Relation of Perioperative Elevation of Troponin to Long-Term Mortality After Orthopedic Surgery

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Myocardial necrosis in the perioperative period of noncardiac surgery is associated with short-term mortality, but long-term outcomes have not been characterized. We investigated the association between perioperative troponin elevation and long-term mortality in a retrospective study of consecutive subjects who underwent hip, knee, and spine surgery. Perioperative myocardial necrosis and *International Classification of Disease, Ninth Revision* −coded myocardial infarction (MI) were recorded. Long-term survival was assessed using the Social Security Death Index database. Logistic regression models were used to identify independent predictors of long-term mortality. A total of 3,050 subjects underwent surgery. Mean age was 60.8 years, and 59% were women. Postoperative troponin was measured in 1,055 subjects (34.6%). Myocardial necrosis occurred in 179 cases (5.9%), and MI was coded in 20 (0.7%). Over 9,015 patient-years of follow-up, 111 deaths (3.6%) occurred. Long-term mortality was 16.8% in subjects with myocardial necrosis and 5.8% with a troponin in the normal range. Perioperative troponin elevation (hazard ratio 2.33, 95% confidence interval 1.33 to 4.10) and coded postoperative MI (adjusted hazard ratio 3.51, 95% confidence interval 1.44 to 8.53) were significantly associated with long-term mortality after multivariable adjustment. After excluding patients with coronary artery disease and renal dysfunction, myocardial necrosis remained associated with long-term mortality. In conclusion, postoperative myocardial necrosis is common after orthopedic surgery. Myocardial necrosis is independently associated with long-term mortality at 3 years and may be used to identify patients at higher risk for events who may benefit from aggressive management of cardiovascular risk factors. **(Am J Cardiol 2015;115:1643−1648)**

Cardiovascular risks of orthopedic surgery impose a significant burden of morbidity and mortality in the United States. More than 110 million adults report a musculoskeletal condition, leading to >1.5 million hip, knee, and spine surgeries each year.[1−3] Although orthopedic procedures have historically been considered to confer only an intermediate risk of death and nonfatal myocardial infarction (MI),[4] cardiovascular events are not uncommon. Perioperative myocardial necrosis and infarction, detected by postoperative elevations in serum cardiac troponin isoforms, occur with an incidence that ranges from 1% to 17%.[5−14] In large prospective registries, peak perioperative troponin elevations correlate with 30-day mortality.[15−17] Although the association between perioperative troponin elevation and short-term outcomes is clear, long-term consequences of postoperative myocardial necrosis remain uncertain.[10,12] We, therefore, investigated the association between perioperative troponin elevation and long-term mortality in a large, retrospective study of subjects who underwent major orthopedic surgery.

Methods

We performed long-term follow-up to a retrospective cohort analysis of consecutive adults who underwent orthopedic surgery. A full description of the methods has been described elsewhere.[8] Briefly, consecutive adults who underwent knee, hip, or spine surgery from November 1, 2008, to December 31, 2009, at 2 hospitals within a large tertiary care academic medical center were eligible. Clinical data were obtained from hospital administrative database (Decision Support System), hospital laboratory database, and from retrospective record review. Data quality was assessed by reviewing a random sample of 10% of all medical and laboratory records. Long-term survival was assessed using the Social Security Death Index database, with the query performed on July 13, 2012. This study was approved by the institutional review board with an informed consent waiver.

Patient baseline demographics, clinical history, and comorbidities were ascertained using a hospital administrative data set. *International Classification of Disease, Ninth Revision* (*ICD-9*) procedure codes were used to identify spinal fusion (81.0x), refusion of spine (81.3x), joint replacement of lower extremity (81.5x), and other procedures on spine (81.6x). *ICD-9* diagnosis codes were used to ascertain

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Table 1
Baseline characteristics

Variable	Overall Population (n=3050)
Age (year), mean	60.84 ± 13.25
Female	1806 (59.2%)
White	1986 (65.1%)
Black	433 (14.2%)
Hispanic	414 (13.6%)
Other	217 (7.1%)
BMI (kg/m^2), mean	29.60 ± 6.63
Admission Type	
Elective	2876 (94.3%)
Emergency or Urgent Surgery	174 (5.7%)
Procedure	
Spine	1144 (37.5%)
Knee	992 (32.5%)
Hip	914 (30.0%)
RCRI Score (Lee et. al, 1999)	
Coronary Artery Disease	326 (10.7%)
Heart Failure	86 (2.8%)
Stroke/Transient Ischemic Attack	18 (0.6%)
Creatinine > 2 mg/dL	15 (0.6%)
Diabetes Mellitus	445 (14.6%)

BMI = body mass index; RCRI = Revised Cardiac Risk Index.

co-morbidities present on admission, including a history of diabetes mellitus (250.x), heart failure (HF) (402.01, 402.11, 402.91, 428, 428.1, 428.2, 428.22, 428.23, 428.3, 428.32, 428.33, 428.4, 428.42, 428.43, 428.9), and stroke (V12.54, 438.0 to 438.9). Coronary artery disease (CAD) was determined by an *ICD-9* diagnosis code indicating previous MI (412.x), previous cardiac revascularization procedure (coronary artery bypass grafting or percutaneous coronary intervention, 36.x), or CAD (412, 414.x).

