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Assessment of 30-day mortality and complication rates associated with extended deep vein thrombosis prophylaxis following hip fracture surgery

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ABSTRACT

Background: DVT is a common complication following lower extremity surgery, occurring in up to 60% of patients undergoing hip fracture surgery without postoperative anticoagulation. The risk of fatal PE continues well-beyond two weeks postoperatively, thus extended DVT prophylaxis beyond 14 days may be warranted. This investigation sought to examine the association between prescription of extended DVT prophylaxis and 30-day postoperative complications following hip fracture surgery.

Methods: This study utilized the ACS NSQIP Hip Fracture Procedure Targeted dataset, a newly available set of patient variables for 2016. The outcome measures were death, occurrence of any postoperative complication, complication subtype, readmission or reoperation within 30-days postoperatively, and length of stay. The primary independent variable was medical DVT prophylaxis continued 28-days postoperatively ("extended DVT prophylaxis"). The control group contains both patients receiving no prophylaxis and those receiving short-duration prophylaxis. Multivariate stepwise logistic regression was employed to control for potential demographic, comorbidity, and procedural/medical confounding factors.

Results: In total, 7533 surgically treated hip fracture patients treated in 2016 were analyzed. Overall, 57.8% of patients (n = 4354) were prescribed extended DVT prophylaxis. On bivariate analysis, prescription of extended DVT prophylaxis was associated with significantly lower incidence of death (7.7% without vs. 2.7% with, $p < 0.0001$) and stroke/CVA (1.4% vs. 0.6%, $p = 0.0016$). In multivariate analysis, prescription of extended DVT prophylaxis was significantly associated with lower odds of death (OR 0.33, $p < 0.0001$), stroke/CVA (OR 0.44, $p = 0.0010$), and acute kidney injury (AKI) (OR 0.31, $p = 0.0010$).

Conclusions: This retrospective cohort study of the 2016 ACS NSQIP found that hip fracture surgery patients prescribed ≥28 days of postoperative DVT prophylaxis exhibited 67% lower odds of death and significantly lower rates of AKI and stroke/CVA as compared to those prescribed short-duration prophylaxis. Given the retrospective and uncontrolled nature of this analysis, these results should be interpreted with caution, and additional prospective randomized controlled trials examining the association between extended DVT prophylaxis and postoperative outcomes are warranted. If these observations accurately reflect real-world experience, these data suggest that ≥28 days of DVT prophylaxis following hip fracture surgery should be strongly considered for patients without explicit contraindications.

Introduction

Deep vein thrombosis (DVT) is a common complication following lower extremity fracture surgery, occurring in up to 60% of historic cohorts of patients undergoing hip fracture surgery without postoperative anticoagulation [1–8]. Fatal pulmonary embolism (PE) may occur secondary to DVT in 5–15% of hip fracture patients not treated prophylactically, compared to <1% of those receiving anticoagulation [3,9–12]. Elderly patients, patients with delayed surgery, and those undergoing general anesthesia account for most hip fracture patients, and each of these characteristics place patients at increased risk for DVT and PE following hip fracture surgery [3].

Anticoagulation is recommended for hip fracture surgery patients to prevent fatal PE. Specifically, the American College of Chest Physicians' 9th edition guideline for "Prevention of Venous

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Thromboembolism (VTE) in Orthopedic Surgery Patients", endorses treatment with antithrombotic prophylaxis for a minimum of 10–14 days (Grade 1C – strong recommendation), and potentially for more than 35 days (2 B – weak recommendation) [13]. These recommendations are supported by a large number of trials indicating decreased incidence of VTE-associated morbidity with thromboembolic prophylaxis [3,6,13–15]. In particular, Todd et al.'s observational study of 580 consecutive hip fracture patients found that fatal pulmonary emboli were significantly less common among those treated with antithrombotic prophylaxis [16]. Despite these 2012 guidelines, however, the proportion of patients receiving appropriate prophylaxis remains low, with incompletely understood ramifications for patient outcomes [17,18].

Retrospective cohort analyses from large, multi-center national databases may add valuable contemporary clinical data to the evolving understanding of postoperative thromboembolism prophylaxis in hip fracture patients. This investigation sought to evaluate the association between prescription of extended DVT prophylaxis and 30-day postoperative complications following hip fracture surgery in the American College of Surgeons National Quality Improvement Program (ACS NSQIP) dataset. This study utilized newly-released hip fracture surgery-specific variables to provide greater depth of information than previously possible.

