Editorial

Will Ticagrelor Help Post-Myocardial Infarction ‘Healing’?

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Conflict of Interest

The author has no financial conflicts of
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The contents of the report are the author's
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► See the article “Rationale and Design of the High Platelet Inhibition with Ticagrelor to Improve Left Ventricular Remodeling in Patients with ST-segment Elevation Myocardial Infarction (HEALING-AMI) Trial” in volume 49 on page 586.

The healing process after myocardial infarction (MI) is known to be a critical factor in subsequent loss of heart function and prognosis of heart failure. Several factors contribute to this process including the time from injury to reperfusion, the degree of inflammation post injury, and chronic left ventricular (LV) remodeling.^{1,2)} This process involves a complex interplay between various cells such as monocytes, macrophages, fibroblasts and even platelets.³⁾

Ticagrelor is a cyclo-pentyl-triazolo-pyrimidine (CPTP), new class of antiplatelet agents, that reversibly binds to the P2Y₁₂ receptor of platelets, resulting in potent inhibition of platelet function.⁴⁾ It has been shown in clinical studies to improve clinical outcomes compared with conventional clopidogrel in patients with acute coronary syndrome including ST-elevation MI. In particular, ticagrelor was shown to reduce all cause death and cardiac death in the Platelet Inhibition and Patient Outcomes (PLATO) trial, triggering several hypotheses that it may have extra-platelet pleiotropic effects.⁵⁾

In animal models, it has been shown that platelet accumulation may promote LV remodeling and rupture, while treatment with ticagrelor may have beneficial protective effects against reperfusion injury and chronic LV remodeling.^{6,7)} In humans, there are conflicting data where one small trial reported reduced infarction size and microvascular obstruction in patients with ST-elevation MI with ticagrelor treatment,⁸⁾ while another did not find any significant benefit.⁹⁾ Further, the potential effects of ticagrelor on or the concept that a potent antiplatelet agent may be protective in chronic LV remodeling have never been verified in humans.

In this edition of the *Korean Circulation Journal*, Park et al.¹⁰⁾ have published the trial design of a very interesting and innovative trial to study whether long-term treatment with ticagrelor compared with clopidogrel, may be associated with an improvement in the remodeling process after ST-elevation MI. They plan to randomize at least 242 patients with suspected ST-elevation MI planned to receive primary percutaneous coronary intervention within 12 hours of symptom onset in a 1:1 manner to ticagrelor (180 mg loading, then 90 mg twice a day) or clopidogrel (600 mg loading, then 75 mg daily). They will perform baseline 3D-echocardiography, N-terminal prohormone of brain natriuretic peptide, high-sensitivity C-reactive protein, and platelet function test with VerifyNow within 3 days of reperfusion,

and follow up with the same tests at 1 month and at 6 months post-reperfusion with the exception of the platelet function test, which will not be performed at 6 months.

This study will be able to address whether loading and maintenance therapy up to 6 months with a potent antiplatelet agent, ticagrelor, can improve post-MI remodeling. The major outcome will be meticulously measured using not only various 3D-echocardiographic parameters, but also biomarkers and cardiac magnetic resonance imaging. As a sub-study, the exploration of various cell counts and levels of inflammatory biomarkers may be able shed valuable light into how they influence the remodeling process after injury. However, there will also be certain issues that this study will not be able to address, such as whether the potential positive effect of ticagrelor on post-MI remodeling, if any, is a function of its potent antiplatelet effect or a drug specific effect unique to ticagrelor. It would be very interesting if any future studies address this question by randomly comparing the effects of ticagrelor vs. prasugrel. I eagerly await the results of this trial and look forward other such innovative trials in the future.

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