**A commentary by Charles Cornell, MD,** is linked to the online version of this article.

# Myocardial Injury in Patients with Hip Fracture

## A HIP ATTACK Randomized Trial Substudy

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**Background:** Myocardial injury after a hip fracture is common and has a poor prognosis. Patients with a hip fracture and myocardial injury may benefit from accelerated surgery to remove the physiological stress associated with the hip fracture. This study aimed to determine if accelerated surgery is superior to standard care in terms of the 90-day risk of death in patients with a hip fracture who presented with an elevated cardiac biomarker/enzyme measurement at hospital arrival.

**Methods:** The HIP fracture Accelerated surgical TreaTment And Care tracK (HIP ATTACK) trial was a randomized controlled trial designed to determine whether accelerated surgery for hip fracture was superior to standard care in reducing death or major complications. This substudy is a post-hoc analysis of 1392 patients (from the original study of 2970 patients) who had a cardiac biomarker/enzyme measurement (>99.9% had a troponin measurement and thus "troponin" is the term used throughout the paper) at hospital arrival. The primary outcome was all-cause mortality. The secondary composite outcome included all-cause mortality and non-fatal myocardial infarction, stroke, and congestive heart failure 90 days after randomization.

**Results:** Three hundred and twenty-two (23%) of the 1392 patients had troponin elevation at hospital arrival. Among the patients with troponin elevation, the median time from hip fracture diagnosis to surgery was 6 hours (interquartile range [IQR] = 5 to 13) in the accelerated surgery group and 29 hours (IQR = 19 to 52) in the standard care group. Patients with troponin elevation had a lower risk of mortality with accelerated surgery compared with standard care (17 [10%] of 163 versus 36 [23%] of 159; hazard ratio [HR] = 0.43 [95% confidence interval (CI) = 0.24 to 0.77]) and a lower risk of the secondary composite outcome (23 [14%] of 163 versus 47 [30%] of 159; HR = 0.43 [95% CI = 0.26 to 0.72]).

**Conclusions:** One in 5 patients with a hip fracture presented with myocardial injury. Accelerated surgery resulted in a lower mortality risk than standard care for these patients; however, these findings need to be confirmed.

**Level of Evidence:** Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

Hip fractures are common and associated with high mortality[1,2]. The fracture initiates inflammatory, hypercoagulable, and stress states, increasing the risk of delirium, infections, bleeding, and vascular events[3,4].

The most common perioperative complication associated with a hip fracture is myocardial injury, which is seen in at least 20% of patients at hospital presentation[5,6]. Myocardial injury is frequently unrecognized, as patients usually do not

**Disclosure:** The HIP ATTACK-1 trial was supported by the Canadian Institutes of Health Research, the Ontario Strategy for Patient Oriented Research Support Unit, the Ontario Ministry of Health and Long-Term Care, the Hamilton Health Sciences Foundation, the Physicians' Services Incorporated Foundation, the Michael G. DeGroote Institute for Pain Research and Care, Smith & Nephew (to recruit patients in Spain), and Indiegogo Crowdfunding. This substudy received funding from a McMaster General Internal Medicine Research Grant. Funders had no role in the study design, conduct, analyses, or manuscript preparation. The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJS/I117).

A **data-sharing statement** is provided with the online version of the article (http://links.lww.com/JBJS/I131).

have typical cardiac ischemic symptoms and routine perioperative troponin screening has not been established as the standard of care. Myocardial injury in patients with a hip fracture is important because it is associated with a poor prognosis and a risk of premature death[5,6]. Due to the complexity of these patients' cases, medical specialists are frequently consulted for preoperative medical assessment and clearance for surgery. Surgical timing is a common dilemma if there is evidence of myocardial injury. Physicians often perceive medical management and testing as a priority; however, the resulting surgical delay may worsen the prognosis[5,7,8].

The impetus for the HIP fracture Accelerated surgical TreaTment And Care tracK (HIP ATTACK) trial[6,9] arose from a patient who presented with a hip fracture and troponin elevation. The HIP ATTACK trial randomized 2970 patients with a hip fracture to receive accelerated surgery (median of 6 hours from orthopaedic diagnosis) or standard care (median of 24 hours from orthopaedic diagnosis). The HIP ATTACK trial demonstrated that accelerated surgery was feasible and safe, even in the subgroup of patients with acute medical conditions.

