G15: Does the use of tranexamic acid reduce the incidence of infection in patients undergoing major orthopedic surgery?

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Response/Recommendations:

Yes. The use of tranexamic acid (TXA) reduces the risk of periprosthetic joint infection (PJI) within two years of joint arthroplasty.

Level Of Evidence: Moderate

Delegate Vote:

Rationale:

Infection following major orthopaedic surgery results in patient morbidity and increased healthcare costs (1). Strategies are sought to minimize the risk of infection, particularly periprosthetic joint infection (PJI), which represents a catastrophic complication (2, 3). Tranexamic acid (TXA) is an anti-fibrinolytic agent that reduces perioperative blood loss and has shown potential in decreasing surgical complications (4-6). However, whether TXA can reduce the risk of infection remains uncertain.

We conducted a meta-analysis of studies that compared TXA administration with no TXA administration for all major orthopedic surgery, with or without metalwork. The primary outcome measure was any surgical site infection within 90 days of surgery (7-64). Since prosthetic joint infection (PJI) can take more than 90 days to present following surgery, we also included joint arthroplasty studies with up to two years of follow-up (55-64). After screening 1326 articles, a total of 58 studies were included (7-64), consisting of 19 randomized controlled trials and 39 cohort studies. A total of 2,510,982 patients were included, with 1,503,126 receiving TXA, and 1,007,856 not receiving TXA as controls.

Surgical Site Infection:

A meta-analysis was performed of 36 studies (7-11, 13-16, 18-22, 24-26, 28-34, 36, 38-46, 50, 53) reporting at least one surgical site infection within 90 days of surgery. Superficial and deep infections were grouped together. There was no difference in infection rates between TXA and controls (OR = 0.93; 95% CI [0.73, 1.18]; p = 0.54; I^2 = 83%) (*Supplementary Appendix A*). There was also no difference in infection rates when restricting the analysis to studies (7, 9, 10, 13, 14,

36, 41, 43, 50) where only topical TXA was administered (OR = 0.74; 95% CI [0.30, 1.82]; p = 0.51; $I^2 = 0$).

We then explored the effect of TXA on superficial and deep infections, separately. A meta-analysis was performed of 29 studies (8, 10, 11, 13, 16, 18-20, 22, 24-26, 29-34, 36, 39-46, 50, 53) reporting at least one superficial infection within 90 days of surgery. There was no difference in superficial infection rates between TXA and controls (OR = 0.91; 95% CI [0.65, 1.28]; p = 0.58; $I^2 = 80\%$). A meta-analysis was performed of 15 studies (7-9, 14, 15, 18-21, 28, 32, 38, 40, 41, 44) reporting at least one deep infection within 90 days of surgery. There was no difference in deep infection rates between TXA and controls (OR = 0.95; 95% CI [0.72, 1.25]; p = 0.69; $I^2 = 82\%$).

Periprosthetic Joint Infection:

A meta-analysis was performed of 20 studies (7-9, 15, 19-21, 28, 32, 38, 40, 41, 44, 56-61, 63) that reported at least one periprosthetic joint infection (PJI) within two years of surgery. TXA administration reduced the incidence of PJI (OR = 0.69; 95% CI [0.53, 0.90]; p = 0.01; $I^2 = 88\%$) (*Supplementary Appendix B*). There was no difference in the incidence of PJI between TXA and controls in studies (7-9, 15, 19-21, 28, 32, 38, 40, 41, 44, 61) reporting outcomes within 90 days of surgery (OR = 0.91; 95% CI [0.69, 1.19]; p = 0.48; $I^2 = 83\%$). There was a reduction in the incidence of PJI with TXA over controls in studies (56-61, 63) reporting outcomes between 90 days and two years of surgery (OR = 0.50; 95% CI [0.38, 0.66]; $p < 0.001$; $I^2 = 47\%$).

Conclusions:

TXA is associated with a reduction in the incidence of PJI, but has not been shown to reduce the incidence of overall surgical site infection within 90 days. There may be inadequate statistical power, and most larger studies were retrospective cohort studies or registry data with potential selection bias. The mechanism of reducing the incidence of PJI is not known, but could represent a reduction in transfusion rates or haematoma formation, that are associated with prosthetic joint infection (65-67). TXA has also demonstrated immunomodulatory properties (68, 69). The optimal route of TXA administration also remains unknown (70). TXA is recommended for all joint arthroplasties for optimal patient blood management and may also reduce the risk of PJI.

