Optimal antithrombotic regimen in patients with cardiogenic shock on ImpellaTM mechanical support: less might be more

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Background: Bleeding and ischemic complications are the main cause of morbidity and mortality in critically ill cardiogenic shock patients, supported by short-term percutaneous mechanical circulatory support (pMCS) devices. Hence, finding the optimal antithrombotic regimen is challenging. Bleeding not only occurs because of heparin and antiplatelet therapy (both required in the prevention of pump and acute stent thrombosis) but also because of device- and disease related coagulopathy. To prevent clotting-related device failure, most centers target full therapeutic heparin anticoagulation levels in left ventricular (LV) Impella™ supported patients in analogy with Veno-Arterial Extracorporeal Membrane Oxygenation. We aimed to investigate the safety (related to bleeding and thrombotic complications) of targeting low-dose versus therapeutic heparin levels in left Impella™-supported cardiogenic shock patients on dual antiplatelet therapy (DAPT).
Methods: In this hypothesis generating pilot study, we investigated 114 patients supported for at least two days by LV Impella™ mechanical support due to cardiogenic shock at three tertiary ICUs, highly specialized in mechanical support. Low-dose heparin (aPTT 40–60s or anti-Xa 0.2–0.3) was compared to standard of care (aPTT 60–80s or anti-Xa 0.3–0.5). Major adverse cardio- and cerebrovascular events (MACCE; composite of death, myocardial infarction, stroke/transient ischemic attack) and BARC bleeding (bleeding academic research consortium classification) during 30 day follow-up were assessed. Inverse probability of treatment weighting (IPTW) analysis was calculated with age, gender, arterial hypertension, diabetes mellitus, smoking, chronic kidney disease, previous stroke, previous myocardial infarction, previous coronary arterial bypass grafting, hypercholesterolemia and DAPT as matching variables. COX regression analysis was conducted to test for robustness.
Results: IPTW revealed 52 patients in the low-dose heparin group and 62 patients in the therapeutic group. Mean age of patients after IPTW was 62±16 years in the intermediate and 62±13 years in the therapeutic group (p=0.99). 25% and 42.2% were male (p=0.92). Overall bleeding events and major (BARC3b) bleeding events were higher in the therapeutic heparin group (overall bleeding: Hazard ratio [HR]=2.58, 95% confidence interval [CI] 1.2–5.5; p=0.015; BARC 3b: HR=4.4, 95% CI 1.4–13.6, p=0.009). Minor bleeding (BARC3a) as well as MACCE and its single components (ischemic events) did not differ between both groups. These findings were robust in the COX regression analysis.
Conclusion: In this pilot analysis, low-dose heparin in 114 LV Impella™ cardiogenic shock patients was associated with less bleeding without increased ischemic events, adjusted for DAPT. Reducing the target heparin levels in critically ill patients supported by LV Impella™ might improve the outcome of this precarious group. These findings need to be validated in randomized clinical trials.