

# The Value of Institutional Protocols and Focused Cardiac Ultrasound During a Case of Ultramassive Transfusion

## Abstract

A 53-year-old female was admitted to the emergency department with an exsanguinating bleed from the rectum which was of unclear origin. In what could be considered an ultramassive transfusion, 60 units packed red blood cells, 23 units fresh frozen plasma, 20 units platelets, 6 units cryoprecipitate, 30 L of crystalloids, 2 L of colloids, and 4 g of tranexamic acid were transfused over the course of 7 h. An arterio-enteric fistula was diagnosed and treated by an interventional radiologist. The patient recovered rapidly thereafter without any major neurologic, pulmonary, cardiac, or hematologic complications.

**Keywords:** Blood components, focused cardiac ultrasound, massive transfusion

## Introduction

Massive transfusion (MT) is most commonly defined as a transfusion of 10 or more units of packed red blood cells (PRBCs) in <24 h.<sup>[1,2]</sup> Several protocols based on varying institutional practices are available. The use of MT protocols (MTPs) is becoming common,<sup>[3]</sup> however, transfusion of more than 30 units in 24 h, which could be referred to as ultra-MT, is rare.<sup>[4,5]</sup> MT is often complicated with hypothermia, coagulopathy, sepsis, immunosuppression, as well as respiratory, cardiovascular, neurologic, and thrombotic complications.<sup>[1]</sup> The 30-day mortality associated with transfusion of PRBC increases from 8.9% with 1–4 units to 21.5% when more than 5 units were given and as high as 57% when the number of units transfused exceeded 50 in 24 h.<sup>[6]</sup>

Blood component based transfusion therapy was introduced in the 1970s to decrease the risk of transmitting infections through whole blood transfusions as well as to maximize the utility of each donated unit of blood. In elective cases, wherein massive blood loss may be expected, coagulation tests are typically used to guide blood component transfusions. However, this strategy may not be practical when managing massive blood loss.<sup>[7]</sup> We present a case in which a massive administration

of blood components and fluids to treat a rapidly exsanguinating patient over a very short-time period resulted in excellent clinical recovery.

## Case Report

A 53-year-old African American female with a body mass index of 27.2 kg/m<sup>2</sup> and a history of coronary artery disease, end-stage renal disease, cervical carcinoma and a right atrial thrombus, presented to our emergency department from an outside hospital bleeding profusely from her rectum. At an outside facility, two self-expanding nasal tampons (Rhino Rockets, Shippert Medical Technologies, Centennial, Colorado, USA) were placed in the rectum to control bleeding and two units of PRBCs were transfused. While still in the emergency department, MTP was started, and 2 g of intravenous tranexamic acid (TXA) were administered.

The patient was emergently taken to the operating room, but surgical efforts failed to control the bleeding as the pelvic radiation therapy she had previously received to treat a cervical carcinoma had distorted her anatomy such that her internal iliac artery could not be visualized. Proctoscopy performed after total colectomy revealed a still massive amount of blood coming from the lower rectum or anal canal. A balloon was fashioned with a Penrose drain and Foley catheter to create a tamponade

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effect in the rectum; however, this was effective for only a short while. Thromboelastography (TEG) results – a normal reaction time (R) time of 7 min, a decreased alpha angle of 40° and decreased maximum amplitude of 36.7 mm – pointed toward a coagulopathy secondary to fibrinogen and platelet deficiency. The patient continued to receive fresh frozen plasma (FFP), cryoprecipitate and platelets. While there was a concern of a coagulopathy related to the apixaban, the patient was prescribed for atrial thrombus, the etiology of bleeding, in this case, was surgical. During the consultation with the interventional radiology service for angioembolization, she was brought to the Surgical Intensive Care Unit (SICU) for interval management with the rectal balloon in place.

In the SICU, two rapid transfuser devices (Level 1, H-1200 Fast Flow Fluid warmer, Dublin, OH, USA) were assembled, and a wide-bore central venous catheter was inserted. MT was continued with a goal mean arterial pressure (MAP) of 50–60 mmHg through the administration of blood products, norepinephrine, and vasopressin infusion and intermittent boluses of epinephrine. Resuscitation was guided by vital signs, bedside echocardiography, serial TEG and perfusion biomarkers such as serum lactate and base deficit. A >14 L blood loss was recorded in the SICU in 90 min.

