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Myocardial Ischemia after Hip and Knee Arthroplasty: Incidence and Risk Factors

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Abstract

Purpose—Because the occurrence of post-operative myocardial ischemia predicts subsequent cardiac morbidity and mortality, we determined the prevalence of and risk factors for myocardial ischemia in hip and knee arthroplasty patients.

Methods—High sensitivity cardiac troponin T (hs-cTnT) was measured on stored samples from post-operative day 2 in 394 hip and knee arthroplasty patients > 65 years of age enrolled in the Genetics-InFormatics Trial (GIFT).

Results—Fifty-three (13.5%) participants had myocardial ischemia, of whom only three were diagnosed clinically during their hospitalization. The risk of myocardial ischemia increased with age (OR 3.52 per decade, 95% CI 2.00-6.19) and diabetes (OR 2.23, 95% CI 1.04-4.77). Myocardial ischemia was rarer with statins (OR 0.74, 95% CI 0.40-1.35) and more common with hypertension, coronary artery disease and tobacco use, although these were not statistically significant.

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Conflict of Interest

The authors have no conflicts of interest.

Conclusions—Subclinical myocardial ischemia occurs frequently after arthroplasty. Diabetic and elderly patients are at highest risk.

Keywords

Postoperative complication; myocardial ischemia; arthroplasty; risk factor; statin; troponin

INTRODUCTION

With the aging of the American population and the increased prevalence of obesity, over 1 million Americans undergo hip or knee arthroplasty each year for osteoarthritis [1]. Based on the National Hospital Discharge database, 1.1% of arthroplasty patients are diagnosed with cardiac complications in the 90 days after surgery [2]. However, most orthopedic surgery patients with myocardial ischemia do not complain of angina. For example, in a study of 200 hip fracture participants, 71 (35%) had an elevated troponin level but only 8% of them complained of chest pain [3]. Therefore the overall incidence of post-operative myocardial ischemia in orthopedic patients is likely much higher than 1.1%.

Understanding the true incidence and risk factors for post-operative myocardial ischemia in orthopedic patients is important for several reasons. First, the occurrence of even asymptomatic post-operative myocardial ischemia predicts subsequent cardiac morbidity and mortality [4-10]. Second, understanding the risk of postoperative myocardial ischemia can help patients make an informed decision about undergoing arthroplasty. Third, identifying patients at elevated cardiac risk can spur preemptive actions, such as giving cardioprotective medications peri-operatively to those that need them. For example, peri-operative beta-adrenergic receptor blockers decrease the risk of post-operative ischemia, although they increase the risk of postoperative ischemic stroke [11]. Likewise, peri-operative aspirin therapy may decrease the risk of post-operative myocardial infarction, cardiac arrest, severe arrhythmia, pulmonary embolism and cardiovascular death, but can cause major bleeding [12-14]. Three(3)-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitors (“statins”) reduce the rate of myocardial infarction by 43%-53% after some non-cardiac surgeries, even when started only 1-30 days before surgery [15-17] but their benefit in orthopedic surgery patients is unknown.

This study was performed in order to quantify the incidence of and risk factors for post-operative myocardial ischemia in orthopedic patients. We conducted a cohort study nested within a multicenter trial of pharmacogenetic vs. clinical dosing of warfarin therapy in individuals undergoing elective hip or knee arthroplasty. We used a fourth generation high sensitivity cardiac troponin T (hs-cTnT) assay to detect post-operative myocardial ischemia.

MATERIALS & METHODS

Participants were recruited as an ancillary study to the Genetics InFormatics Trial (GIFT) of Warfarin Therapy to Prevent DVT. (NHLBI R01 HL097036). As previously described [18], GIFT is an ongoing multi-center randomized trial that utilizes web-based warfarin-dosing algorithms (www.WarfarinDosing.org) in individuals > 65 years of age undergoing hip or knee arthroplasty.

Plasma samples were obtained from consenting GIFT study patients on postoperative day 2, frozen and stored. Batch testing for hs-cTnT was performed at a later date on deidentified samples. Measurement of hs-cTnT was accomplished in the General Core Laboratory of the Weill Cornell Medical College Clinical and Translational Science Center using a quantitative sandwich enzyme immunoassay kit from Meso Scale Discovery (MSD), Catalog Number K151EFC-1 (Gaithersburg, MD, USA), and processed on the MULTI-ARRAY Human Cardiac Troponin T MSD assay using the manufacturer's instructions. The assay had a lower level of detection of 13 ng/L and a coefficient of variation of 7%. This assay has 100% cross-reactivity with Troponin. In this study, myocardial ischemia was defined as an hs-cTnT level ≥ 14 ng/L, the published 99th percentile cutoff for this assay [9].

Deidentified patient demographics and medical history were obtained from the GIFT study database. Demographics were analyzed descriptively.

