

EFFECTIVENESS AND SAFETY OF TRANEXAMIC ACID IN TOTAL KNEE ARTHROPLASTY: A SYSTEMATIC REVIEW AND META-ANALYSIS

DIGITAL CONTENT

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Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Alipour et al. 2013	+	+	+	+	+	+
Aishryda et al. 2013	+	+	+	+	+	+
Alvarez et al. 2008	+	+	-	+	+	+
Alvarez et al. 2019	+	+	+	+	-	+
Antinolfi et al. 2013	+	+	+	+	-	+
Benon et al. 1996	+	+	-	+	+	+
Bidolegui et al. 2014	+	-	+	+	+	+
Bradshaw et al. 2012	+	-	+	+	+	+
Camarasa et al. 2006	+	+	+	+	-	+
Chen et al. 2016	+	+	+	+	-	+
Chiang et al. 2019	+	+	+	+	-	+
Ellis et al. 2001	+	+	+	+	+	+
Engel et al. 2001	+	+	+	+	+	+
Fernandes Guerreir et al. 2017	+	+	+	+	+	+
Georgiadis et al. 2013	+	+	+	+	+	+
Good et al. 2003	+	+	+	+	-	+
Guzel et al. 2016	+	+	+	+	+	+
Hiippala et al. 1997	+	+	+	+	+	+
Hiippala et al. 1995	+	+	+	+	+	+
Huang et al. 2017	+	-	+	+	+	+
Ishida et al. 2011	+	+	+	+	+	+
Jensen et al. 1999	+	+	+	+	-	+
Karaaslan et al. 2015	+	+	+	+	+	+
Kim et al. 2013	+	+	+	+	+	+
Kim et al. 2021	+	+	+	+	+	+
Kundu et al. 2015	+	+	-	+	+	+
Lal Gautam et al. 2011	+	+	+	+	-	+
Lee et al. 2013	+	+	+	+	+	+
Lee et al. 2017	+	+	+	+	+	+
Liu et al. 2018	+	+	+	+	-	+
MacGillivray et al. 2011	+	+	+	+	+	+
Maniar et al. 2012	+	+	+	+	+	+
Molly et al. 2007	+	+	+	-	+	+
Motifard et al. 2015	+	-	+	+	+	+
Onodera et al. 2012	+	+	+	+	+	+
Orpen et al. 2006	+	+	+	+	+	+
Oztaz et al. 2015	+	+	-	+	+	+
Roy et al. 2012	+	+	-	+	+	+
Sa-ngasoongsong et al. 2013	+	+	+	+	+	+
Santias et al. 2020	+	+	+	+	-	+
Shen et al. 2015	+	+	+	+	-	+
Shinde et al. 2015	+	+	+	+	+	+
Sun et al. 2017	+	+	+	+	-	+
Veien et al. 2002	+	+	+	+	+	+
Volquind et al. 2016	+	+	+	+	-	+
Wang et al. 2015	+	-	+	+	+	+
Wong et al. 2010	+	-	+	+	+	+
Yang et al. 2015	+	+	+	+	-	+
Yen et al. 2021	+	+	+	+	-	+
Zhang et al. 2021 (A)	+	+	+	+	+	+
Zhang et al. 2021 (B)	+	+	+	+	-	+
Zohar et al. 2004	+	+	+	+	+	+

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.



Judgement
 Some concerns
 Low

FIGURE S1. A summary table of review authors' judgements for each risk of bias item for each randomized study

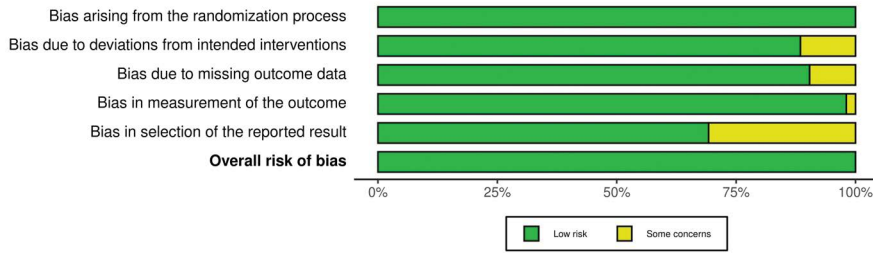


FIGURE S2. A plot of the distribution of review authors' judgements across randomized studies for each risk of bias item

