Author`s Reply

To the Editor,

I read with great interest the letter related to our manuscript entitled “The effects of tirofiban infusion on clinical and angiographic outcomes of patients with STEMI undergoing primary PCI” published

in the Anatolian Journal of Cardiology on December 25, 2014 (Epub ahead of print) by Kaymaz et al. (1). Here, I am going to answer of the abovementioned questions.

As summarized in this letter, our article showed that tirofiban treatment in addition to aspirin, high-dose clopidogrel, and unfractionated heparin prior to primary PCI significantly improves myocardial reperfusion, ST segment resolution, in-hospital sudden cardiac death, and in-hospital all-cause mortality rates in patients with STEMI without an increased risk of major bleeding. The major limitation of our study was the absence of a prospective randomized clinical trial design because of the critical difficulties in the reimbursement of the treatment cost in our country. Despite this important limitation, comparison of the baseline characteristics of the treatment groups permitted us to assess the efficacy and safety issues of tirofiban treatment among the groups. Despite the higher TIMI risk score in the pre-PCI or upstream tirofiban group than those in the other three groups, the benefits in TIMI flow grade, corrected TIMI frame count, ST segment resolution, in-hospital sudden cardiac death, and in-hospital all-cause mortality were also significantly higher in the upstream tirofiban subset than those in the other groups. Our results represent the potential benefit of tirofiban added to aspirin, high-dose clopidogrel, and unfractionated heparin treatment combinations, and should be considered to provide important data concerning the use of tirofiban treatment in the dual antiplatelet therapy (DAPT) era. However, the results of our study are limited to DAPT including aspirin and high-dose clopidogrel, but cannot be generalized to combinations with the novel antiplatelet agents prasugrel and ticagrelor (2). Our rational for bridging treatment with tirofiban in this setting was targeted to minimize the risk of intracoronary rethrombosis within the first hours of primary PCI, in which the level of platelet inhibition still remains sub-therapeutic because of the kinetics of clopidogrel, even with a 600-mg loading dose and well-known procoagulant state of STEMI. Currently, this risk of early rethrombosis and the need for GP IIb/IIIa inhibitors seem to be eliminated with the novel fast-acting and the more potent platelet inhibitors, prasugrel and ticagrelor.

It may not be appropriate to, compare a study based on non-randomized retrospective data with the FINESSE trial that showed no appreciable benefit, but only harm, in starting GP IIb/IIIa inhibitors in the pre-hospital setting for patients progressing to primary PCI (3). The comments of Jeremias et al. (4) were based on formal searches of electronic databases (Medline, Cochrane) from January 1990 to April 2009 and included five trials randomizing 2,937 patients (1,475 in the abciximab group and 1,462 in the placebo group). They concluded that the routine use of abciximab in patients with STEMI treated with primary PCI does not appear to be beneficial in those who receive pre-PCI thienopyridines (4). However, their comments are limited to a meta-analysis from five abciximab series and cannot be compared with the main results of our retrospective study including a total of 994 out of the 1,242 patients with STEMI in whom tirofiban was used prior to, during, or after primary PCI. Indeed, recent studies have confirmed our positive results with upstream tirofiban treatment (5, 6). The first study showed that tirofiban administered with primary PCI following 600 mg clopidogrel improved the primary efficacy outcome at 30-day and 1-year follow-up without an increase in major bleeding (5). In the other study, the upstream use of tirofiban was significantly associated with an increased incidence of spontaneous reperfusion and a decreased incidence of MACE at 30-day as well as 90-day follow-up in patients treated with primary PCI for STEMI (6).

Intracoronary tirofiban injection was the treatment of choice in all patients in the peri-PCI tirofiban group, whereas only the intravenous route was used in the upstream or post-PCI tirofiban treatment groups. Although the median difference in pain-to-balloon time was only 25 min between the upstream and peri-PCI tirofiban groups, the more positive results with upstream treatment can be considered as consistent with the potential benefit of earlier intravenous tirofiban treatment over intracoronary injection of this drug at cath lab.

At the time of enrollment, a manual aspiration catheter was not available in our center. In our opinion, "pain-to-balloon time" instead of "first medical contact-to-balloon time" seems to be a more appropriate measure for the estimation of total ischemic time. Despite the risk of its subjectivity, this definition also includes the time delay from occurrence of the pain to first medical contact. Data from TIMI flow, corrected TIMI frame count, and ST segment resolution in pre-PCI, peri-PCI, and post-PCI subsets can answer question concerning the effect of tirofiban on the no-reflow phenomenon in our study. All patients with no-reflow or a high thrombus burden without satisfactory ST segment resolution underwent repeat angiography after tirofiban infusion. In patients with renal insufficiency, bolus treatment with tirofiban was not followed by infusion. In our study, median pain-to-balloon time (185–210 min) and in-hospital door-to-balloon time (30 min) were included into the analysis. In our study, pain-to-balloon time was not related to the angiographic, electrocardiographic, and clinical benefits of tirofiban.

Finally, I would like to thank the author of this comprehensive letter, which leads to a seminal discussion concerning the use of upstream GP IIb/IIIa inhibitors as an adjunct treatment to DAPT in patients who underwent primary PCI.

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