Statistical analysis

Logistic regression was performed to determine which factors were associated with higher risk myocardial ischemia. We offered the following variables in the backwards stepwise regression model: age, total hip vs. knee arthroplasty, bilateral vs. unilateral total knee arthroplasty, body mass index, coronary artery disease, creatinine clearance, diabetes, hypertension, race, sex, smoker status, use of a statin, and history of stroke. A p-value of 0.5 was used to retain variables in the model, and a two-sided p-value ≤ 0.05 was required to determine statistical significance.

To further quantify the odds ratio of myocardial ischemia in participants prescribed a statin, we used an inverse probability treatment of weighting propensity score (IPTW). The IPTW used the following covariates: age, sex, race, diabetes, coronary artery disease, smoker status, blood pressure, and bilateral arthroplasty (see appendix). A propensity score is the conditional probability of treatment assignment given the observed baseline characteristics. Propensity score conditioning results in unbiased estimates of the average treatment effect [19]. The Shapiro-Wilk test and normal probability plots were utilized to confirm normality. Chi-square goodness-of-fit test was utilized to compare unadjusted and IPTW-adjusted baseline characteristics. Hosmer and Lemeshow goodness-of-fit test determined model fit. The IPTW resulted in a c-statistic of 0.66.

Statistical data were calculated with SAS, version 9.2 (SAS Institute Inc., Cary, NC).

This study was performed in accordance with ethical standards and was approved by the local Institutional Review Board.

Results

Post-operative day 2 (POD2) plasma samples were available for hs-cTnT measurement from 394 hip or knee arthroplasty patients. Two hundred ninety-nine (76%) of these individuals underwent total knee arthroplasty, including 40 (10%) that underwent bilateral knee arthroplasty. The average (standard deviation) age of the patients was 71.8 (6.2) years (Table I).

Fifty-three patients (13.5%) had myocardial ischemia postoperatively (hs-cTnT ≥ 14 ng/L) (Figure 1). The proportion of patients with myocardial ischemia did not differ by site. Only three participants (0.77%) were identified clinically as having myocardial ischemia during their hospital stay. These participants had POD2 hs-cTnT levels of 32.7, 34.1, and 35.6 respectively. The risk of myocardial ischemia increased with age (odds ratio (OR) 3.52 per decade, 95% confidence interval (CI) 2.00-6.19) and diabetes (OR 2.23, 95% CI 1.04-4.77). Myocardial ischemia was less common with a statin (OR 0.74, 95% CI 0.40-1.35) and more common with hypertension, coronary artery disease, and tobacco use, although these were not statistically significant.

After using a propensity score to adjust for the likelihood of being on a statin and performing non-parsimonious stepwise regression, only age and diabetes mellitus were significant predictors of postoperative myocardial ischemia: the odds increased 3.5-fold per decade of life, and 2.2-fold in participants with diabetes mellitus (Table II). Although not statistically significant, the odds of myocardial ischemia were lower in participants on statin therapy and higher in participants with hypertension and coronary artery disease, smokers, and those undergoing bilateral knee arthroplasty (Table II).

Discussion

Over 1 million Americans undergo hip or knee arthroplasty each year [1], and 1%-2% are reported to experience arterial thrombotic complications such as acute stroke, MI or vascular death [2, 20-22]. Using a high sensitivity assay to measure cardiac troponin T (hs-cTnT), we found evidence of myocardial ischemia in 13.5% of patients after hip and knee arthroplasty. Of note, only 0.77% of patients were diagnosed clinically with myocardial ischemia (on the basis of symptoms and troponin measurement) during their hospital stay. The frequency of *clinically apparent* myocardial ischemia noted in our study was similar to the published 0.2-0.7% rate of post-arthroplasty myocardial infarction derived from administrative data [22-25]. The clinical detection of myocardial ischemia in the post-operative setting is difficult, because patients and clinicians are focused on musculoskeletal pain, and opiates used for orthopedic pain can mask angina. We found that many patients with undetected ischemia are discharged without potentially beneficial therapies such as beta antagonists, aspirin, ACE inhibitors, and/or statins.

Fourth generation hs-cTnT assays are highly specific for myocardial ischemia [26]. Although elevated levels can be seen in critically ill patients [9, 27], patients in this study were clinically well. Fourth generation hs-cTnT assays have greater sensitivity to detect myocardial ischemia than traditional assays [26, 28, 29]. In VISION, for example, a study of 15,133 patients over age 45 undergoing non-cardiac surgery, 11.6% of patients were found to have myocardial ischemia postoperatively. Even low levels of ischemia were clinically important in VISION: post-operative hs-cTnT values as low as 20 ng/L or 30 ng/L predicted 30-day mortality [10]. Nagele et al. also found that perioperative hs-cTnT elevations presaged mortality [9]. Hietala et al. demonstrated that perioperative troponin elevation in hip fracture patients was associated with both higher short-term (17% vs 4.7%, $p=0.008$) and long-term (61% vs 40%, $p=0.005$) mortality [30]. There were no deaths in our study, but this was most likely due to the small number of patients analyzed ($n = 394$).