During the HIP ATTACK trial, we recognized that a number of patients presented with an elevated cardiac biomarker/enzyme level at hospital arrival, before randomization. Therefore, we designed this substudy to determine the impact of accelerated surgery versus standard care on the 90-day risk of death and adverse vascular outcomes in patients who presented with a hip fracture and a myocardial injury at hospital arrival.

## Materials and Methods

The HIP ATTACK trial was an international randomized controlled trial (RCT) of 2970 patients aged 45 years or older with a low-energy-mechanism hip fracture requiring a surgical intervention and presenting during the working hours of the individuals carrying out the study. Each center defined their study hours based on the local regular working hours. The main exclusion criteria were the use of therapeutic anticoagulants with no reversing drug available, periprosthetic fracture, and high-energy fracture. The primary objective was to determine the effect of accelerated surgery compared with standard care on the 90-day risk of all-cause mortality and major perioperative complications. The HIP ATTACK protocol and the results of the main trial (NCT02027896 in ClinicalTrials.gov) were published previously[6,9]. We followed the CONSORT (Consolidated Standards of Reporting Trials) recommendations, and a patient flow diagram is shown in Figure 1.

In brief, eligible patients were randomized, stratified by the planned surgery type (open reduction and internal fixation or arthroplasty), in a 1:1 fashion through a central computerized randomization system with randomly varying block sizes to receive accelerated surgery (with a goal of performing it 6 hours after the orthopaedic diagnosis) or standard care. We recruited patients in 69 centers, from 17 countries. All sites obtained local Research Ethics Board approval. All patients provided informed consent before randomization. Patients, health care providers, and research staff were aware of the treatment allocation; however, outcome adjudicators were blinded to the allocation.

All patients had the same structured follow-up for outcome assessment and troponin measurements on post-randomization days 1 through 7 using the assay available at each site. Research personnel followed all patients throughout their index hospitalization and contacted them at 30 and 90 days after randomization to note any trial outcomes. Baseline cardiac biomarker/enzyme levels (>99.9% had a troponin measurement and thus "troponin" is the term used throughout the paper) were measured from the time of the hip fracture to randomization, at the discretion of the physicians involved in the patient's care. Myocardial injury at hospital presentation was defined as a baseline troponin level before randomization that was above the upper limit of normal for each of the site-specific assays except for the high-sensitivity troponin-T assay (hsTnT), for which the threshold was defined as ≥20 ng/L, and for the non-high-sensitivity troponin-T assay (TnT), for which the threshold was defined as ≥0.03 ng/mL, based on perioperative troponin thresholds associated with short-term mortality in noncardiac surgery[10-12].

A committee of independent experts in perioperative medicine, blinded to the participants' allocations, adjudicated the following events: myocardial infarction, recurrent myocardial injury after randomization not meeting the universal definition of myocardial infarction[13], nonfatal cardiac arrest, stroke, pulmonary embolism, proximal deep venous thrombosis, congestive heart failure, infection, sepsis, life-threatening bleeding, and major bleeding. We used the decision of the adjudicators regarding the adjudicated events for all statistical analyses.

For this substudy, we determined a priori that the primary outcome was all-cause mortality 90 days after randomization. Secondary outcomes included a composite of major perioperative vascular complications (i.e., all-cause mortality and non-fatal myocardial infarction, congestive heart failure, and stroke). The individual secondary outcomes were vascular mortality, non-vascular mortality, myocardial infarction, recurrent myocardial injury after randomization not meeting the universal definition of myocardial infarction[13], congestive heart failure, new clinically important atrial fibrillation, and stroke. The duration of the hospital stay after the index admission for hip fracture, delirium, and moderate-to-severe pain as well as the time to first mobilization, standing, and weight-bearing after randomization were also analyzed as secondary outcomes. Tertiary outcomes and definitions of the outcomes are provided in the Appendix.

### *Statistical Analysis*

All randomized participants with baseline troponin measurement before randomization in the HIP ATTACK trial were included in this analysis. As baseline troponin levels were measured at the discretion of the attending physicians involved in the patient's care, there was no specific sample size calculation for this substudy. Patients were analyzed according to the treatment group to which they had been randomized, in accordance with the intention-to-treat principle.

