Point-of-Care Testing for Tranexamic Acid Efficacy: ClotPro TPA-test in Cardiac Surgery

Summary of a Full-Length Article | British Journal of Anaesthesia 2024;132(6):1211-1218 | Yoshii R, Takahashi Y, Tanaka KA, et al.

Why this paper matters to Haemoview

This proof-of-concept study addresses a practical gap in cardiac surgery: tranexamic acid (TXA) is widely used during cardiopulmonary bypass (CPB), but TXA exposure varies between patients and laboratory TXA concentration testing is not clinically available. The authors evaluated whether the **ClotPro TPA-test** can provide a point-of-care functional readout of **TXA-induced inhibition of fibrinolysis**. The study combined an in-vitro evaluation using blood from **six healthy volunteers** with an observational clinical study in **20 cardiac surgery patients** receiving low-dose TXA at the end of CPB.

Study at a glance

Item	Detail
Article type	Peer-reviewed proof-of-concept study combining in-vitro TXA concentration testing and an observational clinical study in cardiac surgery patients
Authors	Yoshii R, Takahashi Y, Tanaka KA, Kawajiri H, Sawa T, Amaya F, Ogawa S - Kyoto Prefectural University of Medicine, University of Oklahoma Health Sciences Center and collaborating departments
Journal	British Journal of Anaesthesia 132(6):1211-1218 (2024); DOI: 10.1016/j.bja.2024.03.023
Clinical scope	Cardiac surgery requiring CPB; in-vitro tPA-triggered fibrinolysis testing; low-dose TXA administered sequentially at the end of CPB
Core finding	The TPA-test detected low TXA concentrations: TXA >=2 mg/L inhibited tPA-induced hyperfibrinolysis in vitro and TXA >=10 mg/L completely inhibited fibrinolysis. In patients, effect was detectable after 0.1 g TXA and complete with TXA >=0.5 g.
ClotPro link	Direct ClotPro link: the TPA-test adds high-concentration tPA to whole blood to assess tPA-inducible fibrinolysis and the functional in-vivo antifibrinolytic effect of TXA.

The clinical gap this paper closes

The article notes that low-dose TXA has been recommended for CPB to reduce complications, while higher TXA exposure is associated with dose-dependent postoperative seizures. Because TXA excretion varies between patients and direct TXA concentration testing is unavailable clinically, clinicians may lack a practical bedside method for assessing residual TXA effect. The TPA-test addresses this gap by evaluating **tPA-inducible fibrinolysis** rather than measuring TXA concentration directly.

Key message: The ClotPro TPA-test was sensitive to low concentrations of TXA and served as a practical monitoring tool for postoperative fibrinolytic activity in cardiac surgery patients, with particular relevance to severe renal impairment.

Key findings in detail

1 | The TPA-test detected low concentrations of TXA in vitro

In whole blood from six healthy volunteers, TXA prolonged lysis time (LT) and lysis onset time (LOT), and decreased maximum lysis (ML), in a concentration-dependent manner. The antifibrinolytic effect between **2 and 5 mg/L** varied between subjects, while **complete inhibition of fibrinolysis** was confirmed in all samples at **TXA >=10 mg/L**.

TXA signal in TPA-test	Observed result	Interpretive meaning
TXA >=2 mg/L	tPA-induced hyperfibrinolysis inhibited in a concentration-dependent manner	Low-concentration TXA effect was detectable
TXA 2-5 mg/L	Antifibrinolytic effect varied between subjects	The assay captured variable low-level response
TXA >=10 mg/L	Complete inhibition of fibrinolysis in all samples	The TPA-test returned a blocked-fibrinolysis pattern

2 | In cardiac surgery patients, TXA effect was detectable after 0.1 g and complete at >=0.5 g

Twenty patients undergoing CPB received sequential TXA doses of 0.1, 0.1, 0.3 and 0.5 g at 2-min intervals at the end of CPB, for a total dose of 1 g. Samples were tested before TXA, after cumulative doses of 0.1, 0.2, 0.5 and 1 g, and at 6, 12 and 18 h after surgery. Baseline TPA-test parameters before TXA were LT 136 (125-160) s, LOT 52 (47-61) s and ML 92 (90-93)%. Antifibrinolytic effects were detected after the 0.1 g bolus, and complete inhibition of fibrinolysis was observed in all patients with TXA >=0.5 g.

