CRITICAL ROUNDS

MICRO LABS LIMITED

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring "CRITICAL ROUNDS" containing latest information in the field of Critical care medicine.

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Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Ltd

Characteristics of Sepsis-2 septic shock patients who do not meet the Sepsis-3 septic shock definition: a real-time data analysis

Background:

In 2016, the American Society of Sepsis and Septic Shock established a new consensus definition of sepsis and septic shock. To be considered to have septic shock, patients must have sepsis (a proven or suspected infection combined with a rise in sequential organ failure assessment score (SOFA) of at least 2 points compared to baseline), persistent hypotension requiring vasopressor therapy to maintain a mean arterial pressure. Patients had to have sepsis (defined as a proven or suspected infection in combination with at least two systemic infammatory response syndrome (SIRS) criteria) and persistent hypotension to meet the old Sepsis-2 consensus definition. When compared to older definitions, the use of SOFA or rapid SOFA (qSOFA) leads in a more accurate prediction of mortality risk.

Objective:

Patients with septic shock according to the new Sepsis-3 definition may have different baseline features and disease severity than those who exclusively follow the Sepsis-2 definition. This study aimed to conduct a retrospective cohort analysis in the ICU of a Belgian tertiary care centre to look for differences between two patient groups and to uncover characteristics linked to no longer satisfying the most recent definition of septic shock.

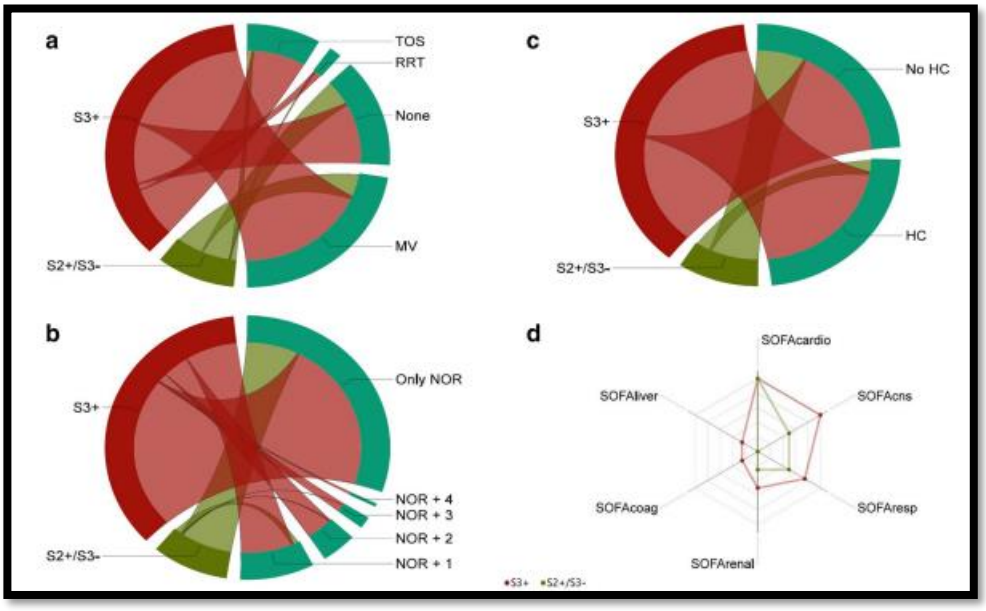
Methods:

Two groups were created according to sepsis 2 definition. The first group of patients was referred to as "S3+." These patients exhibited a rise in lactate above 2 mmol/l at the same timepoint, in addition to vasopressor medication, causing them to comply with the Sepsis-3 shock definition. The remaining patients had only vasopressor medication and had no reported lactate value more than 2 mmol/l, indicating that they did not meet the Sepsis-3 shock definition. These people were dubbed "S2+/S3" patients. The electronic patient record was used to capture outcome parameters. For each patient, the Charlson comorbidity index (CCI), the SOFA score, and the Acute Physiology and Chronic Health Evaluation (APACHE II) score were calculated.

Results:

According to the Sepsis-2 consensus definition, 233 (19.4%) of 1198 individuals with septic shock did not have septic shock according to the Sepsis-3 definition. Patients who solely had septic shock according to the old definition had significantly lower APACHE II and SOFA scores, as well as significantly decreased hospital mortality (31.6 percent vs 55.3 percent, $p < 0.001$).

