text: no changes to text