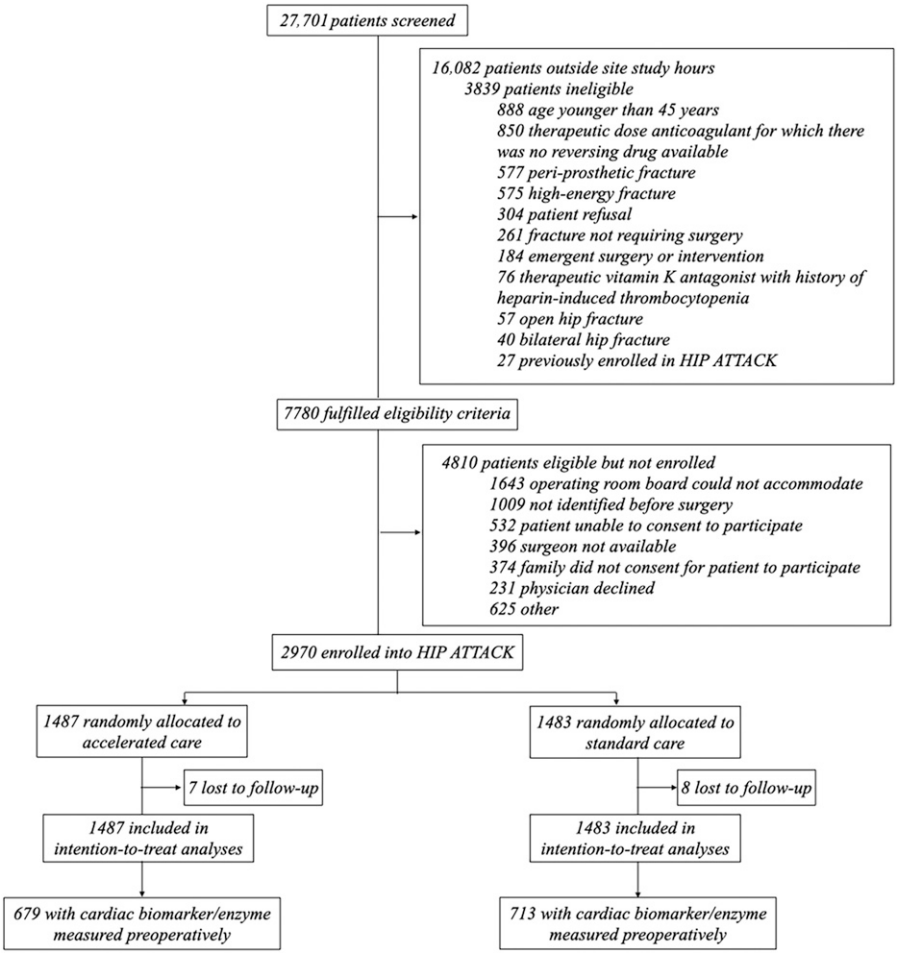


Fig. 1

Patient flow diagram.

For the primary and secondary binary outcomes with an event date, we performed a Cox proportional hazards model with the treatment group as the covariate and adjusted for the stratification variable. We assessed subgroup effects using tests of interaction, with significance defined as a p value of <0.05 for the interaction. The interaction p value informs whether the treatment effect across different subgroups is not attributable to chance. For the primary outcome, we performed a sensitivity analysis including the center where the surgery was performed as a random effect (frailty model). We hypothesized a priori that patients with baseline troponin elevation would benefit more from accelerated surgery compared with standard care than patients with no baseline troponin elevation.

We undertook a post-hoc Cox regression analysis to determine the relationship between baseline troponin measurements and 90-day mortality. The Cox proportionality assumption was met (details provided in the Appendix). The dependent variable was 90-day mortality. Independent variables were age; sex; Revised Cardiac Risk Index (RCRI) score, which includes a history of coronary artery disease, congestive heart failure, cerebrovascular disease, insulin-dependent diabetes, a creatinine level of >177 μmol/L, and high-risk surgery (0 [reference], 1, 2, or ≥3); baseline troponin elevation (no or yes); history of peripheral vascular disease; history of chronic obstructive pulmonary disease (COPD); active cancer; and treatment effect. For all Cox models, we determined the hazard ratio (HR) of each predictor and its associated 95% confidence interval (CI). We repeated this analysis including the baseline troponin level as an independent variable assessed by terciles (with the reference being no elevation). Only observed values were used for analysis; no attempt was made to impute missing values. Patients who were lost to follow-up were censored on their last day of contact during the study or their date of death. All outcomes were compared using 2-sided tests at the 0.05 significance level. The fragility index was estimated to assess the fragility of our results for the primary outcome. The fragility index indicates how many patients would be required to convert a finding from being significant to not significant: the larger the index, the more robust is the data. All analyses were performed in SAS, version 9.4.