3 | Postoperative TXA effect attenuated over 18 h in most patients

No additional TXA was administered after CPB or in the ICU. The antifibrinolytic effect of 1 g TXA on TPA-test parameters was attenuated over time, with no significant difference between before-TXA parameters and 18 h postoperative parameters. Postoperative blood loss was 170 (130-270) mL at 6 h and 355 (249-528) mL at 18 h. No convulsive seizures were observed after surgery.

4 | Residual inhibition was linked to severe renal impairment

Fibrinolytic inhibition remained at 18 h in **four of 20 patients**, defined by LT 7200 s and ML <25%. All four patients with residual antifibrinolytic response had grade 4 or 5 renal dysfunction. Preoperative eGFR correlated significantly with TPA-test parameters, with stronger correlations at 12 h and 18 h than at 6 h; at 18 h, correlations were very strong for LT, LOT and ML (r=0.86-0.92; P<0.0001). The authors concluded that postoperative TXA excretion appeared severely reduced in patients with eGFR <30 mL/min/1.73 m2.

5 | Important limitations for clinical interpretation

- The 1 g TXA regimen was sufficient to block fibrinolysis on the TPA-test, but the article states that clinical outcomes such as bleeding, transfusion, seizure and thrombosis were not evaluated.

- The single bolus practice at the end of CPB was described as uncommon, so results may differ with standard regimens that use a bolus before CPB with or without additional doses.

- The number of patients with severe renal impairment was small, and additional studies with larger populations were warranted.

- The authors did not measure antifibrinolytic proteins or plasmin generation; the TPA-test may reflect comprehensive haemostatic function, not TXA concentration alone.

Relevance to ClotPro users

This article is directly relevant to ClotPro users because the study evaluated the TPA-test as a bedside functional assay for TXA-induced fibrinolytic inhibition. The practical message is not that the TPA-test replaces clinical judgement or TXA concentration testing, but that it may provide a point-of-care view of postoperative fibrinolytic activity when TXA exposure and renal clearance are uncertain.

Paper finding	Relevance to users
TPA-test measured TXA-induced inhibition of fibrinolysis	Provides a direct ClotPro workflow link: the assay challenges the sample with tPA and reports the functional antifibrinolytic effect through LT, LOT and ML.
Low TXA concentrations were detectable	The in-vitro data showed concentration-dependent response from 2-10 mg/L TXA, supporting discussion of assay sensitivity at low concentrations.
Clinical effect was detected after low-dose exposure	In the 20-patient CPB cohort, the TPA-test detected effect after 0.1 g TXA and showed complete inhibition after cumulative TXA >=0.5 g.
Postoperative effect changed over time	After 1 g TXA, the functional antifibrinolytic effect generally attenuated over 18 h, supporting use of serial postoperative fibrinolytic assessment in the study design.
Renal impairment prolonged effect	Residual inhibition at 18 h occurred in four patients, all with grade 4 or 5 renal dysfunction; the article highlights possible usefulness in severe renal impairment.
Clinical validation remains needed	The article concludes that additional clinical studies are needed to evaluate the usefulness of adjusting TXA dosing by testing its antifibrinolytic effect.

Suggested conversation points

- The article frames a practical problem: TXA is common in CPB, but patient excretion varies and direct laboratory TXA concentration testing is not clinically available.

- The ClotPro TPA-test provides a functional assessment of TXA-induced inhibition of fibrinolysis rather than a direct concentration measurement.

- In vitro, the TPA-test responded to 2-10 mg/L TXA and complete inhibition occurred at TXA >=10 mg/L.

- In cardiac surgery patients, the TPA-test detected effect after 0.1 g TXA and complete fibrinolysis inhibition after TXA >=0.5 g.

- Severe renal impairment is an important discussion point because residual antifibrinolytic effect persisted at 18 h in patients with grade 4 or 5 renal dysfunction.

Sources

Yoshii R, Takahashi Y, Tanaka KA, Kawajiri H, Sawa T, Amaya F, Ogawa S. Point-of-care testing for tranexamic acid efficacy: a proof-of-concept study in cardiac surgical patients. British Journal of Anaesthesia. 2024;132(6):1211-1218. DOI: 10.1016/j.bja.2024.03.023.

