Effects of Ticagrelor versus Prasugrel on Coronary Microvascular Function in Patients Undergoing Elective Percutaneous Coronary Intervention: the PROtecting MICROcirculation During Coronary Angioplasty (PROMICRO)-3 Randomized Study

Fabio Mangiacapra, MD, PhD, Emanuele Barbato, MD, PhD

Background
Microvascular injury (MVI) frequently occurs in patients with coronary artery disease undergoing percutaneous coronary intervention (PCI) despite successful revascularization, and is associated with adverse outcome (1). Several mechanisms are involved in the development of MVI, including endothelial dysfunction and increased platelet aggregation (2). In the PROMICRO-2 (PROtecting MICROcirculation during coronary angioplasty) study, more intensive platelet inhibition achieved with a single loading dose of prasugrel, as compared with clopidogrel, was able to protect coronary microcirculation in patients undergoing elective PCI, resulting in lower post-PCI index of microvascular resistance (IMR) and reducing periprocedural myonecrosis (3).

Besides being at least as effective as prasugrel in inhibiting platelet aggregation, ticagrelor has also been shown to have additional properties potentially affecting coronary microcirculation, including inhibition of intracellular adenosine reuptake and increase of adenosine plasma levels (4,5). However, the effects of ticagrelor on coronary microvascular function have not been evaluated in patients with stable coronary artery disease undergoing elective PCI.

Aim of the study
To compare in a prospective, randomized double blind controlled study the effects of ticagrelor (180 mg) and prasugrel (60 mg) on myocardial microvascular function in patients with stable coronary artery disease undergoing elective PCI.
Methods
A total of 50 P2Y12 receptor inhibitor-naïve patients undergoing elective PCI will be recruited in the study and randomized (1:1) to receive currently recommended loading doses of either ticagrelor (180 mg) or prasugrel (60 mg) at least 12 hours before intervention. Coronary microvascular function will be assessed before PCI and at the end of the procedure through a thermo-dilution method that allows accurate and repeatable quantitative absolute coronary flow measurements (ml/min) during catheterization (6). The flow rate, the temperature of the saline entering the coronary artery and the temperature of the blood mixed with the distal part of the coronary artery are assessed using a 4 infusion holes catheter (RayFlow infusion catheter, Hexacath Inc., Paris, France) in combination with a pressure/temperature sensor-tipped guidewire (PressureWire Certus; St. Jude Medical, St. Paul, MN, USA) located approximately 6 cm distal to the tip of the infusion catheter.

Blood samples (40 ml in total) will be drawn in all patients before and 24 h after intervention for cardiac biomarkers assessment (creatine kinase-myocardial band [CK-MB], troponin I [Tn-I]). Patients randomized to the prasugrel group will receive clopidogrel 75 mg once daily from the day after PCI on, whereas patients randomized to the ticagrelor group will receive a 600-mg loading dose on the day after PCI and a 75-mg maintenance dose from the following day on (7).

Exclusion criteria.
Patients will be excluded from the study in the presence of at least one of the following: age >75 years, body weight <60 kg, previous transient ischemic attack (TIA) or stroke, acute coronary syndromes, chronic total occlusion, lesions with extensive calcifications requiring rotational atherectomy, platelet count <70 x 10^9/l, high bleeding risk, coronary bypass surgery in the previous 3 months, severe chronic renal failure (serum creatinine >2 mg/dl).
References


