THE POISE-3 TRIAL

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25/5/2022

Tranexamic Acid in Patients Undergoing Noncardiac Surgery

- PeriOperative ISchemic Evaluation-3
- Devereaux PJ, Marrucci M, Painter D et al
- N Engl J Med 2022 Apr 2. Online

Trial design

- RCT 114 centres, 22 countries,
- Partial factorial design in those taking ≥1 antihypertensive medication
- 30 day follow-up
- Age ≥ 45 yrs
- Inpatient non-cardiac surgery at risk of peri-op bleeding and cardiovascular events
- Excluded: neuro/cardiac, hypertensive cerebral haemorrhage, thyrotoxicosis, phaeochromocytoma, planned use of TXA, CrCl<30ml/min, seizure history

Methods

- Patients undergoing non-cardiac surgery
- 2x2 factorial design:
- TXA 1g bolus at start and end

  or
- Placebo bolus at start and end

  +
- hypotension-avoidance

  or
- hypertension-avoidance strategy

Methods

- Primary efficacy outcome:

  Composite bleeding outcome at 30 days:

  life-threatening, major bleeding, bleeding into critical organ

- Primary safety outcome:

  Composite cardiovascular outcome at 30 days:

  MI/raised troponin, non-haemorrhagic stroke, peripheral arterial thrombosis, symptomatic proximal venous thrombo-embolism

Methods

- Is TXA non-inferior to placebo for composite cardiovascular outcome?
  - Upper boundary of one-sided 97.5% confidence interval for hazard ratio <1.125
  - One-sided P value <0.025

Results

- 9535 patients randomised
- Mean age 70yrs, 44% female
- 79% urgent/emergency surgery
- General 37%, ortho 22%, vascular 15%
- 96.3% received both doses
- 99.9% had 30 day follow-up

Results

Outcome	TXA	Placebo	Hazard ratio
BLEEDING			
Life-threatening bleed	1.6%	1.7%	0.99
Major bleeding	7.6%	10.4%	0.72
Bleeding into critical organ	0.3%	0.4%	0.57
CARDIOVASCULAR			
Myocardial injury	12.8%	12.6%	1.02
Non-haemorrhagic CVA	0.5%	0.3%	1.51
Peripheral arterial thrombosis	0.5%	0.5%	0.96
Symptomatic prox VTE	0.7%	0.6%	1.15
MI	1.4%	1.1%	1.27

Results

Composite bleeding outcome

	TXA	Placebo
Number	433/4757	561/4778
%	9.1	11.7
Hazard ratio (95% CI)	0.76 (0.67–0.87)	
Absolute difference, % points (95% CI)	−2.6 (−3.8—1.4)	
2 sided P value for superiority	<0.001	

Results

Composite cardiovascular outcome

	TXA	Placebo
Number	649/4581	639/4601
%	14.2	13.9
Hazard ratio (95% CI)	1.02 (0.92–1.14)	
Upper boundary of one-sided 97.5% CI	1.14 (needed to be <1.125)	
Absolute difference % points (95% CI)	0.3 (–1.1–1.7)	
One-sided P value for non-inferiority	0.04 (needed to be 0.025)	

