

Assessment of Venous Thromboembolism Rates Following Elective Total Knee and Total Hip Arthroplasties in Patients Receiving Prophylactic Twice Daily Aspirin

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Disclosure Statement

- IRB Status: Approved
- Co-investigator:
 - Cynthia Gary, PharmD, BCPS
- Conflicts of Interest: None
- Project Sponsorship: None

IRB: Institutional Review Board

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Learning Objectives

- List the rate of venous thromboembolism within 90 days following elective total hip or total knee arthroplasty in patients receiving aspirin 325 mg orally twice daily for six weeks
- In patients who underwent elective total hip or total knee arthroplasty, compare the rates of major bleeding between study subjects who received aspirin and a historical control of published literature values

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Background

- Patients who undergo high-risk orthopedic procedures including total hip arthroplasty (THA) and total knee arthroplasty (TKA) are at an increased risk of venous thromboembolic (VTE) events^{1,2}
- Both the American Academy of Orthopaedic Surgeons (AAOS)² and American College of Chest Physicians (ACCP)³ state that aspirin is one of the acceptable medication options for postoperative VTE prophylaxis
 - Neither group specifies the optimal dosing or duration of aspirin therapy

1. Vincent VG, et al. *J Arthroplasty*. 2016;31:2608-16.
 2. American Academy of Orthopaedic Surgeons. http://www.aaos.org/research/guidelines/VTE/VTE_full_guideline.pdf.
 3. American College of Chest Physicians evidence-based guidelines. *Chest*. 2012;141:278-325.

Background

Comparative VTE and Major Bleeding Rates Post-THA or TKA

	Treatment	VTE	DVT	PE	Major Bleeding
2012 ACCP Guidelines ³	Enoxaparin	1.8%	1.25%	0.55%	1.5%
	No prophylaxis	4.3%	2.8%	1.5%	1.2%
2016 Meta-analysis ¹	Aspirin	1.8%	1.2%	0.6%	0.4%
	Other prophylaxis	--	--	--	-

DVT: deep vein thrombosis, PE: pulmonary embolism

- **Billings Clinic**
 - Aspirin 325 mg PO BID used for most elective THA and TKA patients
 - Those who come in on another anticoagulant are typically continued
 - Patients with previous VTEs are often placed on enoxaparin

1. Vincent VG, et al. *J Arthroplasty*. 2016;31:2608-16.
 3. American College of Chest Physicians evidence-based guidelines. *Chest*. 2012;141:278-325.

Purpose

- Compare the rates of VTEs that occurred within 90 days of elective TKA or THA in patients receiving aspirin 325 mg orally twice daily for 6 weeks to literature-derived rates

Methods: Study Design

- Retrospective, single-center, observational study

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Methods: Inclusion Criteria

- Adults (≥ 18 years) who underwent elective THA or TKA between January 2014 and October 2016
- Received a hospital discharge prescription for aspirin 325 mg orally twice daily for 6 weeks
- Had a Billings Clinic primary care provider

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Methods: Exclusion Criteria

- Prescribed other medications at discharge that are efficacious for VTE prophylaxis regardless of indication
- Non-elective THAs or TKAs (e.g., trauma)
- Pregnant or breast feeding

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Methods: Study Group

- Subjects who received a discharge prescription for aspirin 325 mg by mouth twice daily for 6 weeks for VTE prophylaxis following elective THA or TKA
 - Stratified by month and year, then randomly selected
- Subgroups: type of procedure and type of VTE
 - TKA or THA
 - DVT or PE

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Methods: Primary Outcome

- The percentage of eligible patients who experienced symptomatic VTEs within 90 days of surgery

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Methods: Secondary Outcomes

- Rates of symptomatic DVTs or PEs
- Number of days after surgery that the patient experienced a VTE
- Major bleeding within 90 days of surgery¹
 - Intracranial hemorrhage
 - Gastrointestinal bleed
 - Any bleed requiring a return to operating room
- 90-day all-cause mortality post-surgery

1. Vincent VG, et al. *J Arthroplasty*. 2016;31:2608-16.

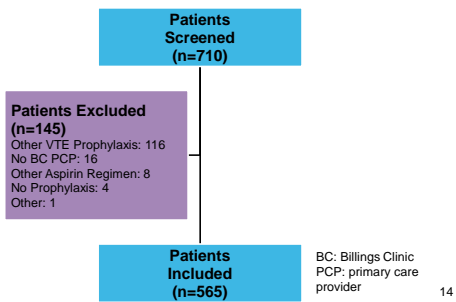
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Methods: Statistics

- Sample Size
 - Alpha 0.05, 80% power
 - Estimated sample size: 750 patients
 - Accounting for 25% non-evaluable data
 - Target sample size: n=563
- Statistical Tests
 - Descriptive statistics
 - Kaplan-Meier survival analysis

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Results: Patient Selection



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Results: Patients

Characteristic	All Participants (n=565)	THA (n=214)	TKA (n=351)	P Value
Age, mean years ± SD	65.4 ± 10	64.4 ± 10.7	66 ± 9.6	0.07
Female, n (%)	324 (57)	120 (56)	204 (58)	0.63
Length of stay, mean days ± SD	2.8 ± 1.8	2.7 ± 1	2.8 ± 1.5	0.63

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Results: VTE Occurrence

Event	All Participants (n=565)	THA (n=214)	TKA (n=351)	P Value
VTE, n (%)	5 (0.9)	1 (0.5)	4 (1.1)	0.41
DVT, n	1	0	1	--
PE, n	4	1	3	--

