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Moderate dosage of tranexamic acid during cardiac surgery with cardiopulmonary bypass and convulsive seizures: incidence and clinical outcome

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Editor's key points

- This is a retrospective data analysis of 4883 patients who underwent cardiac surgery.
- Comparison was made between the use and non-use of tranexamic acid (TA).
- In open-heart surgery, the use of TA was associated with increased mortality.
- The study highlights the need for prospective trials on the safety profile of using TA during cardiac surgery.

Background. Convulsive seizures (CS) occur in ~1% of the patients after cardiac surgery with cardiopulmonary bypass. Recent investigations indicate an up to seven-fold increase in CS in cardiac surgical patients receiving high doses (≥60 mg kg^{-1} body weight) of tranexamic acid (TA).

Methods. In a retrospective data analysis of 4883 cardiac surgical patients, we investigated the incidence of CS in patients receiving a moderate dose of TA (24 mg kg^{-1} body weight) compared with a reference group not receiving TA as a primary endpoint. Secondary endpoints were intensive care unit stay and in-hospital mortality. We performed propensity score (PS)-adjusted logistic regression analysis to test the association between TA use/non-use and clinical outcomes.

Results. Compared with the reference group, the PS-adjusted odds ratio (OR) for CS in the TA group was 1.703 [95% confidence interval (CI): 1.01–2.87; P=0.045; incidence 2.5% *vs* 1.2%]. Log-ICU-stay was significantly longer (P=0.004) and PS-adjusted relative in-hospital mortality risk was significantly higher for the TA group compared with the reference group (OR=1.89; 95% CI: 1.21–2.96; P=0.005). Both the TA-associated CS incidence and the in-hospital mortality risk were only significant in patients undergoing open-heart surgery (OR=2.034, 95% CI: 1.07–3.87; P=0.034 and OR=2.20, 95% CI: 1.32–3.69; P=0.003, respectively) but not in patients undergoing coronary artery bypass grafting (OR=1.21, 95% CI: 0.49–3.03; P=0.678 and OR=1.13, 95% CI: 0.42–3.02; P=0.809, respectively).

Conclusions. In open-heart surgery, even moderate TA doses are associated with a doubled rate of CS and in-hospital mortality. Prospective trials are needed to further evaluate the safety profile of TA in cardiac surgery.

Keywords: blood, coagulation; brain, convulsions; cardiopulmonary bypass; neurological outcome

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After aprotinin was removed from the market, tranexamic acid (TA) has become the mainstay pharmacological blood conservation of antifibrinolytic therapy in cardiac surgery. Although such use of TA has been under investigation for more than 20 yr, dosing regimens vary greatly and no standard regimen has been established yet.[1 2]

The administration of TA in cardiac surgery has not been associated with severe adverse events. However, current studies and case series reports mention an increased incidence of seizures after administration of high TA doses (60–260 mg kg^{-1} body weight).[3–7] In addition, one recent small retrospective analysis associated high TA doses (100 mg kg^{-1} body weight) with an increased mortality risk in patients undergoing open-heart procedures when compared with aprotinin.[3]

At our institution, we use a protocol with a more moderate (~25 mg kg^{-1} body weight) dose, which approximates the suggested dose for achieving an effective inhibition of fibrinolysis during cardiac surgery.[8–10]

We herein report our single-centre experience with this moderate dose of TA on convulsive seizures (CS) and other clinical outcome parameters in a large cohort of cardiac surgery patients.

Methods

Patients and study design

This study was a retrospective, single-centre, cohort study. The institutional database was analysed over a 2 yr period

between January 2008 and December 2009. Out of 6201 consecutive patients who underwent cardiopulmonary bypass (CPB) surgery at the Heart and Diabetes Centre North Rhine-Westphalia, Germany, 4883 patients were finally included in the data analysis (Fig. 1). The database consisted of perioperative data which were prospectively collected. All cardiac surgical patients were asked to give their general written permission before the operation in the scientific analysis and possible publication of anonymized data. The local Ethics Committee had approved this approach. The study was performed according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) Statement for cohort studies (www.strobe-statement.org).

Data collection

All clinical data were collected using the digital patient data management system PDMS (COPRA, Sasbachwalden, Germany). In total, 21 parameters were retrieved for each patient. Among them, 19 patients and surgery characteristics [age, sex, weight, left ventricular ejection fraction, concomitant diagnoses such as stroke, diabetes mellitus, cardiovascular disease, pulmonary disease, peripheral arterial occlusive disease, and hypertension, estimated glomerular filtration rate (eGFR), previous thoracic surgery, aspirin use, open-heart surgery, aortic cross clamp time, duration of CPB, transfusion requirement, and catecholamine requirement], two event categories (CS and in-hospital mortality), and two other outcome parameters [duration of mechanical ventilatory support and intensive care unit (ICU) stay] were assessed.

Primary endpoint

The primary endpoint was the rate of CS observed on the ICU. A CS was considered to have occurred in the case of sudden clonic movement of the patient. The suspicion of the occurrence of a CS was immediately reported from the specially trained nursing staff to the responsible physician who confirmed the diagnosis. Only in the case of re-occurrence or the suspicion of persisting neurological damage, a specialized neurologist was involved and further diagnostics (CT scan and electroencephalogram) were performed.

Secondary endpoints

Secondary endpoints were the duration of mechanical ventilatory support, duration of ICU stay, and in-hospital mortality.

Biochemical analyses

Preoperative creatinine was measured using the Architect autoanalyzer (Abbott, Wiesbaden, Germany). Then, GFR was estimated using the creatinine-based modification of diet in renal disease formula.

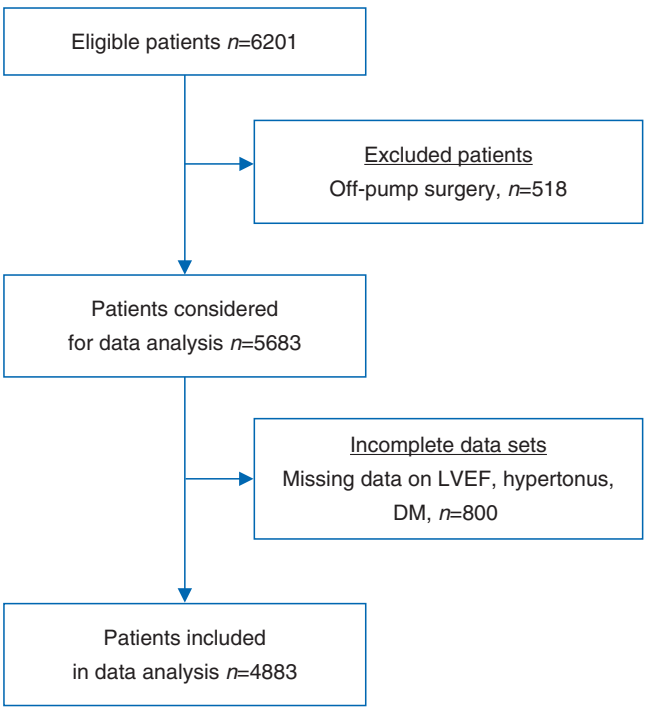

Fig 1 Study flow chart for inclusion of patients into the final analysis according to the STROBE statement. Off-pump, without cardiopulmonary bypass; LVEF, left ventricular ejection fraction; DM, diabetes mellitus.