The risk of myocardial ischemia in our study was higher with advancing age and in patients with diabetes, suggesting that these patients may benefit from cardiac monitoring and troponin testing post-operatively. Ischemia also tended to be more common among patients who had other risk factors for MI (hypertension, CAD, smoking, bilateral TKA, male sex, and African-American race).

Our finding that diabetes is a significant risk factor for silent ischemia confirms prior studies. For example, in a study of 579 individuals undergoing sestamibi stress tests, there was a higher incidence of silent ischemia among diabetic patients [31]. Similarly, in a study of nearly 2000 patients without a history of known myocardial infarction (MI) diagnosis, diabetes was an independent predictor of silent MI (OR 1.5, 95% CI 1.1-1.9, $p=0.004$) [32].

Our finding that silent ischemia is more common in the elderly also is supported by the literature. For example, in a population-based cohort study of 5888 participants ≥ 65 years of age without history of a MI diagnosis, 15.3% of participants had evidence of a MI by baseline ECG studies, 22.3% of which had been unrecognized [33]. Prior studies in orthopedic patients have also demonstrated an association between advanced age and myocardial ischemia. In a study of patients undergoing hip fracture surgery, 44.4% of those ≥ 90 years of age experienced troponin elevations compared with 12.5% of participants < 70 years of age ($p<0.01$) [3].

Our study was limited by insufficient sample size to quantify the effects of statin use on myocardial ischemia. In addition, because ECG testing was not routinely performed we do not know whether patients with elevated hs-cTnT levels had accompanying ECG changes. High sensitivity-cTnT levels were only available from POD2 plasma samples. Although troponin is known to be elevated for seven to ten days, we could not record hs-cTnT levels serially as many patients were discharged within the first three days and we also lacked funding. We also lacked baseline hs-cTnT levels which have also been shown to predict adverse outcomes [9]. These limitations are balanced by strengths, including complete follow-up for all 394 participants and standardized warfarin management (based on the GIFT study protocol).

In contemporary studies, postoperative myocardial infarction occurs at rates similar to those of pulmonary embolism following hip and knee arthroplasty [2, 23-25, 34, 35]. The results of our study suggest that patients at high risk for ischemia, such as diabetics and the elderly, may benefit from postoperative troponin testing. Safe new approaches to cardio-protection are also needed. Given that statin therapy has been shown to reduce the risk of adverse cardiovascular outcomes after a variety of high-risk surgeries [15-17, 36], we propose a randomized trial of statins vs. placebo in patients aged ≥ 65 years undergoing orthopedic surgery.

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Appendix

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Table III
Patient characteristics before and after applying IPTW propensity score

Characteristic	Unadjusted Data		Data Adjusted with the Use of Inverse Probability Weighting			
	No Statin (N=339)	Statin (N=53)	P value	No Statin (N=339)	Statin (N=53)	P value
Age (yr)	71.5 ± 7.3	72.1 ± 4.8	0.286	71.9 ± 6.8	71.9 ± 4.8	0.966
Bilateral TKA (%)	9.1	11.2	0.483	9.6	10.2	0.863
CAD (%)	4.0	13.3	0.001	8.7	8.7	0.983
DM (%)	10.1	19.9	0.006	15.0	14.9	0.988
HTN (%)	15.2	17.5	0.525	17.4	16.8	0.871
Male Sex (%)	25.8	43.4	0.0002	34.4	34.2	0.967
Smoker (%)	4.0	3.6	0.808	3.4	3.4	0.993
Is Black (%)	6.1	4.6	0.516	5.8	5.7	0.966

IPTW = Inverse probability treatment of weighting; TKA = total knee arthroplasty; BMI = body mass index; CAD = coronary artery disease; DM = diabetes; HTN = hypertension

