

## **Title: Myocardial injury in hip fractures: a HIP ATTACK-1 substudy**

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**Background:** Hip fracture is common and associated with important patient outcomes. The HIP ATTACK-1 trial demonstrated that accelerated surgery was feasible and safe. This substudy aims to determine the impact of accelerated surgery versus standard-care on the 90-day risk of cardiovascular outcomes and death in patients who presented with a cardiac biomarker elevation at hospital arrival.

**Methods/Results:** The HIP ATTACK-1 trial was a randomized controlled trial designed to determine whether accelerated surgery for hip fracture (i.e., age >45 years and diagnosed with low-energy mechanism hip fracture requiring surgery) was superior to standard-care in reducing death or major complications. This substudy includes 1392/2970 (47%) patients (61 sites) that had a cardiac biomarker measurement (>99.9% troponins) at hospital arrival. For this substudy, the primary outcome was all-cause mortality, and the secondary outcome was a composite of all-cause mortality, myocardial infarction, stroke, and congestive heart failure at 90-days after randomization. 322/1392 (23%) patients had a cardiac biomarker elevation at hospital arrival. Among patients with elevated cardiac biomarker, the median time from hip fracture diagnosis to surgery was 6 h (IQR 5–13) in the accelerated-surgery group and 29 h (IQR 19–52) in the standard-care group. Patients with an increased cardiac biomarker had a lower risk of mortality with accelerated surgery compared to standard-care (17/163 [10%] in accelerated-surgery patients vs 36/159 [23%] in standard-care patients; HR 0.43 [95% CI 0.24–0.77]); and lower risk of the secondary composite outcome (23/163 [14%] in accelerated-surgery patients vs 47/159 [30%] in standard-care patients; HR 0.43 [CI 95% 0.26-0.72]). Patients with cardiac biomarker elevation >2.5 times the upper limit of normal (ULN) had 30% mortality at 90 days compared to 9% mortality in patients with no cardiac biomarker elevation. Patients with cardiac biomarker elevation >2.5 times ULN had a trend towards lower mortality following accelerated surgery compared with standard-care (2/35 [6%] vs 13/44 [30%]; HR 0.17, CI 95% 0.04-0.77, interaction p=0.09) when compared to patients with lower levels of cardiac biomarker elevation.

**Conclusion:** One in 5 patients with hip fracture present with acute myocardial injury. Mortality is three-fold higher in this population. Myocardial injury reflects patients who are not tolerating the physiological stress associated with the fracture. Accelerated surgery improved mortality and major cardiovascular outcomes at 90 days after randomization compared with standard-care. HIP ATTACK-2 will further explore the effects of accelerated surgery in patients with a hip fracture and myocardial injury identified at hospital presentation.