In a multivariate analysis, respiratory infection (OR 1.485 (95 percent CI 1.56–2.089), p=0.023), a medical admission reason (OR 1.977 (95 percent CI 1.396–2.800), and chronic liver disease (OR 0.345 (95 percent CI 0.181–0.660), $p < 0.001$) were all associated with Sepsis-2 shock patients no longer being defined as such by the Sepsis-3 definition.



a) Chord diagram representing the need for organ support—on top of vasopressor therapy. b) Chord diagram representing administration of hydrocortisone (HC) in septic shock. c) Chord diagram representing the number of adjuvant vasopressor or inotropic agents on top of norepinephrine (NOR). d) Radar plot of the SOFA subscores.

Conclusion:

When the Sepsis-3 shock criteria are implemented, one out of every four patients who have septic shock according to the Sepsis-2 consensus definition is no longer deemed septic. The absence of chronic liver disease, a medical admission cause, and a respiratory infection are all independently linked to no longer being classified as having septic shock by the Sepsis-3 criteria.

Reference:

Vermassen J, Decruyenaere J, De Bus L, Depuydt P, Colpaert K. Characteristics of Sepsis-2 septic shock patients failing to satisfy the Sepsis-3 septic shock definition: an analysis of real-time collected data. Ann Intensive Care. 2021 Oct 30;11(1):154.

Oliguria and the Diagnosis, Assessment, and Mortality of Acute Kidney Injury in

Background:

Acute kidney injury (AKI) is a term that has been used to describe a wide range of acute changes in kidney function, from transitory oliguria to complete kidney failure. AKI is defined as an increase in serum creatinine (sCr) levels relative to a baseline value and/or a decrease in weight-adjusted hourly urine output, according to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines (UO). Both components are thought to be readily available at the bedside, repeatable, and have similar prognostic capabilities. However, the added utility of oliguria over sCr level is questioned, especially if it is merely temporary and not linked to a rise in sCr level.

Objective:

This study aimed to determine the role of oliguria in AKI diagnosis, severity evaluation, and short- and long-term outcomes, as described by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria.

Methods:

Electronic medical records were used to obtain daily sCr levels and hourly UO measures, as well as sociodemographic information and severity assessments. The database was cross-referenced to determine long-term mortality. UO and sCr criteria were used to evaluate the start and severity of AKI according to the KDIGO classification, and their agreement was assessed. The correlation of UO criteria with 90-day mortality was investigated using a multivariable model that took into account baseline characteristics, severity scores, and sCr stages.

	Patients, No. (%)	Mortality, No./total No. (%)[b]	Univariate analysis[a] OR (95% CI)	*P* value
Overall AKI stage				
No AKI	3477 (22.3)	288/3462 (8.3)	1 [Reference]	NA
Stage 1	3027 (19.4)	452/3013 (15.0)	1.94 (1.66-2.27)	<.001
Stage 2	6329 (40.5)	1074/6304 (17.0)	2.26 (1.97-2.59)	<.001
Stage 3	2787 (17.8)	1045/2772 (37.7)	6.67 (5.78-7.69)	<.001
AKI stage according to UO criteria[c]				
No AKI	4466 (28.6)	462/4444 (10.4)	1 [Reference]	NA
Stage 1	2646 (16.9)	410/2635 (15.6)	1.59 (1.38-1.83)	<.001
Stage 2	6390 (40.9)	1120/6365 (17.6)	1.84 (1.64-2.06)	<.001
Stage 3	2118 (13.5)	867/2107 (41.1)	6.03 (5.29-6.86)	<.001
AKI stage according to sCr criteria[d]				
No AKI	9107 (58.3)	1012/9070 (11.2)	1 [Reference]	NA
Stage 1	3422 (21.9)	747/3406 (21.9)	2.23 (2.01-2.48)	<.001
Stage 2	1238 (7.9)	334/1233 (27.1)	2.95 (2.57-3.40)	<.001
Stage 3	1853 (11.9)	766/1842 (41.6)	5.67 (5.06-6.34)	<.001

Table 1: 90-Day Mortality According to AKI Stage by Kidney Disease: Improving Global Outcomes Criteria

Results:

12 143 (77.7%) of the 15 620 patients in the study met AKI criteria (10 330 men [66.1%] with a median age of 65 [IQR, 53-75] years, a median Simplified Acute Physiology Score II score of 40.0 [IQR, 30.0-53.0], and a median follow-up of 67.0 [IQR, 34.0-100.0] months). On AKI diagnosis and staging, serum creatinine and UO criteria demonstrated low agreement (Cohen weighted, 0.36; 95% CI, 0.35-0.37; P < .001). When compared to the use of sCr criteria alone, UO criteria allowed for the detection of AKI in 5630 patients (36.0%). Patients with AKI showed a greater 90-day death rate than those without AKI (724 of 5608 [12.9%] vs 288 of 3462 [8.3%]; P < .001). UO stages 2 and 3 were related with a greater 90-day mortality (odds ratios, 2.4 [95 percent CI, 1.6-3.8; P < .001] and 6.2 [95% CI, 3.7-10.5; P < .001], respectively) on multivariable analysis accounting for sCr stage, comorbidities, and disease severity. All sensitivity analysis confirmed the significance of these findings.

Outcome	Patient group[a]				
			AKI according to KDIGO criteria (n = 12 143)		
	All (N = 15 620)	No AKI (n = 3477)	sCr plus UO (n = 5524)	UO only (n = 5630)	sCr only (n = 989)
LOS, median (IQR), d					
ICU	2.3 (1.1-5.6)	1.1 (0.9-1.9)	5.8 (2.8-12.3)	1.9 (1.0-3.3)	2.8 (1.5-5.5)
Hospital	12.8 (6.8-23.4)	9.2 (4.0-15.8)	18.9 (9.2-34.8)	11.1 (6.5-18.2)	14.4 (7.7-26.2)
KRT during ICU stay	1160 (7.4)	0	1130 (20.5)	0	30 (3.0)
Mechanical ventilation	9640 (61.7)	1624 (46.7)	4335 (78.5)	3168 (56.3)	513 (51.9)
Mechanical ventilation total duration, median (IQR), h	35.7 (10.6-122.2)	10.1 (5.0-22.1)	99.6 (35.5-231.4)	18.2 (7.2-48.8)	46.5 (15.4-128.8)
Mortality					
ICU	1723 (11.0)	147 (4.2)	1129 (20.4)	379 (6.7)	68 (6.9)
Hospital	2306 (14.8)	202 (5.8)	1452 (26.3)	534 (9.5)	118 (11.9)
90-d[b]	2859 (18.4)	288 (8.3)	1673 (30.4)	724 (12.9)	174 (17.7)
1-y[c]	3453 (23.9)	429 (13.2)	1858 (36.7)	930 (17.8)	236 (26.0)
3-y[d]	3630 (31.6)	529 (20.2)	1748 (43.8)	1088 (26.2)	265 (36.0)
5-y[e]	3192 (36.9)	482 (24.0)	1478 (50.1)	996 (31.4)	236 (44.7)

Table 2: Patient Outcomes

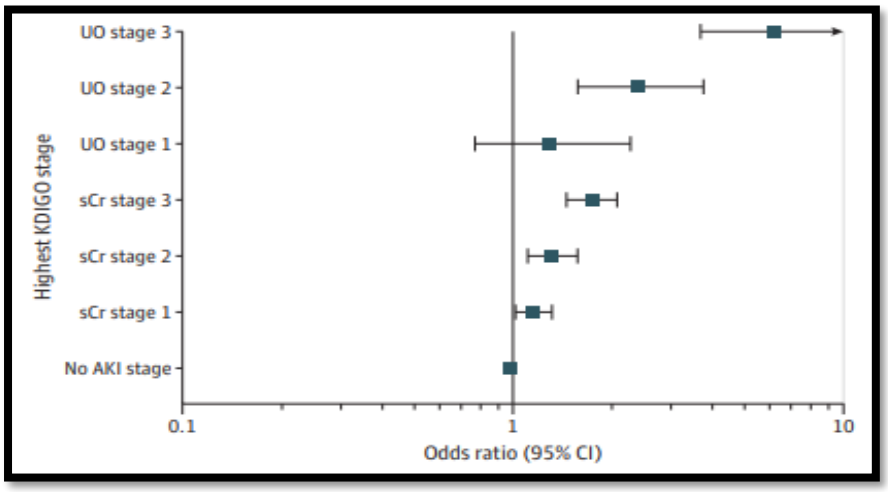
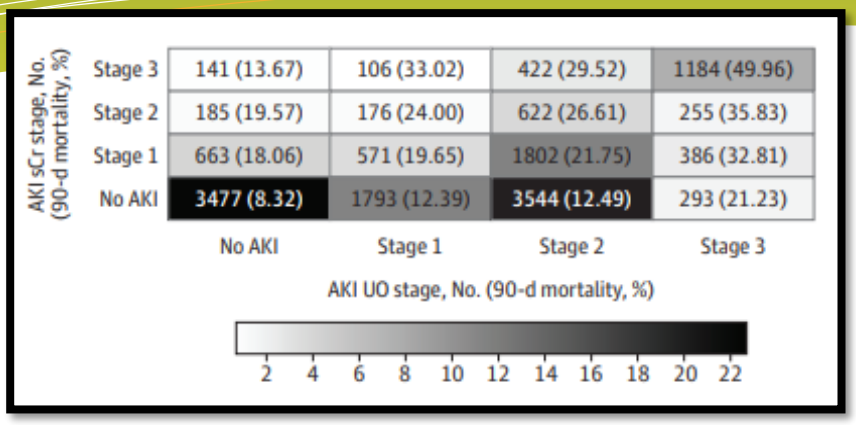