## Results

This substudy included 1392 patients (47% of the 2970 patients recruited in the HIP ATTACK trial), from 61 sites,

who had a troponin measurement at hospital arrival. Appendix Table 1 summarizes the baseline characteristics of all of the HIP ATTACK trial participants. Of the 1392 patients with baseline troponin measurements, 322 (23%) had a troponin elevation at hospital arrival. These patients had a higher baseline risk of complications, based on their greater comorbidities, than the patients with no baseline troponin elevation. They were more likely to be male (36.0% versus 29.1%) and have a history of hypertension (64.6% versus 57.8%), and they had a higher median creatinine level (88.4 versus 74.3 μmol/L) and a lower median hemoglobin level (117 versus 122 g/L) (see Appendix Table 1). However, patients with and without a baseline troponin elevation had similar histories of myocardial infarction (8.7% versus 8.0%), stable angina (2.8% versus 2.7%), coronary artery revascularization (5.0% versus 5.3%), and aortic valve stenosis (1.6% versus 2.0%). These baseline characteristics were also similar to the overall HIP ATTACK trial population (see Appendix Table 1).

Table I summarizes the baseline characteristics in subgroups of patients according to whether the troponin level was elevated and the treatment allocation. Among patients with an elevated troponin level, the median time from hip fracture diagnosis to surgery was 6 hours (interquartile range [IQR] = 5 to 13 hours) in the accelerated surgery group and 29 hours (IQR = 19 to 52 hours) in the standard care group (median absolute difference, 23 hours). Among patients without an elevated troponin level, the median time from hip fracture diagnosis to surgery was 6 hours (IQR = 4 to 8 hours) in the accelerated surgery group and 29 hours (IQR = 9 to 36 hours) in the standard care group (median absolute difference, 23 hours).

Patients with an increased baseline troponin level had a lower risk of mortality with accelerated surgery (17 [10%] of 163) compared with standard care (36 of [23%] 159; HR = 0.43 [95% CI = 0.24 to 0.77]), whereas patients with no elevated troponin level demonstrated no mortality reduction with accelerated surgery (p value for interaction = 0.048) (Table II). The fragility index for the primary outcome was 6.

Among patients with an elevated troponin level, the risk of the secondary composite outcome of major perioperative cardiovascular complications was lower in the accelerated surgery group (23 [14%] of 163) compared with the standard care group (47 [30%] of 159), with an HR of 0.43 (95% CI = 0.26 to 0.72) (Table III). Patients with no elevated troponin level demonstrated no reduction in the composite outcome with accelerated surgery (p value for interaction = 0.0256). Additional secondary and tertiary outcomes are presented in Appendix Tables 2 through 5. Patients with troponin elevation >2.1 times the upper limit of normal had a lower mortality risk following accelerated surgery compared with standard care (3 [6%] of 53 versus 17 [30%] of 56; HR = 0.17 [95% CI = 0.05 to 0.58]). Accelerated surgery lowered the mortality risk in patients with >2.1 times troponin elevation more than it did in patients with less or no troponin elevation (p value for interaction = 0.034; Table IV).

Table V presents the predictors of 90-day all-cause mortality identified with the Cox model, which included all 1392 patients for whom troponin measurements were available. An elevated baseline troponin level was independently associated with 90-day mortality (adjusted HR = 1.80 [95% CI = 1.27 to 2.56]; p = 0.001) when adjusted for age, sex, cardiovascular risk factors, other clinically important comorbidities, and the treatment effect. In multivariable analysis, accelerated surgery was associated with lower all-cause mortality compared with standard care (adjusted HR = 0.66 [95% CI = 0.47 to 0.92]; p = 0.0152).