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Results: Comparative VTE Rates

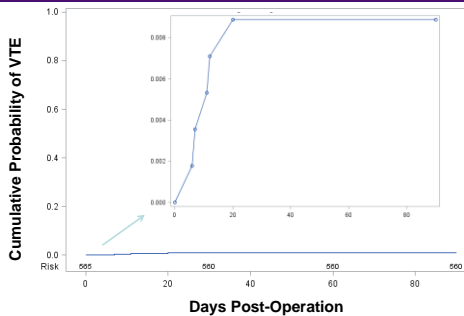
Comparative VTE Rates Post-THA or TKA				
	Treatment	VTE	DVT	PE
2012 ACCP Guidelines ³	Enoxaparin	1.8%	1.25%	0.55%
	No VTE prophylaxis	4.3%	2.8%	1.5%
2016 Meta-analysis ¹	Aspirin	1.8%	1.2%	0.6%
	Other VTE prophylaxis	--	--	--
This Study	Aspirin	0.9%	0.2%	0.7%
	Other VTE prophylaxis	--	--	--

1. Vincent VO, et al. *J Arthroplasty*. 2016;31:2608-16.

3. American College of Chest Physicians evidence-based guidelines. *Chest*. 2012;141:278-325.

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Results: Cumulative Probability of VTE



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Results: Secondary Outcomes

Outcome	All Participants (n=565)	THA (n=214)	TKA (n=351)
VTE occurrence after surgery, mean days \pm SD	13 \pm 6.8	20 \pm 0	13.2 \pm 6.8
Major bleeding, n (%)	1 (0.2)	1 (0.2)	0
90-day all-cause mortality, n (%)	5 (0.9)	1 (0.5)	4 (0.1)

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Results: Comparative Major Bleeding Rates

Comparative Major Bleeding Rates Post-THA or TKA

	Treatment	Major Bleeding
2012 ACCP Guidelines ³	Enoxaparin	1.5%
	No VTE prophylaxis	1.2%
2016 Meta-analysis ¹	Aspirin	0.4%
	Other VTE prophylaxis	--
This Study	Aspirin	0.2%
	Other VTE prophylaxis	--

1. Vincent VO, et al. J Arthroplasty. 2016;31:2608-16.

3. American College of Chest Physicians evidence-based guidelines. Chest. 2012;141:278-325.

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Discussion

- Lower rates of VTE compared to established literature values
- Majority of VTE occurrences happened in 2016
- Very small VTE rates compared to past studies

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Discussion

- Characteristics of subjects who experienced VTE
 - 4/5 were obese
 - 4/5 were women
 - 4/5 were > 40 years old
 - No patient had prior VTE

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Discussion

- 90-day all cause mortality
 - One was related to THA complication
 - None from VTE occurrence
 - Occurred average of 47 days after surgery
- Major bleed only occurred in one patient 82 year old male receiving THA
 - Gastrointestinal bleed
 - Required re-hospitalization

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Limitations

- Compared VTE rates to studies with different designs and criteria for inclusion
- Retrospective design
- Patients were excluded if taking other anticoagulants
- Did not assess aspirin compliance
- Concomitant antiplatelet therapy not assessed
- Quazi-randomization could have missed VTEs

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Conclusions

- In this study, subjects undergoing elective TKA or THA who received aspirin 325 mg orally twice daily for 6 weeks had lower rates of VTE occurrence than historically published literature values
- Very low major bleeding risk with this aspirin regimen

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Future Directions

- Share results with orthopedic surgeons to determine additional actions
 - Develop standardized protocol for VTE prophylaxis medications for patients undergoing elective TKA or THA

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- Statistical Analysis
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- Study Coordinator
 - Melanie Townsend, PharmD, BCPS

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Questions?
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6. Vulcano E, Gesell M, Esposito, et al. Aspirin for elective hip and knee arthroplasty: a multimodal thromboprophylaxis protocol. *Int Orthop*. 2012; 36:1995-2002.
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Supplementary Slides

Results: Comparative VTE and Major Bleeding Rates

Comparative VTE and Major Bleeding Rates Post-THA or TKA					
	Treatment	VTE	DVT	PE	Major Bleeding
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Meta-Analysis Studies

Comparative VTE and Major Bleeding Rates Post THA or TKA				
Study and Year	Study Groups	Intervention	VTE Rates in Aspirin Group	Major Bleeding
Raphael et al. ⁴ 2014	• TKA or THA	• ASA 325 mg PO BID (n=2800) • Warfarin (n=26,123)	• VTE: 0.43% • PE: 0.14% • DVT: 0.29%	--
Lotke et al. ⁵ 2006	• TKA	• ASA 325 mg PO BID (n= 3402)	• VTE: 0.61% • PE: 0.32% • DVT: 0.29%	0.4%
Vulcano et al. ⁶ 2012	• Elective TKA or THA	• ASA 325 mg PO BID (n=1115) • Warfarin (n=426) • Enoxaparin (n=27)	• VTE: 1.2% • PE: 0.36% • DVT: 0.45%	0.3%
Beksac et al. ⁷ 2007	• Bilateral THA	• ASA 325 mg PO BID (n=352) • Warfarin (n=292)	• VTE: 5.7% • PE: 1.13% • DVT: 2.27%	--

Results: Excluded Patients

Reason	Number of Patients
Other VTE prophylaxis	116
Enoxaparin	51
Warfarin	47
Rivaroxaban	17
Dabigatran	1
No Billings Clinic primary care provider	16
Other aspirin regimen	8
No VTE prophylaxis	4
Other	1
Total	145