Figure 2: Multivariate Adjusted Odds Ratios for 90-Day Mortality



Classification of Patients and Corresponding 90-Day Mortality According to the Worst Kidney Disease: Improving Global Outcomes Serum Creatinine (sCr) and Urinary Output (UO) Stages

Conclusion:

This cohort study's finding demonstrated that oliguria lasting more than 12 hours (KDIGO stage 2 or 3) has severe AKI diagnostic implications and is linked to outcomes regardless of increase in sCr level.

Reference:

Bianchi NA, et al. Association of Oliguria With Acute Kidney Injury Diagnosis, Severity Assessment, and Mortality Among Patients With Critical Illness. JAMA Netw Open. 2021 Nov 1;4(11):e2133094

A comprehensive review and meta-analysis of the effects of tranexamic acid on thrombotic events and seizures in bleeding patients.

Background:

Tranexamic acid (TXA) is a synthetic lysine derivative that inhibits fibrinolysis by blocking the lysine binding sites on plasminogen, hence reducing bleeding. One of the most serious issues with TXA therapy is the risk of thrombotic events and seizures. TXA may raise the risk of thrombosis by decreasing fibrinolysis. TXA can pass the blood–brain barrier, and through antagonising inhibitory gammaaminobutyric acid receptor type A (GABAA) in the brain, it may exacerbate seizures. Due to imprecision or methodological constraints, there are still doubts about the risk of thrombotic events and seizures with TXA use, despite the cumulative data.

Objective:

The aim of this systematic review and meta-analysis was to assess the effects of TXA on thrombotic events and seizures in bleeding patients by examining all available RCTs. With subgroup analysis and meta-regression analysis, this study looked at how the effects of TXA change by dose and underlying condition.

Methods:

In bleeding patients, the study included randomised trials comparing intravenous tranexamic acid to placebo or no treatment. Thrombotic events, venous thromboembolism, acute coronary syndrome, stroke, and seizures were the major outcomes. A random effects model was used in the meta-analysis, and meta-regression analysis was used to see how effects differed by dose. The GRADE (grading of recommendations, assessment, development, and evaluations) approach was used to assess the evidence's certainty.

Result:

The meta-analysis includes a total of 234 trials with 102,681 patients. TXA did not enhance the risk of thrombotic events (RR=1.00 [95 percent CI 0.93–1.08]), seizures (1.18 [0.91–1.53]),

venous thromboembolism (1.04 [0.92–1.17]), acute coronary syndrome (0.88 [0.78–1.00]), or stroke (1.12 [0.98–1.27] in bleeding patients. Seizures were increased in individuals taking more than 2 g/day of TXA (3.05 [1.01–9.20]) in a dose-by-dose sensitivity analysis. Increased TXA dose was associated with an increased risk of seizures (p=0.011) in meta-regression.

	Studies	Events, No. / total TXA	Control	RR (95% CI)
Thrombotic events	230	1342/52103	1278/50211	1.00 (0.93-1.08)
Seizures	40	404/30351	351/29847	1.18 (0.91-1.53)
Venous thromboembolism	208	532/50037	454/48447	1.04 (0.92-1.17)
Acute coronary syndrome	107	421/42763	476/41663	0.88 (0.78-1.00)
Stroke	106	446/42924	389/42014	1.12 (0.98-1.27)