In the interventional radiology suite, a fistula between the right common iliac and the rectum was identified as the source of bleeding. A 10 mm × 40 mm covered self-expanding intravascular stent (Fluency, Bard Peripheral Vascular, Tempe, AZ, USA) successfully stopped the bleeding. In total, the patient received 60 units PRBC, 23 units FFP, 20 packs of platelets, 6 units cryoprecipitate, 2 g TXA, 30 L of crystalloid, and 2 L of albumin in <7 h.

Serial focused cardiac ultrasound (FoCUS) guided the resuscitation. Hypothermia, serum lactate, and base deficit improved from 35.4, 7 and – 10–36.8, 1.9 and – 4 respectively, in the next 4 h. By that point, the patient was able to follow commands and required minimal ventilatory support. In the ensuing days, there were no signs of lung injury, volume overload, coagulopathy, or cardiomyopathy. Her abdomen was closed 2 days later, successfully extubated shortly thereafter, and transferred to the floor.

## Discussion

MT is a life-saving intervention with many risks. According to the American College of Surgeons National Surgical Quality Improvement Program, the incidence of MT (>5 units) among all surgical patients was 0.6%–0.7% over a 3-year period. The 30-day mortality for patients receiving MT was 21.5%. Of the 54% of patients, who had major complications, 38% were respiratory and 23% related to infection, sepsis, or septic shock. Other major complications were related to acidosis, coagulopathy, hypothermia, and cardiac dysfunction.<sup>[1,6,8]</sup>

The establishment of an MTP is not a requirement for certification as a trauma center in the US. One study reported that, out of 59 centers, only 85% used MTP-based volume replacement and only 62% included FFP in their first batch.<sup>[9]</sup> This has resulted in widely variable transfusion practices. In general, three components are considered necessary for any MTP: early start while gaining control of the bleeding, anticipation of further transfusion, and the use of laboratory results for goal-directed management.<sup>[3]</sup> The goals are usually set for a hemoglobin level above 8–10 g/dL, platelet count >50 × 10<sup>9</sup>/L, prothrombin time <1.5 times normal, partial thromboplastin time <40, and fibrinogen levels >100 mg/dL depending on the individual institution.

At our institution, MTP is activated by the surgeon, emergency room physician, or physician anesthesiologist. Initially, 4 units of type O PRBCs and 1 unit of type A plasma are delivered by a dedicated transport individual along with a 1 g bolus of intravenous TXA. Transfusion therapy continues while the patient's blood sample is being delivered by the dedicated transport individual to the blood bank for cross-matching. Complete blood count, coagulation studies, fibrinogen, TEG, and chemistries are sent at regular intervals. The second phase of transfusion includes PRBCs, FFP, and platelets in a 2:1:1 ratio and the sequence is repeated until hemostasis is achieved.

Transfusion pathways providing PRBC, FFP, and platelets in a ratio of 1:1:1 were adopted in the military setting,<sup>[10]</sup> but in the civilian setting, the optimum ratio is unknown. Several studies suggest that the optimal ratio is somewhere between 1.5 and 2.5 units of RBC to 1 unit of FFP.<sup>[11]</sup> The 2:1 ratio of RBC to FFP at our institution minimizes patient exposure to the deleterious effects of excessive plasma.<sup>[12]</sup> Clinically significant thrombocytopenia is unlikely to develop until one complete blood volume has been replaced. In our case, dilutional thrombocytopenia was suspected, and platelets were transfused empirically at first, then later, based on platelet count and TEG results. Evidence of the usefulness of preemptive platelet transfusion is lacking. Fibrinogen levels may decrease significantly in consumption coagulopathy, disseminated intravascular coagulation, and hyperfibrinolysis – all of which may be present in the massively bleeding patient. While FFP contains lower levels of fibrinogen as compared to cryoprecipitates, there is no evidence to support the use of one over the other.

