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Review Article

REVIEW ARTICLE

Routine use of viscoelastic blood tests for diagnosis and treatment of coagulopathic bleeding in cardiac surgery: updated systematic review and meta-analysis

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Abstract

Viscoelastic point-of-care tests are commonly used to provide prompt diagnosis of coagulopathy and allow targeted treatments in bleeding patients. We updated existing meta-analyses that have evaluated the clinical effectiveness of viscoelastic point-of-care tests *vs* the current standard of care for the management of cardiac surgery patients at risk of coagulopathic bleeding. Randomized controlled trials comparing viscoelastic point-of-care diagnostic testing with standard care in cardiac surgery patients were sought. All-cause mortality, blood loss, reoperation, blood transfusion, major morbidity, and intensive care unit and hospital length of stay were analysed using random-effects modelling. Fifteen trials that randomized a total of 8737 participants were included for the analysis. None of the trials was classified as low risk of bias. The use of thromboelastography- (TEG®) or thromboelastometry (ROTEM®)-guided algorithms did not reduce mortality [risk ratio (RR) 0.55, 95% confidence interval (CI) 0.28–1.10] without heterogeneity (I^2=1%), reoperation for bleeding, stroke, ventilation time, or hospital length of stay compared with standard care. Use of TEG® or ROTEM® resulted in reductions in the frequency of red blood cell (Risk Ratio 0.88, 95% Confidence Interval 0.79-0.97; I^2=43%) and platelet transfusion (Risk Ratio 0.78, 95% Confidence Interval 0.66-0.93; I^2=0%). Group Reading Assessment and Diagnostic Evaluation (GRADE) assessment demonstrated that the quality of the evidence was low or very low for all estimated outcomes. Routine use of viscoelastic point-of-care tests did not improve important clinical outcomes beyond transfusion in adults undergoing cardiac surgery.

Key words: cardiac surgical procedures; haemorrhage; review, systematic

Coagulopathic bleeding is a common and severe complication of cardiac surgery. Up to 5% of all cardiac surgery patients require emergency re-exploration for bleeding in the immediate postoperative period.[1] This is associated with a four-fold increase in mortality and resource use.[2–4] Viscoelastic point-of-care whole blood tests provide rapid quantitative assessments of global clotting and are commonly used to provide prompt diagnosis of coagulopathy and allow targeted treatment in bleeding patients. Existing National Institute for Health and Care Excellence (NICE) guidance recommends their routine use

Editor's key points

- Viscoelastic testing of whole blood coagulation is widely used to diagnose coagulopathic bleeding and guide treatment in cardiac surgery patients.
- In a systematic review and meta-analysis of randomized controlled trials, use of viscoelastic testing reduced red blood cell and platelet transfusion, but had no effect on mortality or major morbidity, except acute kidney injury.
- Viscoelastic testing is not effective in reducing mortality in cardiac surgery, and further large trials are unlikely to show such a benefit.

in the management of bleeding cardiac surgery patients.[5] A recent Cochrane review concluded that the existing trial evidence was insufficient to demonstrate that use of Viscoelastic testing improved clinical outcomes.[6] They recommended that a pragmatic multicentre randomized controlled trial (RCT) at low risk of bias be performed to address this knowledge gap. Karkouti and colleagues[7] have recently published such a trial, enrolling 7402 patients in 12 Canadian hospitals. The aim of the present study was to update existing meta-analyses that have evaluated viscoelastic tests to include this new evidence, and assess whether this will allow clearer conclusions with respect to the clinical benefits of these devices in cardiac surgery.

Methods

Protocol and registration

Search methods, data extraction, assessment, and presentation were performed as recommended by the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1).[8] The analysis was specified in advance and documented on PROSPERO International prospective register of systematic reviews (CRD:42016033831) on January 31, 2016; http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016033831 (accessed on January 1, 2017).

Eligibility criteria

Randomized controlled trials irrespective of blinding, language, publication status, date of publication, and sample size were considered eligible for this study. Participants of any age undergoing cardiac surgery for acquired or congenital disease or aortovascular disease with or without cardiopulmonary bypass were considered. No age restriction was applied. There were no exclusion criteria.

Type of intervention

We assessed trials evaluating the risks and benefits of the following viscoelastic point-of-care testing devices for coagulopathy: ROTEM (ROTEM® Delta; TEM International GmbH, Munich, Germany; www.rotem.de (accessed on January 18, 2017)), thromboelastography (TEG; TEG® 5000 analyser; Haemonetics Corporation, Niles, IL, USA; www.haemonetics.com (accessed on January 15, 2017)), or Sonoclot® Coagulation and Platelet Function Analyzer (Sienco Inc., CO, USA), alone or combined with platelet function testing.

Comparator

The comparator is represented by a combination of clinical judgement and standard laboratory tests, including prothrombin time (PT), activated partial thromboplastin time (aPTT), activated clotting time, and plasma fibrinogen concentrations. We did not distinguish between these comparators for the purpose of this review.

Outcome measures

The primary outcome was 30 day or hospital all-cause mortality. The secondary outcomes were adverse events, including the following: reoperation for bleeding; red blood cell (RBC), platelet, fresh frozen plasma, fibrinogen, and prothrombin complex concentrate transfusion; acute kidney injury; cerebrovascular accident (stroke); myocardial infarction; ventilation time; and intensive care unit (ICU) and hospital length of stay (LoS).

Information sources

Potentially eligible trials were identified by searching the Cochrane Central Register of Controlled Trials (CENTRAL; Internet), Clinical Trials.gov, MEDLINE (PubMed 1946 to present), EMBASE (Ovid 1975 to present), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus (1979 to present), using a combination of subject headings and text words to identify relevant trials (see Supplementary material for detailed PubMed search criteria). The last search was run on December 3, 2016. In addition to searching databases, we searched in trials registries and we checked reference lists.

Study selection and data items

Two reviewers (G.J.M., G.F.S.) identified trials for inclusion independently of each other. Excluded studies and reasons for exclusion were recorded. Two authors independently screened search output to identify records of potentially eligible trials examining outcomes, the full texts of which were retrieved and assessed for inclusion. A standardized form was used to extract data from included studies for assessment of study quality and evidence synthesis. Extracted information included the following: year and language of publication; country of participant recruitment; year of conduct of the trial; study setting (university teaching hospital, non-university teaching hospital); study population, with inclusion and exclusion criteria; sample size; participant characteristics; baseline characteristics; type of surgery; outcomes and times of measurement; and information for assessment of the risk of bias.

Data extraction forms were completed by one author and checked by a second author. Likewise, quality assessment was done by one author and checked by a second.

Risk of bias in individual studies

The methodological quality of randomized trials was assessed using the Cochrane Collaboration's tools for assessing risk of bias in parallel group[9] and cluster[10] randomized trials. The items assessed for parallel group trials were as follows: (i) sequence generation; (ii) allocation concealment; (iii) blinding of outcome assessor; (iv) incomplete outcome data; (v) selective outcome reporting; and (vi) other sources of bias, including funder bias. Risk of bias was graded as unclear, high, or low. We graded sealed opaque envelopes as unclear evidence of allocation concealment. We also considered the absence of a prespecified protocol or trial registration of trial design as unclear evidence of reporting bias. Risk of bias in cluster-randomized trials was assessed as follows: (i) recruitment bias;