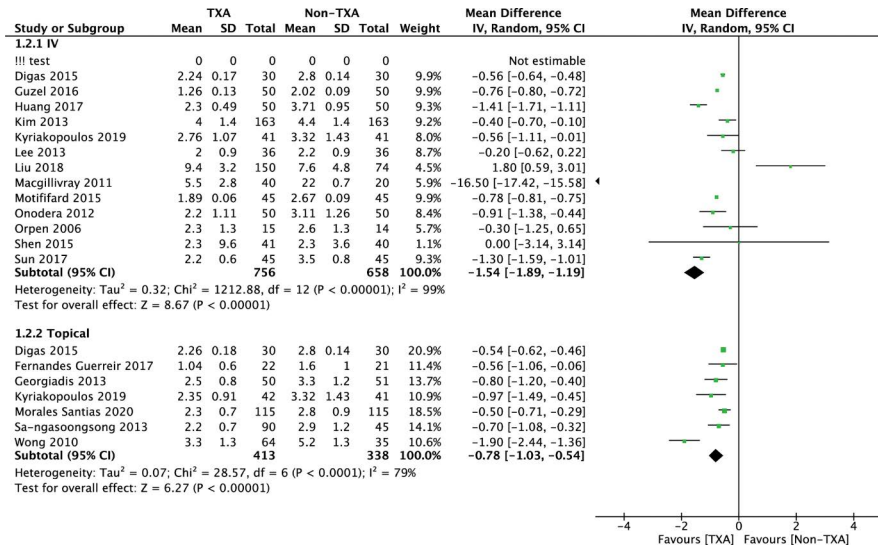


FIGURE S3. Forest plot of hemoglobin changes in 24-hours after surgery among TXA and non-TXA group in subgroup analysis due to TXA administration route

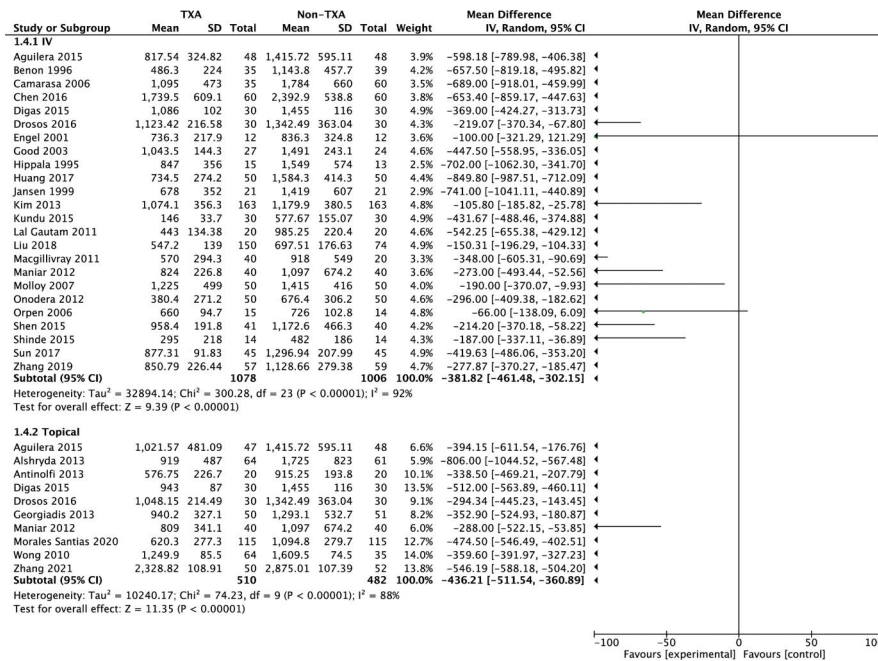


FIGURE S4. Forest plot of total blood loss among TXA and non-TXA group in subgroup analysis due to TXA administration route

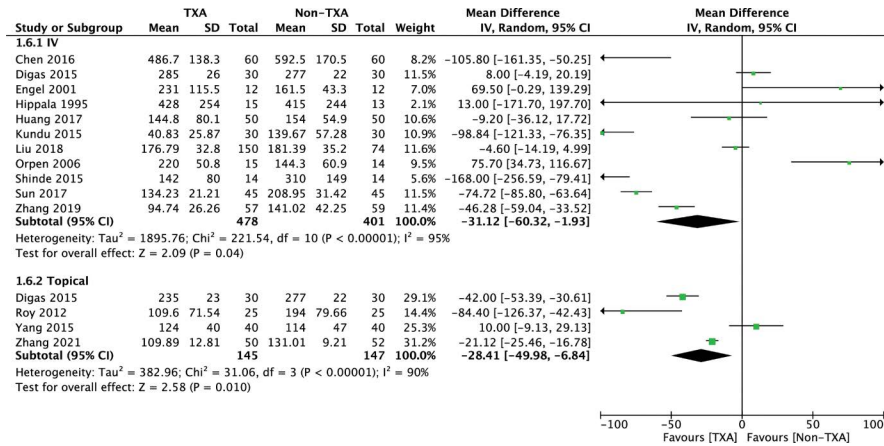


FIGURE S5. Forest plot of intraoperative blood loss among TXA and non-TXA group in subgroup analysis due to TXA administration route