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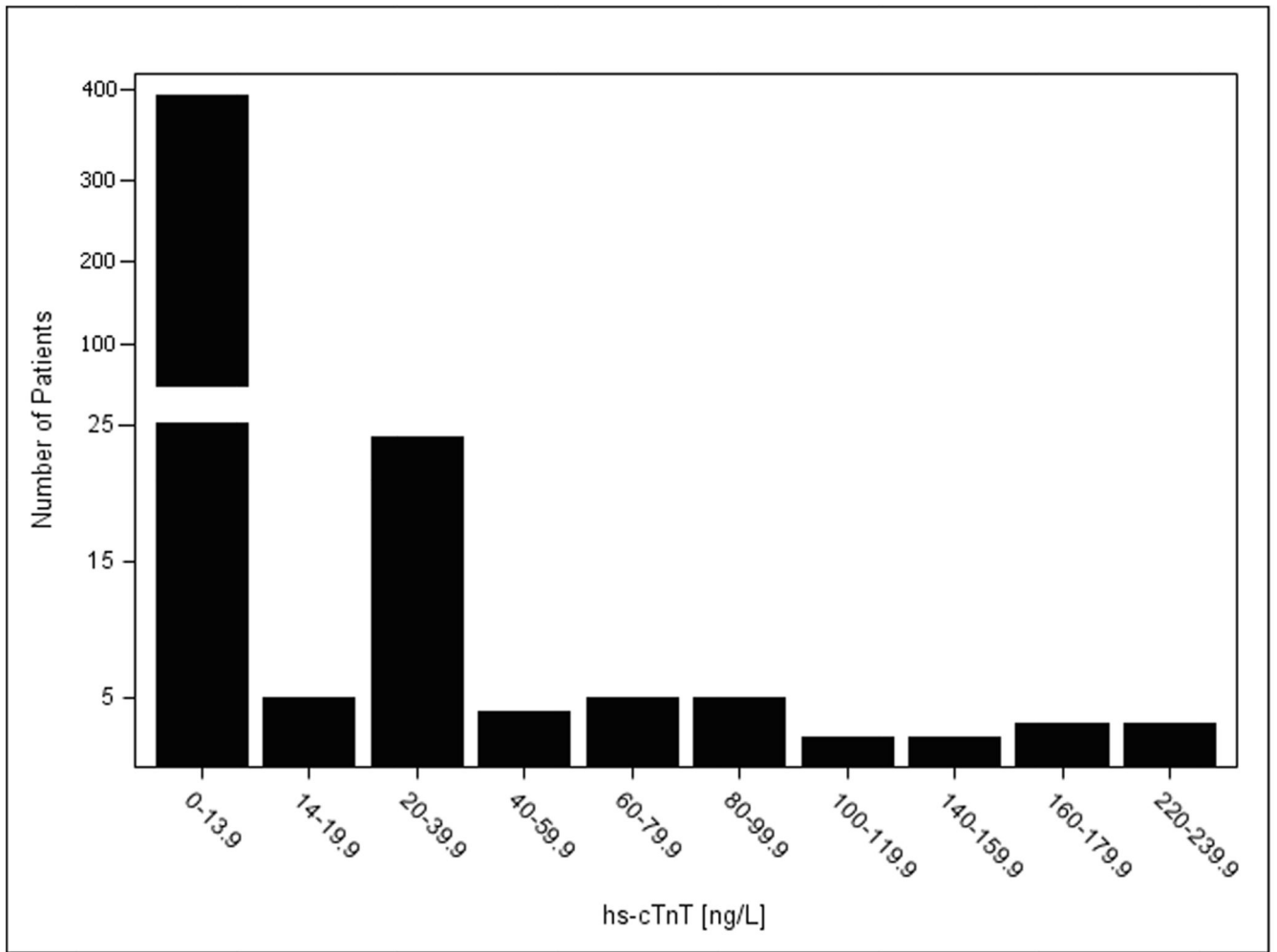


Figure 1.

Table I

Patient characteristics

Group Data			
Characteristic	Total (N=394)	TKA (N=299)	THA (N=95)
Age - yr (mean \pm sd)	71.8 \pm 6.16	71.8 \pm 6.47	71.8 \pm 5.19
CAD (%)	8.7	8.1	9.7
DM (%)	15.0	15.3	13.8
HTN (%)	16.3	15.3	18.3
Male Sex (%)	34.5	32.5	42.6
Smoker (%)	3.8	2.4	8.5
African American (%)	5.3	4.8	7.5
Bilateral (%)	10.2	13.2	1.1

TKA = total knee arthroplasty; THA=total hip arthroplasty; CAD = coronary artery disease; DM = diabetes; HTN = hypertension.

Table II

Risk Factors for Myocardial Ischemia after multivariate analysis with IPTW for statin use

Risk Factor	OR (95% CI)	P value
Statin	0.74 (0.40-1.35)	0.326
Age Per Decade	3.52 (2.00-6.19)	< .0001
Diabetes	2.23 (1.04-4.77)	0.038
Hypertension	1.78 (0.83-3.83)	0.140
CAD	2.15 (0.84-5.46)	0.109
Smoker	2.27 (0.51-10.07)	0.280
Bilateral TKA	1.52 (0.55-4.21)	0.420
Male Sex	1.19 (0.62-2.28)	0.604
Race ¹	1.32 (0.38-4.56)	0.663

IPTW = inverse probability treatment of weighting propensity score; CAD = Coronary Artery Disease; TKA = Total Knee Arthroplasty.

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