

High-dose Aspirin for Extended Venous Thromboembolic Prophylaxis after Total Hip or Total Knee Arthroplasty: An Observational Study Janki Vyas, PharmD Candidate; Cassandra Maynard, PharmD, BCPS

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# BACKGROUND

- Venous thromboembolism (VTE) is a potentially fatal yet preventable complication in patients undergoing total hip arthroplasty (THA) and total knee arthroplasty (TKA)
- Without an appropriate VTE prophylaxis in orthopedic patients, pulmonary embolism (PE) results for 5% to 10% of deaths and deep vein thrombosis (DVT) results in 40-60% in hospitalized patients<sup>1</sup>
- Aspirin Endorsement in current guideline for VTE prophylaxis following THA or TKA. American Academy of Orthopedic Surgeons of 2012: Aspirin as an optimal pharmacotherapy is insufficient. American College of Chest Physicians of 2012: Grade 1B (moderate evidence). UK National Institute of Health and Care Excellence of 2018: Require 10 days of LMWH before receiving aspirin monotherapy or solely receive newer anticoagulants
- VTE prophylaxis with aspirin 325 mg twice daily therapy is still unclear

# OBJECTIVE

 To analyze an adequate population of patients receiving high-dose aspirin (325 mg) twice daily for postoperative VTE prophylaxis following TKA or THA and compare the rates of safety and efficacy to the anticoagulants that are currently used in the literature to determine if aspirin is non-inferior to the anticoagulants that are used as per the guidelines

# METHODS

### Study Design:

Retrospective, cohort, chart review of 50 patients conducted from January 2021 – May 2021 who underwent THA or TKA and received aspirin 325 mg twice daily for 35 days following the arthroplasty

#### Inclusion Criteria:

- Adults aged 18 and 89 years
- Treated with prophylactic high-dose (325 mg) aspirin twice a day for 35 days **Exclusion Criteria:**
- History of bleeding or clotting disorder, history of VTE, current pregnancy, at-risk populations such as prisoners
- Received any non-aspirin thromboprophylaxis medication post-operatively or had incomplete data available for analysis

#### Outcome Measures:

- Primary outcome: Composite of VTE and death occurred within 90 days after the surgery
- Secondary outcomes: Bleeding events, transfusion requirements, rehospitalization within 90 days

#### Statistical Analysis:

- Continuous variables: Mean + standard deviation (SD)
- Categorical variables: frequencies and percentages
- Sample size of 49 patients required to achieve the power of 0.80 and significance level of 0.05

## RESULTS

### **Table 1: Patient Demographics**

CHARACTERISTIC	ASPIRIN N = MEAN (SD)
Age in years	63.38 <u>+</u> 1.33
BMI	29.74 <u>+</u> 0.82
Type of Surgery	
Total Knee Surgery	28 (56%)
Total Hip Surgery	22 (44%)
Comorbidities	
Peptic Ulcer	3 (6%)
Thrombocytopenia	4 (8%)
Liver Disease	9 (18%)
Kidney Disease	5 (10%)

### **Table 2: Primary Outcomes**

PRIMARY ENDPOINT	ASPIRIN ARM N (%)
Composite	2 (4%)
VTE	2 (4%)
Death	0 (0%)

#### **Table 3: Secondary Outcomes**

SECONDARY ENDPOINT	ASPIRIN ARM N (%)
Bleeding Events	5 (10%)
Minor Bleeding Events	3 (6%)
Major Bleeding Events	2 (4%)
Transfusion Requirement	2 (4%)
Rehospitalization Requirement	7 (14%)

### DISCUSSION

- Baseline characteristics inclusive of the general population
- Findings consistent with large observational studies. As per table 2, the composite of VTE and death within 90 days with the aspirin group is 4% which is similar to 3.4% in LMWH group<sup>11</sup>, 4.3% in UFH group<sup>11</sup>, and 3.8% in warfarin group<sup>12</sup>, respectively. Whereas the composite of VTE and death was higher in DOAC group (7.4%)<sup>10</sup> when compared to the aspirin group
- Even though aspirin was associated with 14% rehospitalization rates, only 6% of those were hospitalized due to concerns related to aspirin such as bleeding event or VTE. Available evidence from RCT trials shows bleeding events of 3.37% in LMWH<sup>11</sup>, 7.4% in DOAC<sup>10</sup>, 2.1% in UFH<sup>11</sup>, and 12.1% in warfarin<sup>12</sup>, respectively
- Specific minor and major bleeding events were unable to differentiate in the observational studies due to the different definitions
- Findings consistent with large observational cohorts, which have also reported that aspirin was effective for VTE prophylaxis, and that aspirin had similar or slightly improved effectiveness compared with the commonly used anticoagulants

### STUDY LIMITATIONS

- No control group, observational study
- Small sample size
- Variability in the populations compared (THA, TKA, or both) with the currently available literature
- Limited cross-sectional study that provides a snapshot of aspirin use, might not exhibit the generality of the population
- Unable to differentiate whether the bleeding events were post-operative or related to the aspirin prophylaxis
- Loss of patient follow-up due to change in the area of treatment of care
- Average duration, compliance, and drug-interactions with aspirin and the anticoagulants were unknown

## CONCLUSION

- Aspirin is not significantly different from the anticoagulants used for VTE prophylaxis after THA and TKA for the primary composite outcome
- Some VTE prophylactic agents are becoming less popular in certain regions or countries because of potential drawbacks compared with aspirin and direct oral anticoagulants. For example, LMWH requires daily injections administered by either the patient or health care professionals, and warfarin requires laboratory monitoring
- The lower rates of VTE and death question the superiority of protocols relying on the sole use of expensive, potent anticoagulants for VTE prophylaxis
- This study suggests that aspirin 325 mg twice daily for extended prophylaxis is a potentially safer option following TKA or THA
- Further studies are needed to better understand the association between VTE and extended-duration of prophylaxis with oral anticoagulants and aspirin in relation to THA and TKA

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