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Point-of-care thromboelastography/ thromboelastometry-based coagulation management in cardiac surgery: a meta-analysis of 8332 patients

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ABSTRACT

Objectives: Severe bleeding related to cardiac surgery is associated with increased morbidity and mortality. Thromboelastography (TEG) and thromboelastometry (ROTEM) are point-of-care tests (POCT). Bedside ROTEM/TEG can rapidly detect changes in blood coagulation and therefore provide a goal-directed, individualized coagulation therapy. In this meta-analysis, we aimed to determine the current evidence for or against POCT-guided algorithm in patients with severe bleeding after cardiac surgery.

Methods: We performed a meta-analysis of randomized controlled trials and observational trials retrieved from a literature search in PubMed, EMBASE, and Cochrane Library. Only trials comparing transfusion strategy guided by TEG/ROTEM with a standard of care control group undergoing cardiac surgery were included. In addition, at least one clinical outcome had to be mentioned: mortality, surgical re-exploration rate, sternal wound infection, and acute kidney injury (AKI). Also, surrogate parameters such as transfusion requirements and amount of blood loss were analyzed. The pooled treatment effects (odds ratio [OR] and 95% confidence intervals [CI]) were assessed using a fixed or random-effects model.

Results: The literature search retrieved a total of 17 trials (nine randomized controlled trial and eight observational trials) involving 8332 cardiac surgery patients. POCT-guided transfusion management significantly decreased the odds for patients to receive allogeneic blood products (OR 0.63, 95% CI 0.56-0.71; $P < 0.00001$) and the re-exploration rate due to postoperative bleeding (OR 0.56, 95% CI 0.45-0.71; $P < 0.00001$). Furthermore, the incidence of postoperative AKI (OR 0.77, 95% CI 0.61-0.98; $P = 0.0278$) and thromboembolic events (OR 0.44, 95% CI 0.28-0.70; $P = 0.0006$) was significantly decreased in the TEG/ROTEM group. No statistical differences were found with regard to inhospital mortality, cerebrovascular accident, or length of intensive care unit and hospital stay.

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Conclusions: TEG/ROTEM-based coagulation management decreases the risk of allogeneic blood product exposure after cardiac surgery. Furthermore, it results in significantly lower re-exploration rate, decreased incidence of postoperative AKI, and thromboembolic events in cardiac surgery patients. Results of this meta-analysis indicate that POCT-guided transfusion therapy is superior to the current standard of care.

Introduction

Excessive bleeding after cardiac surgery is associated with transfusion of blood products and enhances the risk of re-exploration resulting in increased morbidity and mortality.[1-3] The main causes for increased bleeding after cardiac surgery include previous dual-antiplatelet therapy, oral anticoagulants, hypofibrinogenemia, residual heparin, prolonged cardiopulmonary bypass, and intraoperative hypothermia.[4,5] The transfusion of packed red blood cells (PRBC), fresh frozen plasma (FFP), and platelets leads to serious adverse events, such as transfusion-related acute lung injury, transfusion-associated circulatory overload, transfusion-related immunomodulation, and nosocomial infections.[1,6-9] Therefore, the indication for transfusion should be well considered.

The standard laboratory tests (SLTs), which include activated partial thromboplastin time, prothrombin time, international normalized ratio, platelet count, and plasma–fibrinogen, are limited due to a lack of real-time monitoring.[10] The turnaround time of SLTs is at least 45-60 min or even longer.[11,12]

The thromboelastography (TEG, Haemonetics, Braintree, MA) and thromboelastometry (ROTEM, TEM International GmbH, Munich, Germany) are so-called point-of-care tests (POCT).[13] Bedside TEG/ROTEM can rapidly detect changes in blood coagulation and, therefore, can provide a goal-directed, individualized coagulation therapy.[14-17] First described by Hartert in 1948, the TEG determines the viscoelastic properties of the developing blood clot *in vitro*.[18,19] In 1995-1997 enhanced in Munich, the viscoelastic test "ROTEM" is less sensitive to vibrations. A preference on one of the viscoelastic tests primarily depends on geography, with TEG and ROTEM favored in North America and Europe, respectively.[20]

The TEG/ROTEM tests are able to detect and quantify the underlying cause of the coagulopathy such as thrombocytopenia, factor deficiency, heparin effect, hypofibrinogenemia, and hyperfibrinolysis.[10,19,21] The TEG/ROTEM-guided transfusion algorithm may potentially save time, reduce complications related to mass transfusion, and provide a balanced transfusion with specific hemostatic drugs and coagulation factor concentrates.[10,16,17] However, the recently published trials and meta-analyses[21] failed to detect any clinical benefits for TEG/ROTEM-guided transfusion regimes.

Therefore, we performed this meta-analysis to determine the current evidence for or against a POCT-guided algorithm with TEG/ROTEM in patients with severe bleeding after cardiac surgery focusing on the clinical relevant end points: mortality, cerebrovascular accident (CVA), acute kidney injury (AKI), thromboembolic events, and re-exploration.

Methods

Selection criteria and search strategy

The current systematic review of the literature was performed in accordance to the guidelines for quality of reporting of meta-analysis[22] and as described elsewhere.[23,24] Randomized controlled trials (RCTs) and observational studies comparing transfusion strategy guided by TEG/ROTEM to SLTs in patients undergoing cardiac surgery were included. In addition, at least one of the following primary outcomes had to be mentioned: mortality, re-exploration rate, AKI, CVA, or thromboembolic events. Moreover, we analyzed surrogate parameters such as transfusion requirements and amount of blood loss. The primary authors' definitions of outcome variables were accepted.

Two authors (A.-C.D. and W.C.) performed an electronic literature search in Medline, EMBASE, and The Cochrane Library using predefined keywords, independently (Supplemental data S1—Search strategy). All potentially relevant abstracts were reviewed after initial abstract identification with subsequent full-text evaluation. References of relevant reports and reviews were screened to identify other eligible studies.

All studies published between 1966 and December 31, 2014 in full-text or abstract forms were eligible for inclusion without applying any language restrictions. Studies not including a control group, animal studies, *in vitro* studies, or trials that exclusively reported other clinical outcomes were not included. Case reports, editorials, comments, and guidelines were also excluded after initial abstract review (Supplemental data S2—References of excluded studies).

Data extraction and quality assessment

All relevant data including authorship, year and type of publication, study design, patient population (sample size, age, gender), method of POCT, perioperative variables, and desired clinical end points were extracted. Independently, two investigators assessed methodologic quality of included studies by using the Downs and Black score (maximum 29 points; good quality [>20 points]; poor quality [<20 points]) for all studies and the Jaded score (maximum 5 points; excellent quality [=5 points]; good quality [<5 points], poor quality [<3 points]) for RCTs.[25,26] Disagreements were resolved by consensus.

Statistical analyses

Statistical analyses were performed using Review Manager (version 5.3; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) and StatsDirect (version 2.7.8; StatsDirect Ltd, Cheshire, UK). I^2 statistics were calculated to