

## Answer Regarding: Potent P2Y12 Inhibitors and Bleeding Complications

Dear colleagues,

**T**hank you for your letter titled "Potent P2Y12 Inhibitors and Bleeding Complications" containing your valuable comments and contributions to our research.<sup>1-2</sup> Your comments will contribute to the evaluation of the results of our study from a different perspective.

In our study, contrary to expectations, we found that patients treated with strong P2Y12 inhibitors when used in combination with tirofiban experienced less in-hospital bleeding than those treated with clopidogrel.<sup>2</sup> However, in further analysis, we determined that this difference was due to the older age of the patients rather than the drug used. As we stated in the discussion part of our study, this finding is consistent with previous studies. Although the bleeding rate is higher with potent P2Y12 inhibitors than with clopidogrel, the antiplatelet effect occurs at a similar rate when used in combination with tirofiban.<sup>3</sup> The disappearance of the difference in bleeding rates in combination with tirofiban may be due to this.

All acute coronary syndrome patients receiving triple antithrombotic therapy in our clinic are given a proton pump inhibitor (PPI) for gastrointestinal protection. In addition, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) is avoided. However, we do not have information about the use of PPIs and NSAIDs before admission to the hospital. In light of previous data, it can be thought that these patients use more NSAIDs due to the older age of the patient group with high bleeding, and this may contribute to the increase in bleeding events.<sup>4</sup> As stated by our colleagues, it is important to use antithrombotic drugs carefully and to take preventive measures in terms of gastrointestinal bleeding in this patient group with a high risk for bleeding.

In our study, contrary to current guidelines, some patients were given tirofiban as pretreatment.<sup>5</sup> However, our study includes patients between the years 2015 and 2020. Some high-risk patients were given pretreatment in accordance with the old guidelines.<sup>6,7</sup> In our study, it can be thought that pretreatment with tirofiban may affect bleeding. However, there was no difference between the patient groups receiving different antiplatelet therapy and also between patients with and without bleeding in terms of pretreatment.

In the ACCOAST study, it was determined that preloading with prasugrel did not provide any benefit in terms of ischemic events but caused an increase in bleeding events.<sup>8</sup> In studies with ticagrelor and clopidogrel, no clear results were found in terms of benefit or bleeding events. In a Swedish registry, no difference was found in terms of long-term ischemic events and mortality in patients pretreated with P2Y12 inhibitors.<sup>9</sup> As a result of this finding, it is not recommended to perform P2Y12 loading before coronary anatomy is observed in patients who will undergo early invasive treatment in current ESC guidelines. In our study, ticagrelor and clopidogrel were loaded on some patients as pretreatment in line with previous guideline recommendations. However, prasugrel was loaded only after the coronary arteries were imaged. Therefore, we think that this will not have a significant effect in terms of bleeding events. However, the number of patients in our study was insufficient to detect small differences. Our findings need to be supported by larger studies.

**Declaration of Interests:** The authors declare that they have no competing interest.

### LETTER TO THE EDITOR AUTHOR'S REPLY

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