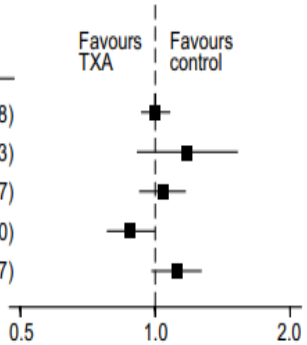


Table 3: Forest plot comparing tranexamic acid and control for primary outcome. TXA, tranexamic acid. RR, risk ratio. CI, confidence interval

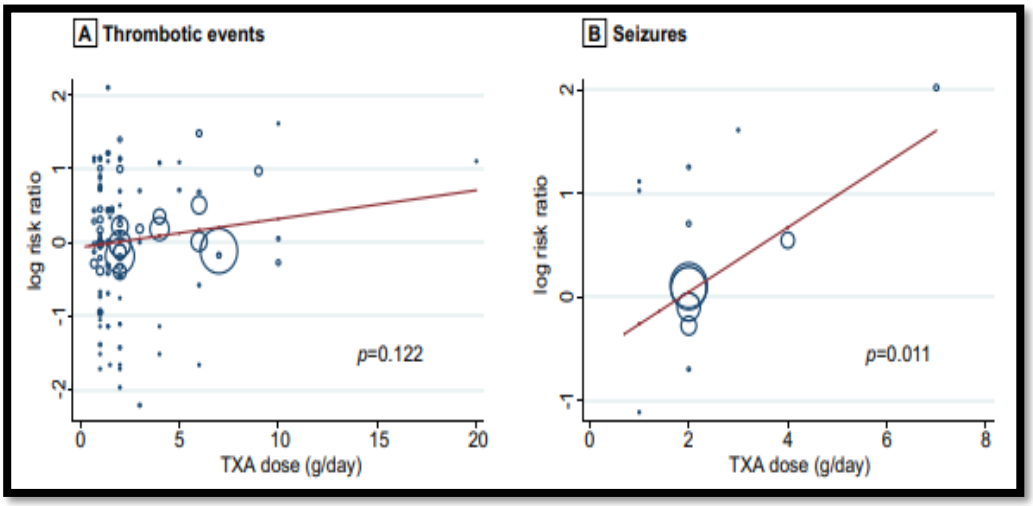
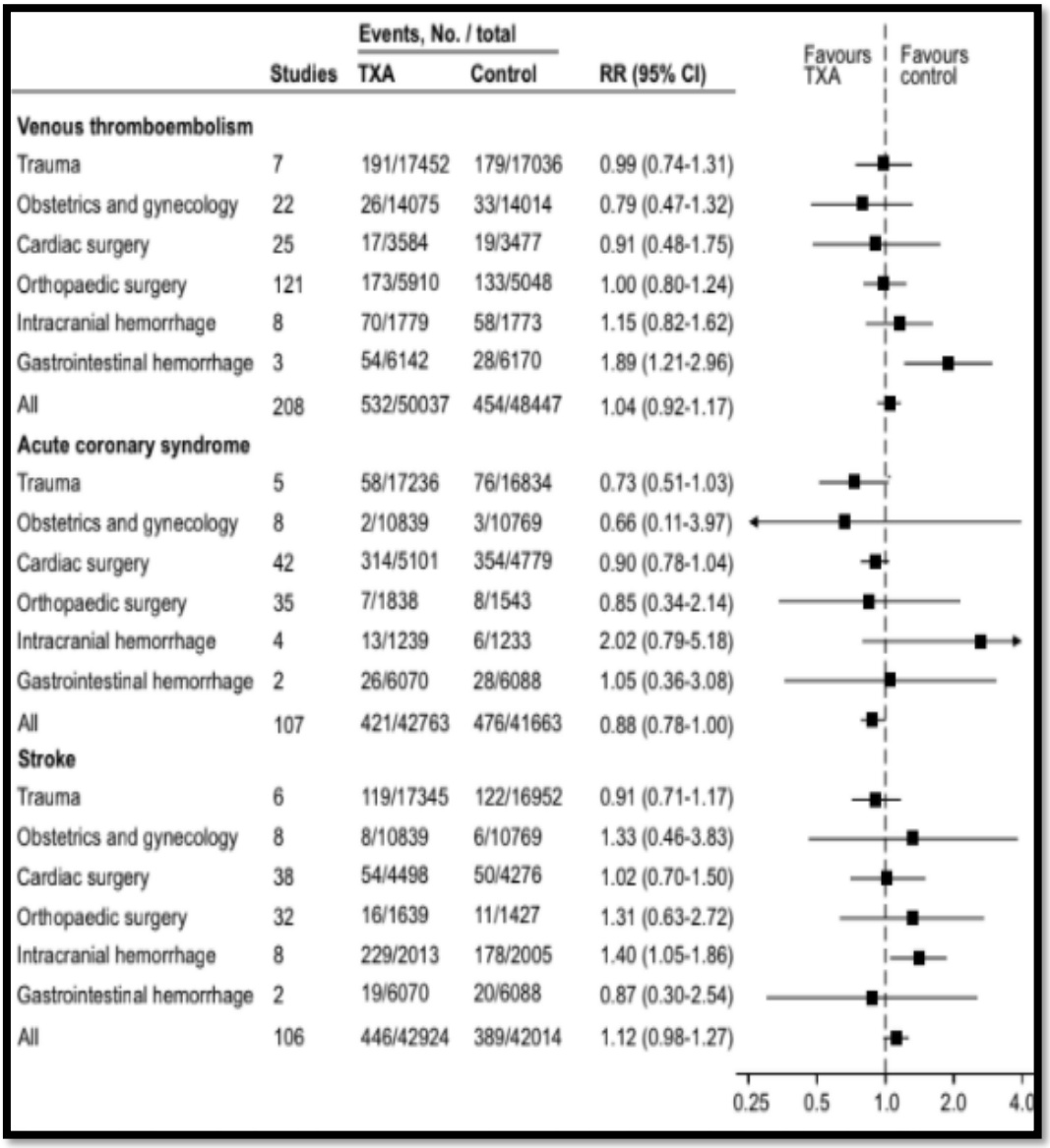