Although it is controversial to restrict the crystalloids in cases of trauma to avoid coagulopathy,<sup>[2]</sup> we used crystalloids for hemodynamic support when the rapid transfusion system tubing had to be replaced, after every 7–10 units of PRBCs. Permissive hypotension during massive volume resuscitation in trauma cases is another factor that has shown survival benefit especially in the immediate postoperative period. Setting MAP goals to

50 mmHg rather than the conventional goal of 65 mmHg, until surgical hemostasis is achieved, has shown to reduce the incidence and severity of postoperative coagulopathy. In our case, we kept the MAP around 55–60 mmHg.<sup>[13]</sup>

Monitoring of the blood coagulation factors is yet another important component of the MTP. Conventional methods to monitor coagulation status were designed to manage anticoagulant therapy and their use in the setting of blood loss is controversial.<sup>[14]</sup> In fact, their value in predicting bleeding tendency in patients receiving MT is poor.<sup>[15]</sup> Furthermore, the long turnaround time is undesirable.<sup>[16]</sup> TEG is a relatively rapid viscoelastic whole blood coagulation test that allows tailoring of fibrinogen, cryoprecipitate, plasma, and to the specific clinical needs of the patients. Furthermore, the use of TEG allows early recognition of hyperfibrinolysis.<sup>[17]</sup> TXA was used in our case to prevent excessive fibrinolysis. Although the effect of TXA in reducing all-cause mortality in profusely bleeding trauma patients is minor, the low cost and favorable side effect profile of TXA make it a valuable adjunct to MTP, especially when the etiology of bleeding is unclear.<sup>[18]</sup> The time to administration of the first unit of blood may be another important prognostic factor. A recent systematic review examining the utility of MT policies suggested that shorter times to initiating transfusion result in improved survival.<sup>[19]</sup>

Adequacy of volume resuscitation is difficult to assess in these situations. Monitoring of cardiac filling pressure is fraught with fallacies due its dependence on several factors including changes in venous capacitance, ventricular function as well as effect of mechanical ventilation and abdominal pressure.<sup>[20,21]</sup> Moreover, unless there is a dedicated central line to measure central venous pressure (CVP), the ongoing large volume resuscitation through the existing central line prevents the ability to transduce the line to obtain any meaningful CVPs, as in our patient. Pulse pressure variability is another modality often used to guide fluid resuscitation; however, it is dependent on several factors including controlled mechanical ventilation, respiratory system compliance of  $\geq 30$  mL cm H<sub>2</sub>O and tricuspid annular peak velocity of  $\geq 0.15$  m/s.<sup>[22]</sup> FoCUS has, therefore, become a rapidly available first line tool in these emergent situations, where it can substitute comprehensive echocardiography in the assessment of volume status, pericardial effusion, cardiac global and regional systolic function, right and left ventricular enlargement as well as to guide pericardiocentesis and transvenous pacing wire placement.<sup>[23]</sup> It involves five views, namely the parasternal short axis, parasternal long axis, apical four chamber, subcostal inferior vena cava (IVC) and subcostal four chamber. Furthermore, in a mechanically ventilated patient, transthoracic echocardiographic assessment of IVC distensibility during inspiration has been utilized to assess fluid responsiveness. A lack of any variation points toward a fluid nonresponder, although just like CVP, it has its own limitations.<sup>[24]</sup> In our case, in addition

to quick assessment of volume resuscitation, it allowed us to not interrupt administration of volume and/or vasoactive medications during CVP measurements. At the conclusion of the transfusion, the patient had no respiratory variations in the IVC diameter and adequate left ventricular end-diastolic volume.

## Conclusion

This case emphasizes the role of a strict disciplinary approach that should include an aggressive and timely resuscitation with blood products, close coordination with the blood bank, prompt management of physiological derangements and guidance by both FoCUS as well as clinical and biochemical parameters. Although reports of ultra-MT in the medical literature are not unusual, we believe that the patient's size and comorbidities, the difficulty in detecting the source of bleeding, and the rapid recovery devoid of transfusion-related complications make for a particularly valuable educational case.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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