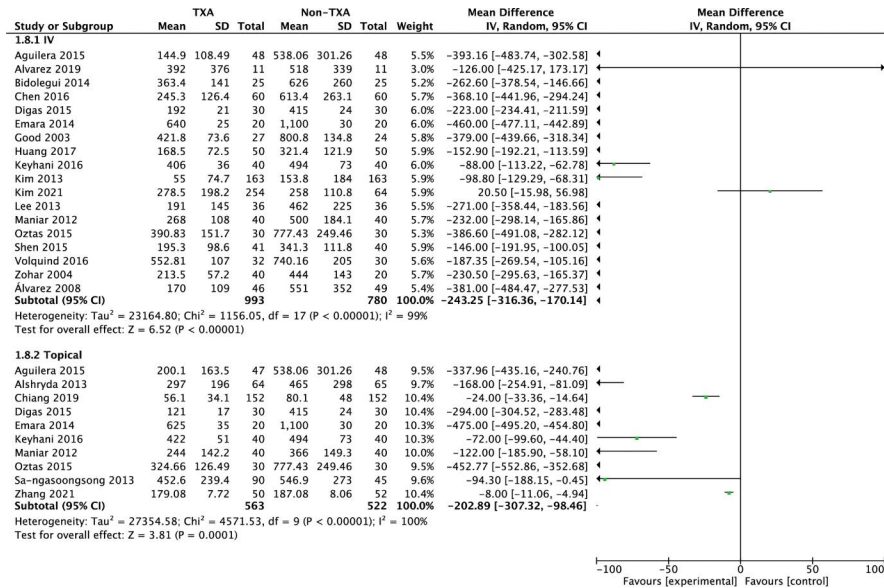


FIGURE S6. Forest plot of 24-hours blood loss from the drain among TXA and non-TXA group in subgroup analysis due to TXA administration route

