Early vs Delayed Anticoagulant Initiation:
Venous thromboembolism risk after a total knee replacement/revision

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Introduction

- Despite appropriate pharmacological prophylaxis, venous thromboembolism (VTE) occurs in ~1–3% of patients within 14 days after a total knee replacement or revision (TKR); postoperative bleeding occurs in ~3–4%.[1]
- Guidelines support the use of pharmacological prophylaxis for at least 14 days after TKR surgery, with no clear preference for one medicine over another.[2-3]
- *'Early'* initiation of prophylaxis is defined as within 12 hours post-surgery, however this is arbitrary, and the optimal timing remains uncertain.[2-3]
- Tranexamic acid (TXA) is widely adopted to reduce perioperative blood loss, with meta-analysis showing no increased risk of VTE in lower limb arthroplasty.[4]

Aim

To investigate if the time of anticoagulant administration after a total knee replacement or revision (TKR) impacts the rates of VTE.

Methodology

A retrospective observational study was conducted in Cabrini Health Malvern from January 2022 to December 2024

A total of 1697 surgeries were identified and patient characteristic data extracted via the Patient Administration System (PAS)

Cohort matched against electronic medication management (eMM) charts, anticoagulant administration record and administration record of post-operative TXA in the first 24 hours after TKR surgery

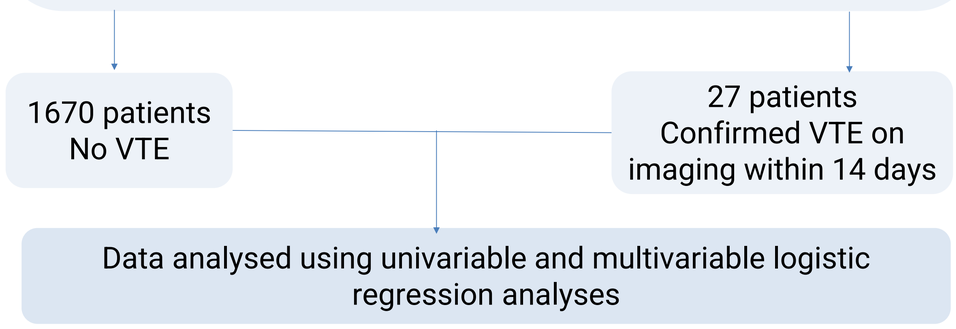

Figure 1: Flow Diagram

Results

Table 1: Patient Characteristics

	No VTE (N = 1670)	VTE (N = 27)	p-value
Age, years [mean (SD)]	71 (8.5)	70 (6.95)	0.363
Gender, male [number (%)]	715 (42.8%)	8 (29.6%)	0.239
Length of stay [median (IQR)]	4 [3, 5]	6 [3, 8.5]	**0.029**
Charlson Comorbidity Index [mean (SD)]	2.68 (0.97)	2.60 (0.96)	0.492
Tranexamic Acid (TXA) [number]	353	6	0.816
Time of anticoagulant administration post-surgery			
<12 hours [number (%)]	894 (98.9%)	11(1.1%)	0.243
>12 hours [number (%)]	776 (98.0%)	16 (2.0%)	
Anticoagulant administered			
Enoxaparin [number (%)]	1144 (98.9%)	13 (1.1%)	0.107
Rivaroxaban [number (%)]	508 (97.3%)	14 (2.7%)	
Others [number (%)]	18(100%)	0 (0.0%)	

