

REVIEW

## Presenting Baseline Coagulation of Infra Renal Ruptured Abdominal Aortic Aneurysm: A Systematic Review and Pooled Analysis

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### WHAT THIS PAPER ADDS

This first systematic review and pooled analysis on the presenting baseline coagulation of ruptured abdominal aortic aneurysm (rAAA) demonstrates that the majority of rAAAs do not present with coagulopathy and significant coagulopathy is present in a limited proportion of individuals.

**Background:** The incidence of coagulopathy in patients presenting with rAAA is not clear. The lack of high-quality evidence has led to various speculations, reliance on anecdotal experience, and suggestions about their appropriate haemostatic resuscitation. The aim of this systematic review is to establish the baseline coagulation status of infra renal ruptured abdominal aortic aneurysms (rAAA) against defined standards and definitions.

**Methods:** An electronic search of literature in Medline, CINAHL, Scopus Embase, and Cochrane library was performed in accordance with the PRISMA guidelines. Quality assessment of articles was performed using the Oxford critical appraisal skills programme (CASP) and their recommendation for practice was examined through National Institute for Health and Care Excellence (NICE). Information on platelet count, international normalisation ratio (INR), activated partial prothrombin time (aPTT), prothrombin time (PT) fibrinogen and D-dimer was extracted, and pooled analysis was performed in accordance with the definition of coagulopathy and its subtypes. Pooled prevalence of coagulopathies and 95% CI were estimated with a variance weighted random effects model.

**Results:** Seven studies, comprising 461 patients were included in this systematic review. Overall weighted prevalence of coagulopathy was 12.3% (95% CI 10.7–13.9), 11.7% for INR (95% CI 1–31.6), 10.1% for platelet count (95% CI 1–26.8), and 11.1% for aPTT (95% CI 0.78–31). Fibrinogen serum concentration level was normal in 97%, and 46.2% ( $n = 55$ ) of patients had elevated D-dimer. Only 6% of the entire population demonstrated significant coagulopathy. DIC was noted in 2.4% of the population.

**Conclusion:** This first systematic review of literature on baseline coagulation of rAAAs suggests that the majority of these patients do not present with coagulopathy and only a minor proportion of patients present with significant coagulopathy.

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### INTRODUCTION

In the last decade, there has been a significant change in the resuscitation protocol of patients presenting with major haemorrhage to the emergency services. The traditional first line fluid strategy with crystalloids and colloids solution has been replaced by blood and blood component transfusions.<sup>1</sup> The coagulopathy associated with trauma and haemorrhage is now believed to be the consequence of anticoagulant protein C pathway activation and not their

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consumption as highlighted in an earlier report.<sup>2</sup> Alteration in the coagulation cascade has been attributed to the presence and duration of tissue hypo perfusion following haemorrhage, worsened by hypothermia and acidaemia.<sup>3</sup> However, these studies are not free of methodological limitations (e.g. survival bias, heterogeneity) and their application in the resuscitation of all types of haemorrhage including those with ruptured abdominal aortic aneurysm, is not currently supported by the literature.<sup>4</sup>

Furthermore, individuals with ruptured abdominal aortic aneurysm (rAAA) have a number of demographical differences. Patients are much older, suffer with more comorbidities and are exposed to a different mechanism and type of volume depletion. In addition, aneurysmal degeneration of the aorta is a time-dependent process (chronic) and indulges the coagulation cascade at various molecular and endothelial levels, which is variant to the sudden impact of trauma and its implications.<sup>5</sup>

The lack of high-quality evidence regarding the coagulation status of patients with rAAAs has led to speculations, reliance on anecdotal experience, and suggestions about their appropriate haemostatic resuscitation. To optimise patient care, diminish disparities, and objectify the current protocols, the first systematic review of the literature was performed to establish the baseline coagulation status of infra renal ruptured abdominal aortic aneurysms. This review did not settle for the term “coagulopathy” alone, rather investigations were made of the subtypes in detail (mild versus significant) against the defined standards and definitions provided by the literature.

## MATERIAL AND METHODS

### Search strategy

A systematic search of the literature from 1966 to July 2015 was conducted in Medline, CINAHL, Scopus Embase, and Cochrane library. The following keywords and/or medical subject headings (MeSH) were used: “ruptured abdominal aortic aneurysm” and/or “ruptured infra renal abdominal aortic aneurysm” and/or “coagulation” and/or “coagulopathy.” The search was performed in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>6</sup> Bibliographies of the retrieved articles were also manually checked for any additional studies not identified in the primary search. All abstracts were retrieved and reviewed by two separate investigators (AK and AA). Studies that appeared to fulfil the eligibility criteria but had insufficient information in the abstracts were also retrieved and examined in full. The extraction of the data was also performed by two separate investigators (AK and AA).

### Exclusion criteria

The following articles were excluded: non-human and non-adult studies, abstracts and conference proceedings, case reports, narrative reviews, commentary and opinions. Other studies that did not report the outcomes of coagulation/coagulopathy or investigated coagulopathy post rAAA repair

were also excluded. Articles that were not in English language were excluded.

### Quality assessment and analysis

To achieve an informed conclusion and an evidence-based approach, the included articles were assessed for their validity, bias, applicability, and inference using a critical appraisal tool provided by the Oxford Critical Appraisal Skills Programme (CASP).<sup>7</sup> Lack of consistency and uniformity of the provided data, as well as heterogeneity in the population across the studies, meant that a meaningful statistical analysis (meta-analysis) was not deemed plausible. However, the data were presented in a tabulated format and a pooled analysis was performed. The pooled analysis was conducted by calculation of the mean value in addition to pooled prevalence of coagulopathies, and 95% CI were estimated with a variance weighted random effects model. This was done using MedCalc statistical Software version 16.1. Data extraction included the type of the studies, number of recruited individuals, coagulation factors, outcome, and conclusion. The strength of evidence and their recommendation for future practice was also assessed through the National Institute for Health and Care Excellence (NICE) checklist.<sup>8</sup> In addition, recommendations for future research were formulated based on the current systematic review outcome.

### Standards and definitions

To avoid heterogeneity and create a uniform approach, all terms were defined according to their respective and acceptable definitions.<sup>4,9</sup>

1. Coagulopathy was defined as a condition in which clot formation was impaired. Therefore, patients with aPTT >40 seconds and/or international normalised ratio of >1.2 and/or platelet count of <150 × 10/L<sup>9</sup> were deemed coagulopathic in the broader terminology. In addition, the following definitions were also applied:
  - a. Mild coagulopathy was defined as APTT >40 seconds and/or international normalised ratio between 1.2 and 1.5 and/or platelet count of 100 × 10/L<sup>9</sup>–150 × 10/L<sup>9</sup>.
  - b. Significant coagulopathy was defined as APTT >40 seconds and/or international normalised ratio of >1.5 and/or platelet count of <100 × 10/L<sup>9</sup>.
2. Disseminated intravascular coagulation (DIC) was defined as an acquired syndrome defined by the intravascular activation of the coagulation cascade with loss of localisation arising from different causes.
3. No robust definition of contained versus free rupture of abdominal aortic aneurysm could be identified in the included manuscript and/or the literature.

## RESULTS

The electronic search returned a total of 71 studies (Fig. 1).<sup>6</sup> A further manual search revealed two more articles. Of the

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