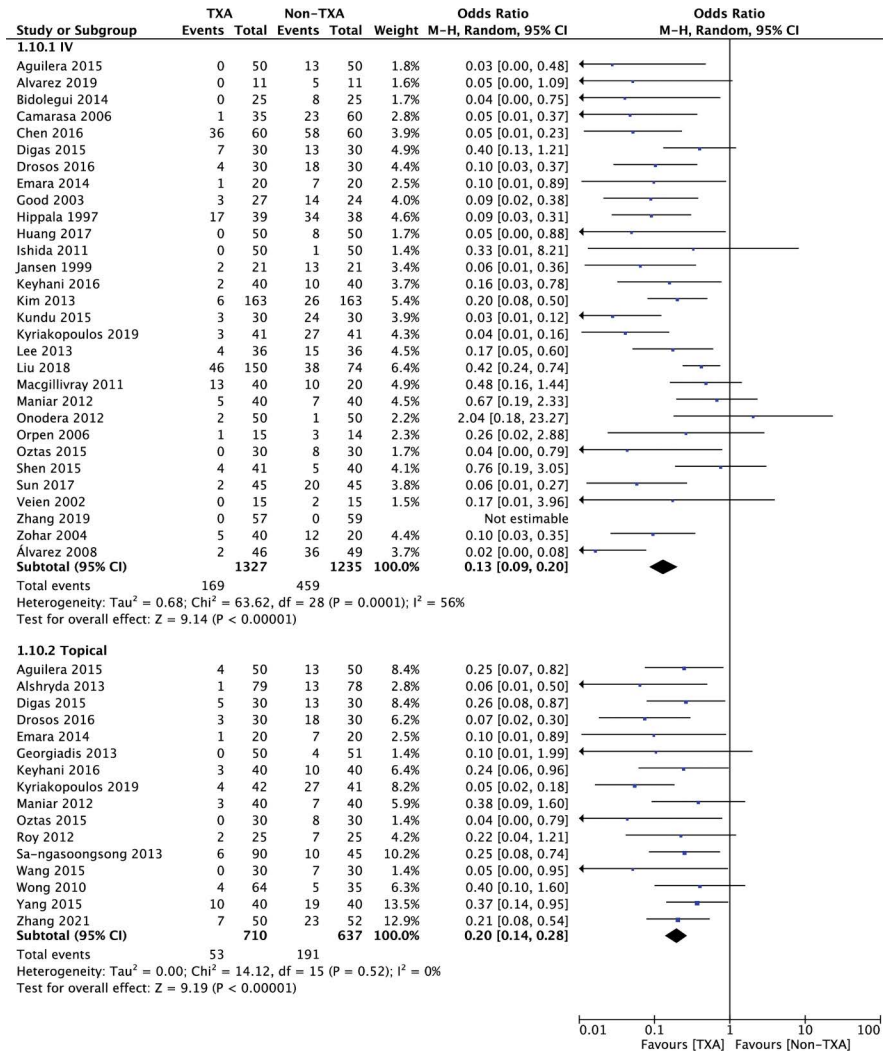


FIGURE S7. Forest plot of blood transfusion occurrence among TXA and non-TXA group in subgroup analysis due to TXA administration route

Table S1. Characteristics of included studies

Study	Country	Study design	TXA group			Non-TXA group		
			No. of patients	Age	Sex, male	No. of patients	Age	Sex, male
Alipour et al. 2013	Iran	RCT	26	68.6 ± 10	11 (42.3%)	27	63.11 ± 12.4	16 (59.3%)
Alshryda et al. 2013	UK	RCT	79	65.5 ± 9.6	30 (38.0%)	78	67.1 ± 10.2	44 (56.4%)
Álvarez et al. 2008	Sapin	RCT	46	71 ± 9	7 (15.2%)	49	72 ± 7	10 (20.4%)
Álvarez et al. 2019	Sapin	RCT	11	70 ± 7.5	3 (27.3%)	11	72.4 ± 7.1	2 (18.1%)
Antinolfi et al. 2013	Italy	RCT	20	71.9 ± 5.1	11 (55.0%)	20	70.7 ± 7.3	10 (50.0%)
Benon et al. 1996	Sweden	RCT	43	76 ± 7	13 (30.2%)	43	74 ± 7	10 (23.3%)
Bidolegui et al. 2014	Argentina	RCT	50	71.5 ± 9.4	NS	50	72 ± 6.8	NS
Bradshaw et al. 2012	Australia	RCT	26	67.1 ± 9.4	14 (53.8%)	20	68.2 ± 9.8	13 (65.0%)
Camarasa et al. 2006	Spain	RCT	35	73 (61-84)	9 (25.7%)	60	72 (52-85)	12 (20.0%)
Chen et al. 2016	China	RCT	60	66.5 ± 7.1	16 (26.7%)	60	64.2 ± 6.2	14 (23.3%)
Chiang et al. 2019	Taiwan	RCT	151	25.7 ± 8.4	125 (82.8%)	149	27.6 ± 6.9	119 (79.9%)
Ellis et al. 2001	Israel	RCT	10	71 ± 5	4 (40.0%)	10	72 ± 8	3 (30.0%)
Engel et al. 2001	Germany	RCT	12	71 ± 9	4 (33.3%)	12	66 ± 11	4 (33.3%)
Fernandes Guerreir et al. 2017	Brasil	RCT	22	68.36 (55-86)	4 (18.2%)	21	69.14 (55-81)	7 (33.3%)
Georgiadis et al. 2013	USA	RCT	50	67.0 ± 9.0	19 (38.0%)	51	64.5 ± 8.2	12 (23.5%)
Good et al. 2003	Sweden	RCT	27	72 (46-83)	9 (33.3%)	24	72 (50-84)	6 (25.0%)
Guzel et al. 2016	Turkey	RCT	50	66.5 ± 5.1	7 (14.0%)	50	67 ± 4.5	10 (20.0%)
Hiippala et al. 1997	Finland	RCT	39	70 ± 7	4 (10.3%)	38	69 ± 5	8 (21.1%)
Hippala et al. 1995	Finland	RCT	15	70(56-92)	2 (13.3%)	13	70 (63-78)	3 (23.1%)
Huang et al. 2017	China	RCT	100	66.1 ± 7.6	34 (34.0%)	50	65.8 ± 6.3	15 (30.0%)
Ishida et al. 2011	Japan	RCT	50	73.3 ± 5.0	6 (12.0%)	50	73.5 ± 6.1	6 (12.0%)
Jensen et al. 1999	Belgium	RCT	21	70.7 (62-80)	5 (23.8%)	21	71 (64-84)	3 (14.3%)
Karaaslan et al. 2015	Turkey	RCT	41	65.9 ± 8.0	6 (14.6%)	40	65.6 ± 7.0	8 (20.0%)
Kim et al. 2013	Korea	RCT	90	73.5 ± 5.5	11 (12.2%)	90	71.9 ± 55.9	12 (13.3%)