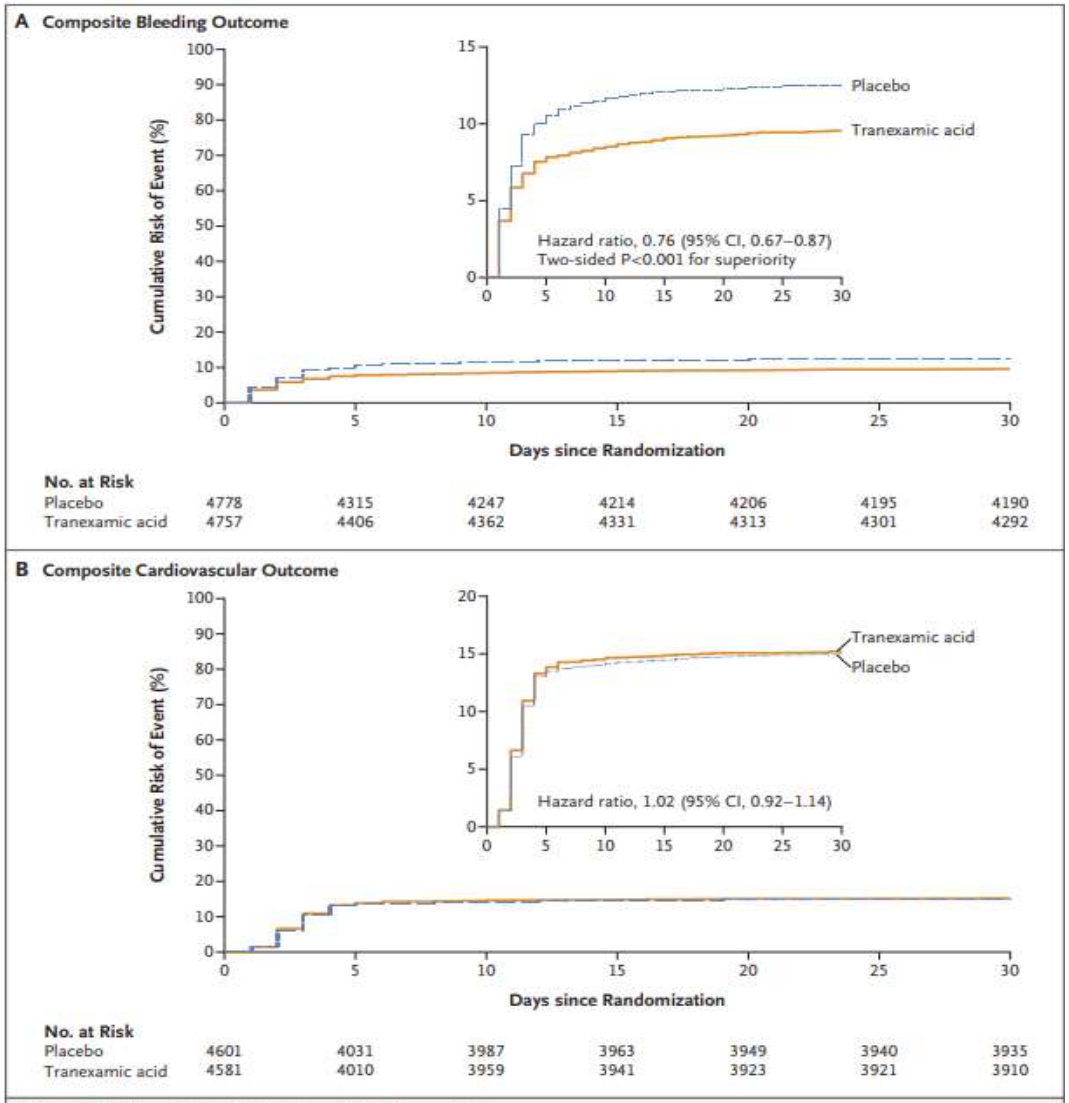

Figure 1. Kaplan–Meier Estimates of the Primary Outcomes.

The composite bleeding outcome (Panel A) was a composite of life-threatening bleeding, major bleeding, and bleeding into a critical organ at 30 days. The composite cardiovascular outcome (Panel B) was a composite of myocardial injury after noncardiac surgery, nonhemorrhagic stroke, peripheral arterial thrombosis, and symptomatic proximal venous thromboembolism at 30 days. The insets show the same data on an expanded y axis.

Conclusions

- Incidence of composite bleeding outcome significantly lower with TXA cf. placebo
- Although between-group difference in composite cardiovascular outcome small, non-inferiority of TXA was not established
- However 96% probability that we are inside the non-inferiority safety margin
- Trial of 10,000 stopped early due to financial deficit from slow recruitment (COVID)

Conclusions

- ‘Health care providers and patients will have to weigh a clear beneficial reduction in the incidence of composite bleeding outcome events against the low probability of a small increase in the incidence of composite cardiovascular outcome events’

Conclusions

- Short of 30m units of blood globally
- Surgery is 40% of all transfusions
- 300m adults have surgery each year worldwide
- Could prevent about 8m bleeding events resulting in transfusions annually globally
- Further trials in hepatic and cardiac surgery, topical TXA