## Discussion

We found that 1 in 5 patients with a hip fracture had myocardial injury identified by an elevated troponin measurement when they presented to the hospital. In patients who received standard care for a hip fracture, the presence of myocardial injury before surgery was associated with close to 3 times higher mortality at 90 days (22.6% versus 8.7% mortality in patients with and without troponin elevation, respectively). In a multivariable analysis, a baseline troponin elevation was an independent predictor of 90-day all-cause mortality (adjusted HR = 1.80 [95% CI = 1.27 to 2.56]; p = 0.001); thus, this laboratory test offers information in addition to that provided by clinical predictors, including the RCRI score. Accelerated surgery lowered the risk of mortality compared with standard care in patients with a baseline elevated troponin level (HR = 0.43; 95% CI, 0.24 to 0.77), an effect that was not seen in patients without a baseline elevated troponin level (HR = 0.88 [95% CI = 0.58 to 1.34]; p value for interaction = 0.048).

Our results are similar to those in previous cohort studies demonstrating that preoperative myocardial injury is common (rates ranging from 15% to 30%) in patients with a hip fracture and is associated with a poor prognosis[5,7,14,15]. Currently, there are no clinical guidelines on how to manage these patients. Conventional treatment focuses on medical management of the myocardial injury. Usually, physicians proceed to hip surgery only when they believe that the myocardial injury has been stabilized[7,16]. This typically prevents hip surgery from being performed for at least 24 hours after the hip fracture diagnosis. However, with the current standard care approach, 23% of patients presenting with a hip fracture and myocardial injury die within 90 days. This short-term mortality rate is much worse than the outcome for patients with a hip fracture who do not have an elevated troponin level (9%).

Most likely the myocardial injury is a consequence of the physiologic stress induced by the hip fracture and is a marker of a poor cardiac reserve. Although troponins are specific for myocardial injury[17], multiple different etiologies play a role in the perioperative setting. These include dehydration, hypoperfusion, bleeding, inflammation, and ischemia. These are also common causes of type-2 supply-demand-mismatch myocardial infarction[18]. Patients are commonly managed accordingly to acute coronary syndrome (ACS) guidelines[16], despite patients with a hip fracture being frequently excluded from ACS trials. Indeed, coronary artery thrombosis is uncommon in the perioperative setting, and physicians' judgment of thrombosis etiology is frequently inaccurate[19,20].