Table S1. Characteristics of included studies

Study	Country	Study design	TXA group			Non-TXA group		
			No. of patients	Age	Sex, male	No. of patients	Age	Sex, male
Kim et al. 2021	Korea	RCT	254	69.8 ± 6.4	24 (9.4%)	64	67.2 ± 5.1	6 (9.4%)
Kundu et al. 2015	India	RCT	30	60.3±12.56	8 (26.7%)	30	59.6 ± 12.2	7 (23.3%)
Lal Gautam et al. 2011	India	RCT	20	65.65±6.27	8 (40.0%)	20	64.65 ± 9.75	8 (40.0%)
Lee et al. 2013	Korea	RCT	36	69.7 ±7.9	5 (13.9%)	36	69.2 ± 7.7	5 (13.8%)
Lee et al. 2017	China	RCT	94	70 ± 8	31 (33.0%)	95	68 ± 8	29 (30.5%)
Liu et al. 2018	China	RCT	150	63.5 ± 6.8	64 (42.7%)	74	61.85 ± 6.4	31 (41.9%)
MacGillivray et al. 2011	United Arab Emirates	RCT	40	63.5 ± 4.3	15 (37.5%)	20	66 ± 7.5	5 (25.0%)
Maniar et al. 2012	India	RCT	80	67.8 ± 8.5	16 (20.0%)	40	66.2 ± 7.2	4 (10.0%)
Molly et al. 2007	Ireland	RCT	50	NS	NS	50	NS	NS
Motififard et al. 2015	Iran	RCT	45	67.04 ± 8.01	10 (20.2%)	45	65.66 ± 4.97	13 (28.9%)
Onodera et al. 2012	Japan	RCT	50	70.4 ± 10.1	8 (16.0%)	50	70.5 ± 8.3	9 (18.0%)
Orpen et al. 2006	UK	RCT	15	73 (70-78)	8 (53.3%)	14	69 (63-74)	3 (21.4%)
Oztaz et al. 2015	Turkey	RCT	60	67.5 ± 6.3	9 (15.0%)	30	67.03 ± 6.15	5 (16.7%)
Roy et al. 2012	India	RCT	25	66.04 ± 7.15	15 (60.0%)	25	66.56 ± 8.03	9 (36.0%)
Sa-ngasoongsong et al. 2013	Thailand	RCT	90	67.9 ± 8.1	8 (8.9%)	45	66.2 ± 7.3	2 (4.4%)
Santias et al. 2020	Spain	RCT	115	71.1 ± 7.9	35 (30.4%)	115	70.0 ± 8.0	41 (35.7%)
Shen et al. 2015	China	RCT	41	65.7±8.2	8 (19.5%)	40	64.9 ± 7.9	11 (27.5%)
Shinde et al. 2015	India	RCT	14	66.79 ± 6.12	3 (21.4%)	14	63.79 ± 8.85	1 (7.1%)
Sun et al. 2017	China	RCT	45	68.1 ± 7.9	10 (22.2%)	45	67.4 ± 8.4	8 (17.8%)
Veien et al. 2002	Denmark	RCT	15	70.5 ± 9.5	4 (26.7%)	14	69.5 ± 9.0	1 (7.1%)
Volquind et al. 2016	Brazil	RCT	32	67.87 ± 5	10 (31.3%)	30	63.96 ± 4	9 (30.0%)
Wang et al. 2015	China	RCT	30	64.90 ± 6.38	9 (30.0%)	30	64.97 ± 6.75	6 (20.0%)
Wong et al. 2010	Canada	RCT	64	65.9 ± 11.2	20 (31.3%)	35	68.4 ± 10.4	13 (37.1%)
Yang et al. 2015	China	RCT	40	69 ± 5	12 (30.0%)	40	67 ± 6	10 (25.0%)

Table S1. Characteristics of included studies

Study	Country	Study design	TXA group			Non-TXA group		
			No. of patients	Age	Sex, male	No. of patients	Age	Sex, male
Yen et al. 2021	Taiwan	RCT	34	NS	NS	35	NS	NS
Zhang et al. 2021 (A)	China	RCT	57	65.21 ± 8.23	10 (17.5%)	59	64.78 ± 6.63	11 (18.6%)
Zhang et al. 2021 (B)	China	RCT	50	65.19 ± 6.87	16 (32.0%)	52	64.81 ± 7.08	18 (34.6%)
Zohar et al. 2004	Israel	RCT	40	69 ± 9	12 (30.0%)	20	73 ± 7	7 (35.0%)

RCT — randomized controlled trial; NS — not specified