ADP-receptor antagonists in patients with acute myocardial infarction complicated by cardiogenic shock: a pooled IABP-SHOCK II and CULPRIT-SHOCK trial sub-analysis

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Purpose: The purpose of this pooled analysis is to compare the clinical outcome of patients with acute myocardial infarction complicated by cardiogenic shock treated with either clopidogrel or the newer, more potent ADP-receptor antagonists prasugrel or ticagrelor. Patients from the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) and Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) trial were included.

Methods and results: For the current analysis, the primary endpoint was 1-year mortality and the secondary safety endpoint was moderate or severe bleedings until hospital discharge with respect to three different ADP-receptor antagonists. Eight hundred fifty-six patients were eligible for analysis. Of these, five hundred seven patients (59.2%) received clopidogrel, one hundred seventy-eight patients (20.8%) prasugrel and one hundred seventy-one patients (20.0%) ticagrelor as acute antiplatelet therapy. The adjusted rate of mortality after 1-year did not differ between prasugrel and clopidogrel (hazard ratio [HR]: 0.81, 95% confidence interval [CI] 0.60–1.09, padj=0.17) or between ticagrelor and clopidogrel treated patients (HR: 0.86, 95% CI 0.65–1.15, padj=0.31). In-hospital bleeding events were significantly less frequent in patients treated with ticagrelor vs. clopidogrel (HR: 0.37, 95% CI 0.20–0.69, padj=0.002) and not different in patients treated with prasugrel vs. clopidogrel (HR: 0.73, 95% CI 0.43–1.24, padj=0.24), see Table 1.

Conclusion: This pooled sub-analysis is the largest analysis on safety and efficacy of three oral ADP-receptor antagonists and shows that an acute therapy with either clopidogrel, prasugrel or ticagrelor is no predictor of 1-year mortality. Treatment with ticagrelor seems to be associated with less in-hospital moderate and severe bleeding events in comparison to clopidogrel.

Table 1. Regression analysis of bleeding events

Hospital bleeding events (moderate & severe)	unadjusted OR (95% CI)	P value	adjusted OR (95% CI)	P value
Prasugrel vs. Clopidogrel	0.72 (0.45 - 1.17)	0.18	0.73 (0.43 – 1.24)	0.24
Ticagrelor vs. Clopidogrel	0.49 (0.28 – 0.84)	0.01	**0.37 (0.20 – 0.69)**	**0.002**
1 - year bleeding events (moderate & severe)	**unadjusted HR (95% CI)**	**P value**	**adjusted HR (95% CI)**	**P value**
Prasugrel vs. Clopidogrel	0.74 (0.49 - 1.11)	0.14	0.83 (0.54 – 1.28)	0.40
Ticagrelor vs. Clopidogrel	0.50 (0.30 – 0.83)	0.007	**0.43 (0.25-0.72)**	**0.002**

Legend to Table 1:
This table shows the regression analyses of bleeding events with the different ADP-receptor inhibitors as dependent variable in comparison to clopidogrel. Adjusted odds and hazard ratios were calculated with an adjustment for the variables shown in the methods section. P-values: Pearson chi-squared test or Mann-Whitney-Wilcoxon test.