In-Hospital Survival After Out of Hospital Cardiac Arrest

We read with keen interest the description of etiology and determinants of in-hospital survival after an out of hospital cardiac arrest (OHCA).[1] Among the noncardiac causes, pulmonary embolism (PE) is reported to be the most common. It is particularly challenging to diagnose pulmonary (PE) as a cause of OHCA, but it often presents as a nonshockable rhythm, which was predictive for nonsurvival. The emergence of mobile-application based ultrasound systems where the ubiquitous smartphones can be transformed into an ultrasound by plugging in a transducer or through a Bluetooth will facilitate the diagnosis of PE in OHCA.[2] These patients should receive thrombolytic therapy if rapid imaging with a device confirms the suspicion of PE. We have demonstrated that cardiopulmonary resuscitation after a dose of lytic with the bolus agent tenecteplase, should range from 60 to 90 minutes[3] preferably with a manual compression device. Prolonged CPR gives time for the lytic agent to act. The outcomes may improve in those with noncardiac causes and nonshockable rhythms, especially if PE is the cause of OHCA.

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Meta-Analysis of the Efficacy and Safety of Genotype-Guided Strategy for Selection of $P2Y_{12}$ Inhibitors in Coronary Artery Disease

Despite the development of newer and more potent antiplatelet medications, clopidogrel remained the most prescribed $P2Y_{12}$ inhibitor after percutaneous coronary intervention (PCI) in the United States.[1,2] Clopidogrel is a pro-drug, which requires activation through cytochrome P450 pathway (*CYP2C19*) to be effective. Due to genetic variation in the *CYP2C19* gene, up to 30% of the US population are poor metabolizers of clopidogrel, and are at higher risk of thrombotic complications after PCI.[1–3] Ticagrelor and prasugrel metabolism are not affected by these genetic polymorphisms. Given their increased potency, they carry a higher risk of bleeding complications.[4] In a previous meta-analysis, we reported reduced rates of major adverse cardiovascular events (MACE) in acute coronary syndrome (ACS) patients who underwent treatment with genotype-guided strategy (GGS) utilizing *CYP2C19* testing versus conventional strategy (CS).[5] The recently published Tailored Antiplatelet Initiation to Lessen Outcomes Due to Decreased Response after Percutaneous Coronary Intervention (TAILOR-PCI) trial did not show any benefit of *CYP2C19*-guided treatment.[6] The trial was possibly underpowered since the study had lower than expected event rates, and was powered to detect a large effect size of a 50% reduction in the primary endpoint with GGS. Therefore, we sought to analyze further evidence using pooled data form multiple published randomized controlled trials (RCTs).

Ethical approval: This study is exempted from ethical/IRB approval, as it is conducted utilizing publically available database.

We conducted a comprehensive search of electronic databases for all RCTs that evaluated the safety and efficacy of GGS for selection of oral $P2Y_{12}$ inhibitors in patients who underwent PCI or those with ACS. Studies with a minimum follow-up of 6 months were included. Two authors extracted and analyzed the data using Review Manager Version 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, 2014). Risk ratios (RR) and corresponding 95% confidence intervals were calculated and combined using random effects model meta-analysis. The primary outcome of our study was the rate of MACE defined as a composite of cardiovascular (CV) mortality, myocardial infarction (MI), and stroke. Secondary outcomes were individual components of MACE, stent thrombosis, and major bleeding (based on the Bleeding Academic Research Consortium 3-5 [BARC].

A total of 6,329 patients (3,143 in the GGS group and 3,186 in the CS group) were analyzed from 6 RCTs with a mean follow-up of 11.6 months (mean age 63.2 ± 4.1 years, 26% women, 61.6% with hypertension, 26% with diabetes mellitus, 40.7% with dyslipidemia, 41.5% with tobacco use [former/current], and 86.5% with ACS).[5–7] Analysis showed significant reduction in MACE (4.8% vs 6.9%; RR 0.69, 95% CI: 0.51 to 0.93, p = 0.01, $I^2 = 43\%$), MI (1.9% vs 3.29%; RR 0.59, 95% CI: 0.42 to 0.84, p = 0.004, $I^2 = 14\%$), and stent thrombosis (0.31% vs 0.91%; RR 0.36, 95% CI: 0.18 to 0.76, p = 0.007, $I^2 = 0\%$) with GGS compared with CS. No significant difference was found with respect to CV mortality, stroke, and major bleeding (Figure 1) A sensitivity analysis that restricted the study population to only ACS subjects showed similar results.

In this meta-analysis, we found a significant benefit of *CYP2C19* genotype-guided initiation of oral $P2Y_{12}$ inhibitors in patients who underwent PCI or those with ACS compared with conventional treatment without genotype testing. Our analysis showed lower risk of MACE, MI, and stent thrombosis. Although not statistically significant, there were trends toward lower risk of CV mortality and stroke with a GGS.