Disclaimer

PROOF-OF-CONCEPT STUDY

POINT-OF-CARE TESTING FOR TRANEXAMIC ACID EFFICACY IN CARDIAC SURGICAL PATIENTS

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The TPA-test is sensitive to low concentrations of TXA and serves as a practical monitoring tool for postoperative fibrinolytic activity in cardiac surgery patients.

BACKGROUND

Low-dose tranexamic acid (TXA) reduces bleeding in cardiac surgery, but the optimal dose and duration are unclear. A point-of-care test for TXA concentrations is not available.

STUDY AIM

To evaluate the performance of the TPA-test on the ClotPro® system in vitro and in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB).

METHODS

IN VITRO STUDY

- Whole blood from **6 healthy volunteers**
- tPA added to trigger fibrinolysis
- TXA added at 0, 1, 2, 5, 10, 20, 50, 100 mg L^{-1}
- Measured with TPA-test on **ClotPro® system**

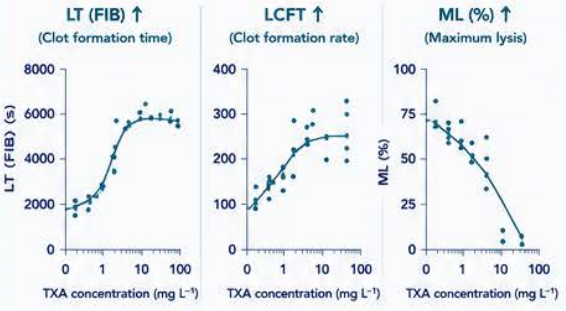
CLINICAL OBSERVATIONAL STUDY

- 20 patients undergoing cardiac surgery with CPB
- TXA administration:
  - 0.1 g bolus at the end of CPB (all patients)
  - Additional doses at surgeon's discretion (total 0.1–1.0 g)
- TPA-test at baseline (after CPB), 6 h, 12 h, and 18 h after surgery

RESULTS

1. IN VITRO: TXA INHIBITS tPA-INDUCED FIBRINOLYSIS

tPA-triggered fibrinolysis was inhibited by TXA in a concentration-dependent manner and completely inhibited at ≥10 mg L^{-1}.

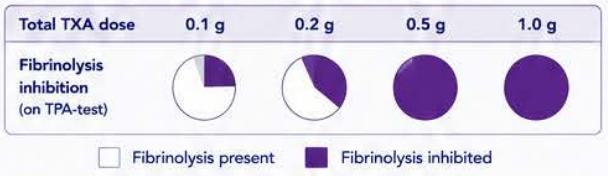


Complete inhibition of fibrinolysis was achieved at **TXA ≥10 mg L^{-1} *in vitro*.**

2. CLINICAL: TPA-TEST REFLECTS TXA DOSE AND TIME

Antifibrinolytic effect after TXA bolus

Effect was detectable after 0.1 g bolus at the end of CPB and complete inhibition achieved with ≥0.5 g.



Time course after surgery (1.0 g TXA)

Antifibrinolytic effect gradually attenuated over 18 h after surgery.

3. RENAL FUNCTION INFLUENCES TXA EFFECT AT 18 h

In patients with eGFR ≤30 ml min^{-1} 1.73 m^{-2} (n=4), antifibrinolytic effect persisted at 18 h.

eGFR had strong correlations with TPA-test parameters at 18 h:

LT (FIB)	LCFT	ML (%)
r = 0.92	r = 0.89	r = 0.86
P < 0.0001	P < 0.0001	P < 0.0001

CONCLUSION

The TPA-test is sensitive to low concentrations of TXA and serves as a practical monitoring tool for postoperative fibrinolytic activity in cardiac surgery patients. It may be particularly useful in patients with severe renal impairment.

CLINICAL IMPLICATIONS

- The TPA-test allows real-time assessment of TXA efficacy.
- Low-dose TXA (0.1–0.5 g) can achieve effective fibrinolysis inhibition.
- Renal function should be considered when determining TXA dosing and monitoring duration.

Yoshii R, Takahashi Y, Tanaka KA, Kawajiri H, Sawa T, Amaya F and Ogawa S. *Br J Anaesth* 2024;132:1211–1218. doi: 10.1016/j.bja.2024.03.023

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