**TABLE I Characteristics of Participants in the Troponin Substudy***

| | Participants with No Troponin Elevation | | Participants with Troponin Elevation | |
|---|---|---|---|---|
| | Accelerated Care | Standard Care | Accelerated Care | Standard Care |
| Randomized | 516 | 554 | 163 | 159 |
| Age† *(yr)* | 77.7 (11.5) | 78.6 (11.1) | 81.8 (11.1) | 81.5 (11.5) |
| Male | 152 (29.5%) | 159 (28.7%) | 64 (39.3%) | 52 (32.7%) |
| History before hip fracture | | | | |
| Assistance with activities of daily living | 145 (28.1%) | 190 (34.3%) | 59 (36.2%) | 60 (37.7%) |
| Current nursing home residence | 107 (20.7%) | 131 (23.6%) | 29 (17.8%) | 32 (20.1%) |
| Tobacco use | 142 (27.5%) | 138 (24.9%) | 31 (19.0%) | 23 (14.5%) |
| Total smoking pack years† | 34.7 (31.0) | 33.2 (27.9) | 36.6 (30.4) | 27.9 (24.1) |
| Stroke | 52 (10.1%) | 33 (6.0%) | 11 (6.7%) | 19 (11.9%) |
| Subarachnoid hemorrhage | 4 (0.8%) | 3 (0.5%) | 5 (3.1%) | 1 (0.6%) |
| Transient ischemic attack | 22 (4.3%) | 29 (5.2%) | 7 (4.3%) | 7 (4.4%) |
| Myocardial infarction | 46 (8.9%) | 40 (7.2%) | 12 (7.4%) | 16 (10.1%) |
| Unstable angina | 11 (2.1%) | 6 (1.1%) | 2 (1.2%) | 2 (1.3%) |
| Stable angina | 14 (2.7%) | 15 (2.7%) | 4 (2.5%) | 5 (3.1%) |
| Pulmonary embolism | 3 (0.6%) | 4 (0.7%) | 3 (1.8%) | 4 (2.5%) |
| Deep venous thrombosis | 8 (1.6%) | 16 (2.9%) | 4 (2.5%) | 5 (3.1%) |
| CABG | 17 (3.3%) | 14 (2.5%) | 4 (2.5%) | 2 (1.3%) |
| PCI | 16 (3.1%) | 17 (3.1%) | 6 (3.7%) | 6 (3.8%) |
| CABG or PCI | 29 (5.6%) | 28 (5.1%) | 9 (5.5%) | 7 (4.4%) |
| Peripheral vascular disease | 14 (2.7%) | 15 (2.7%) | 6 (3.7%) | 7 (4.4%) |
| Aortic stenosis | 10 (1.9%) | 11 (2.0%) | 3 (1.8%) | 2 (1.3%) |
| Paroxysmal atrial fibrillation | 17 (3.3%) | 16 (2.9%) | 6 (3.7%) | 6 (3.8%) |
| Chronic atrial fibrillation | 27 (5.2%) | 32 (5.8%) | 10 (6.1%) | 9 (5.7%) |
| Congestive heart failure | 33 (6.4%) | 21 (3.8%) | 12 (7.4%) | 12 (7.5%) |
| Hypertension | 284 (55.0%) | 334 (60.3%) | 98 (60.1%) | 110 (69.2%) |
| Diabetes | 113 (21.9%) | 104 (18.8%) | 33 (20.2%) | 37 (23.3%) |
| COPD | 44 (8.5%) | 55 (9.9%) | 16 (9.8%) | 6 (3.8%) |
| Active cancer | 24 (4.7%) | 24 (4.3%) | 5 (3.1%) | 7 (4.4%) |
| Renal failure requiring dialysis | 1 (0.2%) | 2 (0.4%) | 3 (1.8%) | 2 (1.3%) |
| Dementia | 71 (13.8%) | 107 (19.3%) | 33 (20.2%) | 31 (19.5%) |
| Osteoporosis prior to fracture | 69 (13.4%) | 88 (15.9%) | 20 (12.3%) | 17 (10.7%) |
| Previous hip fracture | 31 (6.0%) | 41 (7.4%) | 9 (5.5%) | 11 (6.9%) |
| Physiological measurements before randomization† | | | | |
| Systolic blood pressure *(mmHg)* | 142.4 (24.5) | 142.5 (26.1) | 140.0 (126.0-159.0) | 140.0 (126.0-157.0) |
| Diastolic blood pressure *(mmHg)* | 76.9 (13.0) | 76.8 (13.0) | 80.0 (70.0-87.0) | 77.0 (70.0-82.0) |
| Heart rate *(bpm)* | 81.0 (13.5) | 80.8 (13.6) | 80.0 (70.0-87.0) | 81.0 (72.0-90.0) |
| Baseline laboratory assessments† | | | | |
| Creatinine *(μmol/L)* | 82.2 (38.8) | 83.5 (40.8) | 88.4 (70.7-122.0) | 90.5 (69.8-124.6) |
| Hemoglobin *(g/L)* | 123.0 (109.0-134.0) | 122.0 (110.0-134.0) | 118.5 (103.0-131.5) | 115.5 (101.0-125.5) |

*CABG = cardiac artery bypass, PCI = percutaneous coronary intervention, COPD = chronic obstructive pulmonary disease. †The values are given as the mean with the standard deviation in parentheses or as the median with the interquartile range in parentheses as appropriate.

Our results suggest the possibility of a beneficial paradigm shift in perioperative medicine. Based on a strong biologic rationale and encouraging preliminary data, we propose expedited surgery for patients with a hip fracture and myocardial injury at hospital presentation. Similar to other causes of myocardial injury, for which the standard of care is to control the trigger (e.g., upper gastrointestinal bleeding), earlier surgical repair of a hip fracture seems to reduce the risk

**TABLE II 90-Day All-Cause Mortality in Patients with and without Baseline Elevated Troponin Measurement According to Treatment Allocation Group**

| | No. of Deaths/Total No. of Patients (%) | | | |
|---|---|---|---|---|
| | Accelerated Care | Standard Care | HR (95% CI) | P Value for Interaction* |
| Overall series | 140/1487 (9.4) | 154/1483 (10.4) | 0.91 (0.72-1.14) | |
| Non-elevated troponin | 39/516 (7.6) | 48/554 (8.7) | 0.88 (0.58-1.34) | 0.048 |
| Elevated troponin | 17/163 (10.4) | 36/159 (22.6) | 0.43 (0.24-0.77) | |

*P value for interaction for the subgroup analysis comparing the treatment effect on patients with non-elevated troponin level versus treatment effect on patients presenting with elevated troponin level.