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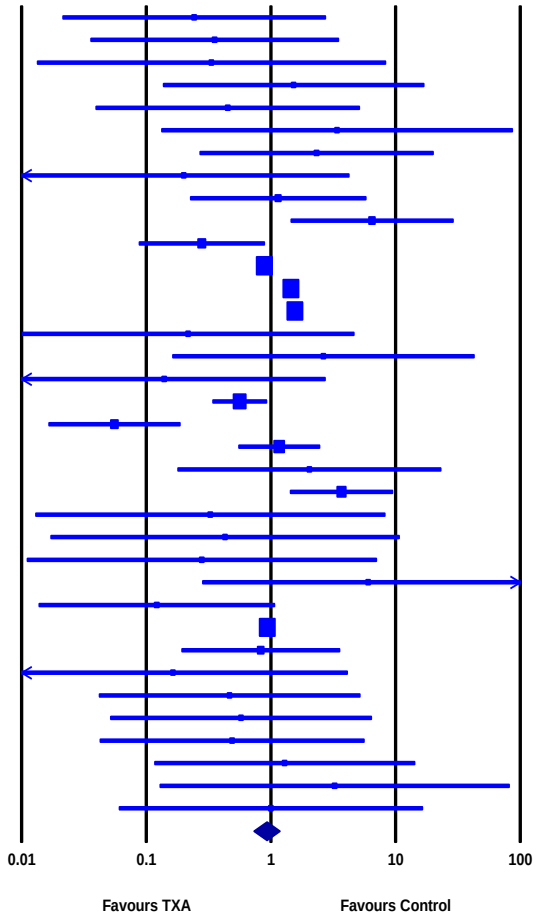
Appendix 1:

Surgical Site Infection Within 90 Days

Study name	Subgroup within study	Odds ratio	Lower limit	Upper limit	p-Value
Aguilera 2015	DI	0.24	0.02	2.74	0.25
Ali 2022	Combined	0.35	0.04	3.49	0.37
Alshryda 2013	DI	0.33	0.01	8.31	0.50
Cao 2019	SI	1.52	0.14	16.86	0.73
Chen 2020	SI	0.45	0.04	5.14	0.52
Costain 2021	SI	3.39	0.13	86.43	0.46
Davis 2024	DI	2.33	0.27	20.03	0.44
FÃ-gar 2017	DI	0.20	0.01	4.23	0.30
Formby 2015	SI	1.14	0.23	5.78	0.87
Gettleman 2024	Combined	6.48	1.45	28.97	0.01
Goh 2021	Combined	0.28	0.09	0.89	0.03
Heckmann 2023	Combined	0.89	0.84	0.93	0.00
Hong 2021	DI	1.45	1.29	1.62	0.00
Hsu 2023	SI	1.56	1.41	1.72	0.00
Johansson 2005	SI	0.22	0.01	4.63	0.33
Kelly 2022	SI	2.64	0.16	42.67	0.49
Khatib 2024	SI	0.14	0.01	2.73	0.19
Klement 2020	DI	0.56	0.34	0.92	0.02
Kramer 2020	SI	0.06	0.02	0.19	0.00
Liu 2017	SI	1.16	0.55	2.46	0.69
Lubberdink 2013	SI	2.04	0.18	23.09	0.57
Moore 2022	Combined	3.68	1.43	9.47	0.01
Ni 2021	SI	0.33	0.01	8.21	0.50
Palanisamy 2018	SI	0.43	0.02	10.69	0.61
Qiu 2019	SI	0.28	0.01	7.02	0.44
Steinmetz 2020	DI	6.03	0.28	128.30	0.25
Tan 2022	SI	0.12	0.01	1.07	0.06
Thapaliya 2024	Combined	0.94	0.83	1.05	0.27
Tzatzairis 2016	Combined	0.83	0.19	3.56	0.80
Wang 2016	SI	0.16	0.01	4.11	0.27
Witmer 2022	SI	0.47	0.04	5.17	0.53
Wu 2019	Combined	0.58	0.05	6.39	0.65
Xie 2015	SI	0.49	0.04	5.59	0.56
Xie 2019	SI	1.29	0.12	14.22	0.84
Yue 2014	SI	3.25	0.13	81.63	0.47
Zhou 2019	SI	1.00	0.06	16.44	1.00
		0.93	0.73	1.18	0.54



Appendix 2:

Prosthetic Joint Infection Within Two Years

Study name	Subgroup within study	Odds ratio	Lower limit	Upper limit	p-Value
Aguilera 2015	DI	0.24	0.02	2.74	0.25
Ali 2022	DI	0.35	0.01	8.98	0.53
Alshryda 2013	DI	0.33	0.01	8.31	0.50
Drain 2020	DI	0.52	0.35	0.76	0.00
FÃ-gar 2017	DI	0.20	0.01	4.23	0.30
Goh 2021	DI	0.44	0.14	1.41	0.17
Gorbaty 2023	DI	0.89	0.51	1.54	0.67
Heckmann 2023	DI	0.91	0.86	0.98	0.01
Hong 2021	DI	1.45	1.29	1.62	0.00
Klement 2020	DI	0.56	0.34	0.92	0.02
Lacko 2020	DI	0.12	0.01	0.94	0.04
Moore 2022	DI	7.26	0.86	61.39	0.07
Prieto 2018	DI	0.48	0.02	12.37	0.66
Shohat 2022	DI	0.38	0.29	0.48	0.00
Steinmetz 2020	DI	6.03	0.28	128.30	0.25
Thapaliya 2024	DI	0.83	0.73	0.94	0.00
Tzatzairis 2016	DI	1.53	0.06	38.36	0.80
Waddell 2016	DI	1.00	0.24	4.25	1.00
Wu 2019	DI	0.38	0.02	9.47	0.56
Yazdi 2020	DI	0.47	0.34	0.66	0.00
		0.69	0.53	0.90	0.01