# The iTACTIC (implementing Treatment Algorithms for the Correction of Trauma Induced Coagulopathy) study primary publication

## Introduction

Bleeding trauma patients are known to quickly develop a blood abnormality referred to as Trauma induced coagulopathy (TIC). This is a disruption of blood clotting specific to trauma patients. Personalised blood transfusion for bleeding trauma patients may help to correct TIC.

Currently, when a bleeding trauma patient is admitted to hospital, the trauma clinicians follow a set of guidelines, referred to as the major haemorrhage protocol (MHP), which allow them to quickly access blood products to give the patient. These come in prepared packs, and contain blood products that have been separated out from whole blood.

Whole blood can be separated into several different blood products:

Red blood cells – carry oxygen around the body and provide the patient volume to fill-up empty or under filled blood vessels.

Fresh frozen plasma (FFP) - provides some proteins that help with blood clotting and provide cell protection, whilst also delivering volume.

Cryoprecipitate – is rich in clotting proteins, especially fibrinogen which is key for making a strong blood clot. Our previous work has shown that fibrinogen levels rapidly decrease in bleeding trauma patients, and that replacing it early may help reduce mortality.

Platelets – are tiny cell fragments which, when activated, change shape and stick together within a scaffold of fibrinogen to form a blood clot.

By performing blood tests on a patient, doctors can tailor the blood products a patient receives to what their body is lacking. They do this by using tests referred to as conventional coagulation tests (CCT). These CCTs look at the level of fibrinogen and number of platelets in the patients’ circulation, as well as a laboratory test which shows how quickly their blood can make a blood clot.

Another way of investigating blood clotting is by using a rotational thromboelastometry (ROTEM) or thromboelastography (TEG). These are both types of viscoelastic haemostatic assays (VHA). A blood sample taken from a patient can be analysed within minutes to see the time it takes the blood to clot, and how much fibrinogen and platelets are in the blood clot.

Both CCT and VHA test results can then be checked against expected ranges and if below normal can trigger a doctor to order the specific blood product to correct this deficit (the treatment algorithms).

## Aim

iTACTIC was designed to investigate whether trauma patients, who were displaying a bleeding abnormality (known as being coagulopathic), had better outcomes if they received personalised blood transfusions guided by CCT or VHA treatment algorithms.

## Hypothesis

The team hypothesized that personalising blood transfusion using VHA technology would improve survival and reduce the need for ten or more units of red blood cells to be transfused in the first 24 h after injury (referred to as a massive transfusion).

## Patients included

Adult trauma patients were enrolled if the doctors thought they were bleeding, had given the patient a transfusion of red blood cells and were going to treat the patient according to the MHP. The patient also had to be included within three hours of their injury occurring, and one hour of admission to the emergency department.

## Consent

Consent for inclusion in to the trial was initially provided by a nominated consultee, usually an independent doctor in charge of the patients’ care.

## Procedures

All patients received the standard MHP, plus TXA – a drug that stops blood clot breakdown and limited use of saline fluid.

In both groups, blood samples were taken for analysis after enrolment and then again after every four units of RBCs until the patient stopped bleeding (haemostasis).

## Outcomes

The primary outcome of this study was the proportion of subjects who were alive and free of massive transfusion 24 h after their injury. Secondary endpoints included:

* survival at 6 h, 24 h, 28 days, and 90 days after injury
* total blood components usage
* ventilator use
* length of time spent on the intensive care unit (ICU)
* total length of time spent in hospital
* the proportion of patients who
  + had a blood clot after they stopped bleeding
  + developed multiple organ dysfunction
  + had a serious adverse event

## Results

396 patients were included in the analysis. Two thirds of these patients had a blunt injury and were classified as being severely injured. The average injury to admission time was 69 mins, and patients received an average of two red blood cell transfusions before being enrolled.

Patients were equally allocated to either the VHA or CCT treatment arms. 67% of VHA patients received an intervention whereas only 36% of CCT received a trial guided blood product. Blood products were given ~20 mins earlier in the VHA arm compared to the CCT arm, and 64% of the participants in the VHA arm received a trial blood transfusion within 3hrs of injury, vs just 45% in CCT arm of the trial.

From the baseline blood sample to the patient stopping bleeding, patients in both arms of the trial received on average of three red blood cell transfusions and four FFP transfusions. Patients in the VHA arm were allocated to receive more fibrinogen products, equivalent to four grams of fibrinogen in the VHA or 0g in the CCT arm.

At 24 h after injury, there was no difference in the proportion of patients who were alive and free of massive transfusion regardless of whether patients received VHA or CCT supplemented treatment.

There were no statistically significant differences in any of other secondary outcomes between the two study arms.

However, when researchers looked at a subgroup of 74 patients who had a severe traumatic brain injury (TBI), 64% of patients in the VHA arm were alive and free of massive transfusion 24 hours after injury compared to 46% in the CCT arm.

## Discussion

This trial compared the ability of CCT versus VHA to personalise blood transfusion for bleeding trauma patients. The team saw no difference overall in primary or secondary outcomes between CCT and VHA guided blood transfusion.

While this study aimed to explore the effect of VHA directed assessment and treatment of coagulopathy in trauma patients, the prevalence of coagulopathy in the patients recruited was lower than expected. Nearly three quarters of the patients were not coagulopathic at baseline and very few subsequently developed coagulopathy.

The reduction in 28-day mortality in coagulopathic patients with a severe brain injury who received seen VHA guided blood transfusion was unexpected and may have occurred due to chance. However, other studies have also shown that managing coagulopathy in patients with a brain injury may improve survival. Further investigation of this phenomena will form the basis of future work within the group.

## Take‑home message

When the MHP is used to deliver blood transfusion in bleeding trauma patients using VHA to personalise blood transfusions did not improve clinical outcomes when compared to CCT interventions.