Subjects were stratified by whether troponin measurement was performed in the postoperative period as previous analyses suggest that subjects in whom postoperative troponins are not measured have fewer cardiovascular risk factors and may be at a lower risk for events.[18] Plasma cardiac troponin I (cTnI) was measured using the VITROS cTnI ES assay (Ortho-Clinical Diagnostics, Rochester, New York) or the ST AIA-PACK second-generation cTnI assay (Tosoh Bioscience, Tokyo, Japan). Myocardial necrosis was defined by any elevation in troponin level ≥99th percentile upper reference limit of the assays (0.04 and 0.06 ng/ml, respectively). MI was defined by *ICD-9* diagnosis code 410.x, not present on admission. The primary study outcome was long-term mortality based on the Social Security Death Index database. Long-term survival was not available for 32 subjects (1.0%); these patients were excluded from the analysis.

Continuous variables were displayed as means ± SD and were compared using the Student's *t* test. Categorical variables were displayed as frequencies and percentages and were compared by the chi-square and Fisher's exact tests. Baseline characteristics associated with outcomes were estimated with univariate logistic regression models and reported as odds ratios with 95% confidence intervals (CIs). Time-to-event Cox proportional hazards analyses reported as hazard ratios (HRs) were used to examine the association between dichotomized myocardial necrosis and mortality, while controlling for potential demographic, clinical, and procedural confounders. Multivariate models were adjusted for age, gender, race, urgent surgery, procedure type, diabetes mellitus, CAD, HF, stroke, and creatinine >2 mg/dl. Kaplan-Meier plots were generated to illustrate long-term survival by postoperative troponin. Statistics were calculated using SPSS 20 (IBM SPSS Statistics, Armonk, New York). Two-tailed p values <0.05 were considered to be statistically significant for all tests.

Results

A total of 3,050 subjects underwent orthopedic surgery of the spine, hip, or knee and were included in the analysis. Baseline patient characteristics, cardiovascular co-morbidities, and procedural characteristics are displayed in Table 1. Troponin was measured in 1,055 subjects (34.6%). Myocardial necrosis occurred in 179 cases (17.0% of subjects who had a troponin measured and 5.9% overall). Mean follow-up was 3.0 ± 0.5 years after surgery. Over 9,015 patient-years of follow-up, 111 deaths (3.6%) occurred, with 53 (1.7%) and 90 (3.0%) by 12 and 24 months, respectively. Univariate predictors of long-term mortality are displayed in Table 2. The incidence of perioperative myocardial necrosis was significantly higher in subjects who died during long-term follow-up overall (27.0% vs 5.0%, p <0.0001). The incidence of coded perioperative MI was also significantly higher in subjects who died during long-term follow-up in comparison with surviving subjects (6.3% vs 0.4%, p <0.001).

The 179 subjects who developed perioperative myocardial necrosis had significantly higher long-term mortality (16.8% vs 2.8%, p <0.0001) after orthopedic surgery. In multivariable models adjusting for demographic and clinical variables, perioperative troponin elevation was associated with long-term mortality (Table 3). Associations between positive postoperative troponin and long-term mortality persisted in landmark analyses of events up to 12 months (adjusted HR 2.45, 95% CI 1.12 to 5.34), between 12 and 24 months (adjusted HR 2.90, 95% CI 1.13 to 7.42) but not after 24 months (adjusted HR 0.97, 95% CI 0.17 to 5.39). Of the subjects with myocardial necrosis, 20 had an *ICD-9*–coded postoperative MI. Subjects with coded postoperative MI had significantly higher mortality over study follow-up (35.0% vs 3.4%, p <0.0001). Postoperative MI was also strongly associated with mortality in multivariable analysis (adjusted HR 3.51, 95% CI 1.44 to 8.53). After excluding patients with coded MI, myocardial necrosis remained significantly associated with long-term mortality (adjusted HR 2.10, 95% CI 1.14 to 3.88).

Subjects who underwent urgent rather than elective orthopedic procedures had a higher frequency of perioperative troponin measurement (67.2% vs 32.8%, p <0.0001), myocardial necrosis (19.0% vs 5.1%, p <0.0001), and greater long-term mortality (26.4% vs 2.3%, p <0.0001). After excluding subjects who underwent urgent surgery from the analysis, perioperative troponin elevation was still significantly associated with long-term mortality (HR 3.40, 95% CI 1.65 to 7.03).

Measurement of perioperative serum troponin, regardless of the outcome of the laboratory test, was also associated with mortality. Long-term mortality was 16.8% (30) in subjects with an abnormally elevated troponin, 5.8% (51) for those