of additional medical complications and all-cause mortality. Hip fractures result in pain, bleeding, inflammation, and hypercoagulation, which can precipitate myocardial injury[21-27]. Patients undergoing hip fracture surgery have higher risk-adjusted mortality and major complications than patients undergoing elective hip surgery[28]. This suggests that the hip fracture,

**TABLE III Secondary Outcomes at 90 Days in Patients with and without Baseline Elevated Troponin Measurement According to Treatment Allocation Group**

| Outcome/Baseline Troponin Elevation | No. of Events/Total No. of Patients (%) | | HR (95% CI) | P Value | P Value for Interaction* |
|---|---|---|---|---|---|
| | Accelerated Care | Standard Care | | | |
| Secondary composite outcome† | | | | | 0.0256 |
| No | 65/516 (12.6) | 81/554 (14.6) | 0.86 (0.62-1.19) | 0.3602 | |
| Yes | 23/163 (14.1) | 47/159 (29.6) | 0.43 (0.26-0.72) | 0.0011 | |
| Vascular mortality | | | | | 0.2509 |
| No | 21/516 (4.1) | 32/554 (5.8) | 0.71 (0.41-1.23) | 0.2219 | |
| Yes | 10/163 (6.1) | 22/159 (13.8) | 0.41 (0.19-0.87) | 0.0196 | |
| Non-vascular mortality | | | | | 0.0844 |
| No | 18/516 (3.5) | 16/554 (2.9) | 1.22 (0.62-2.39) | 0.5647 | |
| Yes | 7/163 (4.3) | 14/159 (8.8) | 0.46 (0.19-1.15) | 0.0967 | |
| Myocardial infarction | | | | | 0.2903 |
| No | 29/516 (5.6) | 35/554 (6.3) | 0.89 (0.54-1.45) | 0.6305 | |
| Yes | 9/163 (5.5) | 16/159 (10.1) | 0.52 (0.23-1.18) | 0.1189 | |
| Stroke | | | | | 0.0725 |
| No | 3/516 (0.6) | 5/554 (0.9) | 0.64 (0.15-2.70) | 0.5479 | |
| Yes | 0/163 (0) | 4/159 (2.5) | — | 0.9949 | |
| Congestive heart failure | | | | | 0.2647 |
| No | 5/516 (1.0) | 8/554 (1.4) | 0.67 (0.22-2.05) | 0.4809 | |
| Yes | 1/163 (0.6) | 5/159 (3.1) | 0.18 (0.02-1.55) | 0.1183 | |
| New clinically important atrial fibrillation | | | | | 0.2488 |
| No | 8/516 (1.6) | 9/554 (1.6) | 0.96 (0.37-2.49) | 0.9308 | |
| Yes | 0/163 (0) | 1/159 (0.6) | — | 0.9975 | |
| Recurrent myocardial injury after randomization | | | | | 0.6033 |
| No | 110/516 (21.3) | 146/554 (26.4) | 0.80 (0.63-1.03) | 0.0851 | |
| Yes | 37/163 (22.7) | 50/159 (31.4) | 0.68 (0.44-1.04) | 0.0775 | |

*P value for interaction for the subgroup analysis comparing the treatment effect on patients with non-elevated troponin level versus treatment effect on patients presenting with elevated troponin level. †All-cause mortality, non-fatal myocardial infarction, non-fatal stroke, and non-fatal congestive heart failure.

**TABLE IV 90-Day All-Cause Mortality by Troponin Terciles According to Treatment Allocation Group***

| Elevation of Troponin Level* | Accelerated Care Events/Patients (%) | Standard Care Events/Patients (%) | HR (95% CI) | P Value | P Value for Interaction† |
|---|---|---|---|---|---|
| Not elevated | 39/516 (8) | 48/554 (9) | 0.88 (0.58-1.34) | 0.552 | 0.0340 |
| >1-1.32 × ULN | 4/54 (7) | 7/53 (13) | 0.54 (0.16-1.88) | 0.335 | |
| 1.33-2.1 × ULN | 10/56 (18) | 12/50 (24) | 0.71 (0.31-1.66) | 0.431 | |
| >2.1 × ULN | 3/53 (6) | 17/56 (30) | 0.17 (0.05-0.58) | 0.005 | |

*ULN = upper limit of normal for the site-specific assay. †P value for interaction for the subgroup analysis comparing the treatment effect on patients with non-elevated troponin level versus treatment effect on patients presenting with elevated troponin level.

independent of surgery, increases patient risk. Typical medical treatments for myocardial injury such as antithrombotics and beta-blockers may worsen physiological effects resulting from the hip fracture by way of increased bleeding and hypotension[29,30]. Additionally, performing multiple preoperative cardiac tests delays surgical access, prolongs the aforementioned stress state, and frequently does not change perioperative clinical management[31]. Thus, accelerated hip surgery has the potential to quickly restore a patient's overall physiologic health and reduce the risk of death compared with standard care.