Figure 3: Meta-regression plot. Plots show the relation between the log risk ratio of A thrombotic events and B seizures with tranexamic acid and tranexamic acid dose (g/day). TXA, tranexamic acid



	Studies	Events, No. / total TXA	Control	RR (95% CI)
Venous thromboembolism				
Trauma	7	191/17452	179/17036	0.99 (0.74-1.31)
Obstetrics and gynecology	22	26/14075	33/14014	0.79 (0.47-1.32)
Cardiac surgery	25	17/3584	19/3477	0.91 (0.48-1.75)
Orthopaedic surgery	121	173/5910	133/5048	1.00 (0.80-1.24)
Intracranial hemorrhage	8	70/1779	58/1773	1.15 (0.82-1.62)
Gastrointestinal hemorrhage	3	54/6142	28/6170	1.89 (1.21-2.96)
All	208	532/50037	454/48447	1.04 (0.92-1.17)
Acute coronary syndrome				
Trauma	5	58/17236	76/16834	0.73 (0.51-1.03)
Obstetrics and gynecology	8	2/10839	3/10769	0.66 (0.11-3.97)
Cardiac surgery	42	314/5101	354/4779	0.90 (0.78-1.04)
Orthopaedic surgery	35	7/1838	8/1543	0.85 (0.34-2.14)
Intracranial hemorrhage	4	13/1239	6/1233	2.02 (0.79-5.18)
Gastrointestinal hemorrhage	2	26/6070	28/6088	1.05 (0.36-3.08)
All	107	421/42763	476/41663	0.88 (0.78-1.00)
Stroke				
Trauma	6	119/17345	122/16952	0.91 (0.71-1.17)
Obstetrics and gynecology	8	8/10839	6/10769	1.33 (0.46-3.83)
Cardiac surgery	38	54/4498	50/4276	1.02 (0.70-1.50)
Orthopaedic surgery	32	16/1639	11/1427	1.31 (0.63-2.72)
Intracranial hemorrhage	8	229/2013	178/2005	1.40 (1.05-1.86)
Gastrointestinal hemorrhage	2	19/6070	20/6088	0.87 (0.30-2.54)
All	106	446/42924	389/42014	1.12 (0.98-1.27)

Figure 4: Forest plot of venous thromboembolism, acute coronary syndrome and stroke: subgroup analysis by underlying disease. TXA, tranexamic acid. RR, risk ratio. CI, confidence interval

Conclusion:

There is no indication that tranexamic acid raises the risk of thrombotic events or seizures, thus it can be taken safely in patients who are bleeding. High doses, on the other hand, should be avoided due to the possibility of a dose-dependent increase in the risk of seizures.

Reference:

Murao, S., *et al.* Effect of tranexamic acid on thrombotic events and seizures in bleeding patients: a systematic review and meta-analysis. *Crit Care* **25,** 380 (2021).