Antithrombotic Therapy and Their Association with Periprosthetic Joint Infection Risk After Total Knee Arthroplasty: A 12-Year Review

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INTRODUCTION:

Management of postoperative antithrombotic therapy (ATT) after total knee arthroplasty (TKA) continues to evolve, yet its relationship to infection risk remains unclear. This study evaluated temporal trends in ATT use over a 12-year period and association of different medication types with periprosthetic joint infection (PJI) after primary TKA at a single, high-volume academic center.

METHODS:

We retrospectively reviewed 20,376 primary TKAs performed from 2013 to 2025. Postoperative ATT medications, prescribed from date of admission through one-week post-discharge, were reviewed and further categorized as either antiplatelet (AP) or anticoagulant (AC) category. Patients were assessed for PJI by cross referencing with our institutional infection database, which uses the 2018 International Consensus Meeting (ICM) definition of PJI for inclusion. Statistical analyses including Fisher's exact test and Cramér's V were performed to assess for associations between medication type and PJI incidence.

RESULTS:

Use of aspirin alone rose from 2% in 2013 to >80% by 2018 and the declined to 55% by 2025. Enoxaparin use sharply declined from 87% to under 1% over 12 years. Apixaban usage increased gradually, reaching 10% by 2025. Overall, non-aspirin ATT use declined from 96% to 16% over the study period. Aspirin alone was associated with a lower risk of PJI compared to non-aspirin regimens (1.11% vs. 1.51%, p = 0.017). In contrast, enoxaparin (2.10% vs. 1.11%, p = 0.0001) and fondaparinux (3.62% vs. 1.22%, p = 0.028) were associated with higher infection risk. Use of any AC or AP regimens without aspirin also showed increased PJI risk (1.72% vs. 1.07%, p = 0.0004). Other agents, including DOACs, P2Y12 inhibitors, and unfractionated heparin, showed no significant associations. Effect sizes were small (Cramér's V < 0.03).

DISCUSSION AND CONCLUSION:

Over the past decade, aspirin has emerged as the most commonly used postoperative ATT agent following TKA and is associated with reduced risk of PJI. Conversely, declining use of enoxaparin and other non-aspirin regimens was observed and was also found to be associated with higher infection risk, albeit with small effect sizes.

Table 1: Risk of infection following TKA correlated with medication type.

Drug group/Subgroup	Infection w/ Drug	Infection w/o drug	*p*-value	Effect size
Antiplatelets				
Aspirin Alone	1.11%	1.51%	**0.017**	0.011
Aspirin with other *ATT*	1.21%	1.32%	0.549	0.004
P2Y12 Inhibitors	0.73%	1.24%	0.999	0.003
Clopidogrel *(Plavix)*	0.84%	1.24%	0.999	0.007
Prasugrel *(Effient)*	0.00%	1.24%	0.999	0.002
PDE Inhibitors, Cilostazol *(Pletal)*	0.00%	1.24%	0.999	0.002
Anticoagulants				
Warfarin *(Coumadin)*	1.80%	1.23%	0.464	0.004
DOAC (Direct Oral Anticoagulants)	1.18%	1.24%	0.999	0.001
Apixaban *(Eliquis)*	1.28%	1.23%	0.883	0.000
Rivaroxaban *(Xarelto)*	1.02%	1.25%	0.670	0.004
Dabigatran *(Pradaxa)*	4.55%	1.23%	0.239	0.009
Unfractionated heparin	4.35%	1.23%	0.248	0.009
Enoxaparin *(Lovenox)*	2.10%	1.11%	**<0.001**	0.030
Fondaparinux *(Arixtra)*	3.62%	1.22%	**0.028**	0.017
Antiplatelet + Anticoagulant (no aspirin)	4.35%	1.23%	0.110	0.013
Anticoagulant or Antiplatelet (no aspirin)	1.72%	1.07%	**<0.001**	0.025

ATT, antithrombin therapy;

Figure 1: Temporal trends in postoperative ATT medication use following TKA (2013–2025)