Overall, our results suggest that patients presenting with myocardial injury are not tolerating the additional cardiac stress associated with a hip fracture and could benefit from expedited surgical care. These patients are frequently asymptomatic from a cardiac perspective and will not be identified without routine preoperative troponin screening. Additionally, if troponin is monitored only postoperatively, the myocardial injury could be attributed to the surgical stress rather than to the hip fracture. A common concern regarding troponin testing is that elevated measurements result in surgical delays and cancellations. However, it is clear these patients are at very high risk and are not being identified. Instead of ignoring this problem, we should identify these patients and propose new strategies to improve their prognosis. The HIP ATTACK trial, which to our knowledge is the first trial that provides insights on this topic, suggested that accelerated surgery may be the best approach. Despite the fact that the first participants in HIP ATTACK were enrolled a decade ago, current practice has not changed[7].

**TABLE V Cox Model for Predictors of 90-Day All-Cause Mortality***

| Variable | HR (95% CI) | P Value |
|---|---|---|
| Elevated troponin vs. not elevated | 1.80 (1.27-2.56) | 0.0010 |
| RCRI score: 1 vs. 0 | 1.39 (0.93-2.07) | 0.1098 |
| RCRI score: 2 vs. 0 | 1.95 (1.15-3.33) | 0.0140 |
| RCRI score: ≥3 vs. 0 | 2.56 (1.20-5.48) | 0.0151 |
| Age | 1.04 (1.02-1.06) | <0.0001 |
| Male vs. female | 1.62 (1.14-2.30) | 0.0067 |
| History of peripheral vascular disease | 1.11 (0.52-2.38) | 0.7791 |
| History of COPD | 1.63 (0.99-2.66) | 0.0526 |
| Active cancer | 1.57 (0.81-3.03) | 0.1823 |
| Accelerated vs. standard care | 0.66 (0.47-0.92) | 0.0152 |

*RCRI = Revised Cardiac Risk Index, COPD = chronic obstructive pulmonary disease.

Our study has some limitations. Reasons for troponin elevation before randomization were not recorded. However, according to the site reports, only 19 (6%) of the 322 patients (13 in the accelerated surgery group and 6 in the standard care group) presented with an acute myocardial infarction between hip fracture and randomization. These low numbers did not allow any solid comparisons; however, the fact that more patients in the accelerated care group than in the standard care group presented with an acute myocardial infarction—and usually physicians are more concerned about the possibility of causing harm to such patients—suggests that the results of our study (i.e., the beneficial effect of accelerated care for patients with troponin elevation) could be conservative. Indeed, regardless of the etiology of the myocardial injury, its presence identifies the potential benefit of accelerated surgery. Sites used multiple different troponin assays. Therefore, it was not possible to establish specific troponin thresholds that were independently associated with mortality. We thus performed analysis by terciles. The data presented are based on a post-hoc analysis, meaning that the study was not sufficiently powered to be a definitive practice-changing trial, to suggest additional strategies (such as use of a specific type of anesthesia) to improve outcomes, or to make definitive statements on secondary exploratory outcomes. The ongoing HIP ATTACK-2 trial will include 1100 participants (NCT04743765 in ClinicalTrials.gov), and is powered to determine if accelerated surgery is superior to standard care with regard to improving the 90-day risk of death of patients with a hip fracture who present with an elevated troponin level at hospital arrival.

In conclusion, 1 in 5 patients with a hip fracture present with myocardial injury. Mortality is 3-fold higher in this population compared with the patients with a hip fracture who do not have a myocardial injury. Accelerated surgery has the potential to improve mortality rates and major cardiovascular outcomes compared with standard care. These findings must be confirmed in additional trials.

## Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJS/I118). ■

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