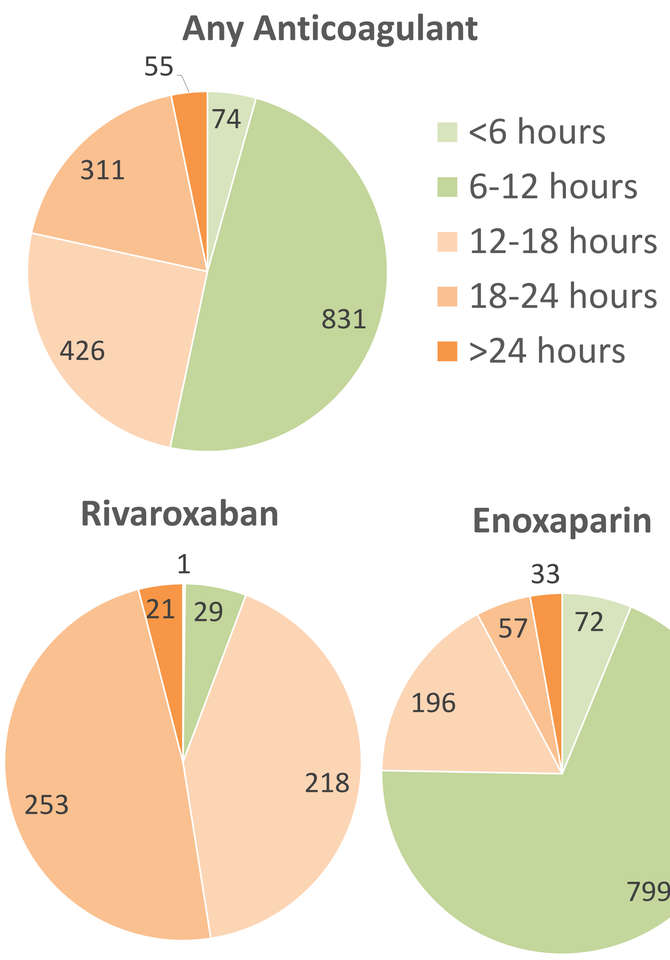

Figure 2: Timing of first dose of anticoagulant administration after TKR surgery

Table 2: Factors affecting outcome

Variable	Risk Ratio (95% CI)	p value
Enoxaparin ≤12 hours	1 [Reference]	
Enoxaparin >12 hours	0.9 (0.2 - 3.0)	0.672
Rivaroxaban ≤12 hours	2.9 (0.2 - 16.3)	0.283
Rivaroxaban >12 hours	**2.3 (1.0 - 5.5)**	**0.044**
Enoxaparin (any time)	1 [Reference]	
Rivaroxaban (any time)	**2.7 (1.2 - 6.1)**	**0.017**
Enoxaparin <24 hours with TXA	1 [Reference]	
Rivaroxaban <24 hours with TXA	**2.5 (1.0 -5.9)**	**0.038**

Early administration (≤12 h post-surgery) of any anticoagulant **did not** significantly alter VTE rates when compared **to delayed administration** (>12 h post-surgery) .

Delayed administration of **rivaroxaban** occurred in 94% of patients, and the risk of VTE was **2.3 times** higher **compared** to **early administration** of **enoxaparin**.

Rivaroxaban combined with TXA administration was associated with increased risk of VTE when compared to enoxaparin with TXA.

Discussion

This study found no significant difference in a 14-day VTE rate between ≤12 h and >12 h initiation of any anticoagulant after a TKR, aligning with prior literature.[1,3] Overall VTE rates were within published ranges.[1]

By medicine, VTE occurred in 2.7% with rivaroxaban and 1.1% with enoxaparin. The landmark studies assessing the efficacy of rivaroxaban after a TKR administered rivaroxaban ~6–10 hr after a TKR and direct factor Xa inhibitors are associated with a decrease rate of VTE compared to enoxaparin.[5] The majority of patients in this cohort were administered rivaroxaban (94%) more than >12 h after surgery compared to enoxaparin (25%). This pattern highlights that rivaroxaban may be less efficacious compared to enoxaparin when delayed, warranting further medicine-specific time-to-anticoagulation analysis.

The impact of TXA remains uncertain; TXA alone was not independently associated with VTE, yet rivaroxaban and TXA showed ~2.5-fold higher risk. The extent to which delayed rivaroxaban initiation contributed to this finding is unclear and has not been previously reported.[4]

Implications

- Findings highlight the importance of optimizing the timing of rivaroxaban initiation to align with guideline recommendations.
- Larger studies are needed to clarify the interaction between TXA, delayed anticoagulant initiation, and patient-specific VTE risk factors.

Limitations

This retrospective, single-centre study is subject to potential misclassification bias and unmeasured confounding factors. The relatively small sample size and low number of VTE events limit the ability to establish causality. The findings are not generalisable beyond the study setting, and bleeding outcomes could not be captured.

Conclusion

This study found that initiation of any anticoagulant within 12 hours versus later did not significantly change 14-day VTE rates. Higher rates were observed with rivaroxaban compared to enoxaparin, especially when administration was delayed by more than 12 hours. These findings highlight the need for medicine-specific analyses of time-to-anticoagulation and suggest that optimising rivaroxaban initiation may be important to minimise postoperative VTE.

References

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