Methods

Data sources

Data for this study was from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) and the Hip Fracture Procedure Targeted Public Use File (HFPT PUF) for year 2016. The NSQIP collects data from participating hospitals for major surgical procedures. The HFPT PUF, a new addition to the NSQIP, contains supplementary variables of interest for hip fracture patients specifically and can be merged with the general public use file for a corresponding time period using unique, de-identified case IDs. A full list of additional variables can be found on the ACS NSQIP PUF website [19]. As the NSQIP is both publicly available and de-identified, this study was exempt from formal IRB approval.

Patient selection

All patients undergoing hip fracture surgery and included in the Hip Fracture Procedure Targeted PUF were preliminarily included in the study. The following inclusion criteria were subsequently applied: patients aged $\geq$60 years-old, orthopaedic surgeon specialty, inpatient status, non-pathological fracture, and American Society of Anesthesiologists (ASA) classification 1 to 4, as well as absence of preoperative ventilator dependency, ascites, renal failure, dialysis, disseminated cancer, congestive heart failure within 30 days preoperatively, open/infected wound, and pathologic weight loss. Of 9390 patients in the Hip Fracture Procedure Targeted PUF, 7533 met these criteria and were included in the study.

Outcome measures

The outcome measures in this study were death, occurrence of any postoperative complication, complication subtypes, readmission or reoperation within 30-days postoperatively, and length of stay. Complication subtypes included: DVT, PE, pneumonia, urinary tract infection (UTI), stroke/cerebrovascular accident (CVA), transfusion, surgical site infection (SSI), acute kidney injury, major adverse cardiac events (MACE, includes cardiac arrest and myocardial infarction), and sepsis/septic shock.

Primary independent variable

The primary independent variable was medical DVT prophylaxis continued 28-days postoperatively ("extended DVT prophylaxis"). The NSQIP considers patients as receiving extended prophylaxis if "the patient is prescribed [anticoagulative therapy] for any reason, including as prophylactic treatment or therapeutic management through 28 days from the date of operation." Patients who were intended to receive $\geq$28 days postoperative prophylaxis but deceased prior to the 28-day threshold were still considered as having been prescribed extended prophylaxis "if the DVT prophylaxis was continued up until the day of death" [20]. The group not receiving extended prophylaxis thus presumably includes a combination of both patients not receiving prophylaxis and patients receiving only short-duration prophylaxis. Patients receiving any of the following anticoagulation modalities were included: mechanical devices (excluding compression hose alone) such as sequential compression devices (SCDs), aspirin 325 mg BID (with or without other anticoagulation), low molecular weight heparin, unfractionated heparin, Warfarin, fondaparinux sodium, oral factor Xa inhibitors, or direct thrombin inhibitors.

Potential confounding variables

Additional covariates examined included demographic factors (patient age and sex), comorbidities (diabetes, smoking, dyspnea, functional health status, COPD, hypertension requiring medication, chronic steroid use, bleeding disorder, preoperative transfusion, preoperative sepsis, dementia, delirium, preoperative bone protection medication prescription, and ASA classification), and procedural/medical factors (anesthesia type, operative duration, surgical technique, medical co-management, standardized hip fracture care program, and fracture anatomic location/type).

Statistical analysis

Analyses were conducted utilizing SAS 9.4 (SAS Institute, Cary, NC) and R 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria). Length of stay was Winsorized at the 5th and 95th percentiles to minimize the influence of outliers and was also log-transformed for analysis. Descriptive statistics were generated and stratified by extended DVT prophylaxis status. Bivariate analyses (Chi-Square and linear regression) between outcomes and extended prophylaxis status were conducted. Multivariate analyses for binary outcomes utilized multiple stepwise logistic regression, with threshold α for variable entry and retention of 0.2 and 0.1, respectively. Multivariate analyses for length of stay utilized multiple stepwise linear regression, with models built to optimize the Akaike Information Criterion. Extended prophylaxis status was exempted from selection. Collinearity between candidate predictors was assessed with variable tolerance in a generalized linear model, with no concerning values noted. Logistic regression model discrimination and fit were analyzed with the c-statistic and Hosmer-Lemeshow Goodness-of-Fit test, respectively. Patients with missing data were excluded on a listwise basis. Given the large number of comparisons made in this investigation, $p < 0.005$ was considered statistically significant.

Results

Descriptive statistics

In total, 7533 hip fracture surgery patients were analyzed. Overall, 57.8% of patients (n = 4354) were prescribed extended DVT prophylaxis, and 42.2% (n = 3179) were not prescribed extended prophylaxis. Females were most prominently represented (72.5%, n = 5460), as were patients aged 80–89 (42.4%, n = 3197). The vast majority of patients were ASA classification 3 (63.8%, n = 4806). The majority of fractures were intertrochanteric (54.8%, n = 4125),

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