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LIMITATIONS OF AVAILABLE BLOOD PRODUCTS FOR MASSIVE TRANSFUSION DURING MASS CASUALTY EVENTS AT US LEVEL 1 TRAUMA CENTERS

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ABSTRACT—**Introduction:** Exsanguination remains a leading cause of preventable death in traumatically injured patients. To better treat hemorrhagic shock, hospitals have adopted massive transfusion protocols (MTPs) which accelerate the delivery of blood products to patients. There has been an increase in mass casualty events (MCE) worldwide over the past two decades. These events can overwhelm a responding hospital's supply of blood products. Using a computerized model, this study investigated the ability of US trauma centers (TCs) to meet the blood product requirements of MCEs. **Methods:** Cross-sectional survey data of on-hand blood products were collected from 16 US level-1 TCs. A discrete event simulation model of a TC was developed based on historic data of blood product consumption during MCEs. Each hospital's blood bank was evaluated across increasingly more demanding MCEs using modern MTPs to guide resuscitation efforts in massive transfusion (MT) patients. **Results:** A total of 9,000 simulations were performed on each TC's data. Under the least demanding MCE scenario, the median size MCE in which TCs failed to adequately meet blood product demand was 50 patients (IQR 20–90), considering platelets. Ten TCs exhaust their supply of platelets prior to red blood cells (RBCs) or plasma. Disregarding platelets, five TCs exhausted their supply of O- packed RBCs, six exhausted their AB plasma supply, and five had a mixed exhaustion picture. **Conclusion:** Assuming a TC's ability to treat patients is limited only by their supply of blood products, US level-1 TCs lack the on-hand blood products required to adequately treat patients following a MCE. Use of non-traditional blood products, which have a longer shelf life, may allow TCs to better meet the blood product requirement needs of patients following larger MCEs.

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INTRODUCTION

The past two decades have seen resuscitation efforts at trauma centers (TCs) shift from crystalloid-based resuscitation to damage control resuscitation, which uses a combination of surgery, permissive hypotension as a bridge to definitive control, and resuscitation with a high ratio of blood products (1, 2). The administration of balanced blood products, in a 1:1:1 ratio of platelets:plasma:red blood cells (RBCs), results in decreased mortality rates and increased rates of hemostasis (3, 4). Balanced transfusion of blood products within 6 h of injury is also associated with decreased mortality (3). However, the mean time to death from hemorrhage still occurs between 100 and 180 min (3, 4). Despite these advancements in management, exsanguination remains a leading cause of preventable death in trauma patients, accounting for 40% of injury-related mortality (5).

Both globally and in the United States (US), mass casualty events (MCEs) have increased during the past two decades (6, 7). A MCE is defined as greater than 10 living victims arriving to a responding facility following an event (8). Terrorist and criminal activity are the primary drivers of the MCE increase, with approximately 50% of global terrorist attacks using explosive mechanisms (6, 7). Explosively generated MCEs tend to result in more patients, who are more severely injured, and who require more blood products (7, 9, 10). The rapid influx of patients immediately following such an event can overwhelm a treating facility's resources, resulting in limited or no care for a portion of patients.

Retrospective analysis of blood product consumption during MCEs demonstrates that between 20% and 40% of admitted patients require blood products (9–11). Though only 4% to 10% of admitted patients require massive transfusion, these patients consume between 45% to 65% of RBCs, 65% to 85% of plasma, and $\geq$80% of platelets during the event (8–10). Additionally, between 60% and 75% of RBCs used to treat patients are consumed within the first 4 h (8, 11, 12). Though there is wide variation, roughly a quarter of transfused RBCs are given as uncross-matched (UCM) RBCs (8, 9, 12, 13). Additionally, resupply timelines following MCEs may be greater than the mean time of exsanguination and outside the 6-h window for component products to be beneficial (14).

Analyses of past events can serve as a baseline for developing computer models for analyzing blood product consumption during MCEs (15). In 2016 Glasgow et al. (15) used discrete event simulation (DES) computer modeling to simulate the effect of varying on-shelf RBCs stock and resupply with regards to RBC consumption and increased casualty loads in MCEs. Their model demonstrated that limited size MCEs (<20 patients) threatened to overwhelm RBCs supplies at UK TCs (15). Other computer simulations have examined other factors affecting a TC's surge capacity (16, 17). To date, there has been no study to model blood product consumption during MCEs using MTPs taking into consideration the multiple factors which affect type-specific blood product consumption.

The main objective of this simulation study was to evaluate US level-1 TCs' ability to meet the blood product requirements of patients following a MCE based solely on their initial blood product supply. Each TC's blood bank was evaluated on: its ability to treat patients following MCEs using MTPs to treat MT patients, the maximum number of MT patients treated, and type-specific blood products exhausted. We hypothesized that the limiting factor in a TC's ability to provide care to patients of a MCE is their initial supply of UCM blood products and platelets.

METHODS

This study was deemed exempt from review by the institutional review board of the University of Texas Health Science Center Houston. A cross-sectional survey of on-hand blood products was sent to 25 large academic level-1 trauma centers with replies from 17 centers. A unit of RBCs was defined as approximately a 300 mL bag. A standard six packs of platelets was counted as one unit. A unit of plasma was defined as approximately a 300 mL bag. Jumbo units of plasma were defined as a 500 mL bag of plasma and were counted as two standard units of plasma. A unit of whole blood was defined as approximately a 450 mL bag which was counted as one unit of RBCs and one unit of plasma. Surveys were e-mailed from the trauma fellowship director at McGovern Medical School to trauma surgeons or staff at each institution. Surveys were completed by either the trauma director, blood bank director, or as directed by either of the aforementioned positions and e-mailed back to McGovern Medical School. For cases where there was not a reply within 6 weeks of the initial e-mail a follow-up e-mail was sent. If there was no reply after an additional 4 weeks, a phone call was made. A total period of 12 weeks was allotted for responses.

Model development

A computerized DES model was constructed using MATLAB SimEvents and Simulink software (R2017b, Natick, Mass). DES modeling uses customizable queues and algorithms to allow entities, with defined attributes, to flow through a model in discrete time intervals, consuming resources while experiencing events and interacting with the model (18). DES is particularly useful for modeling consumption of limited resources when resource allocation is dependent upon multiple patient characteristics, and when what happens next is dependent upon what happened previously (18). Ultimately, entities must complete a series of events before exiting the model. Running multiple iterations of the same scenario, using different rand number seeds each time, allows for meaningful trends to be identified (18).

The model was designed to reflect a busy, urban level-1 US TC responding to a MCE. Only aspects of patient care related to blood product consumption were considered. Blood product resources were neither able to be regenerated once consumed, nor could they be increased once the model began. The model did not consider other limitations such as prehospital care, bed space, diagnostics, or staffing issues. Model parameters were based on a review of the literature with consultation of subject matter experts when the literature was insufficient. A complete list of model parameters can be found in the appendix, http://links.lww.com/SHK/B205. A list of model assumptions can be found in Table 1 and a model schematic can be found in Figure 1.

Upon generation, each patient's attributes are specified in accordance with the model parameters and scenario specifications. Specified attributes are: gender, age, blood type, admission type, priority status, and blood product requirements. Patients are assigned to one of three admission types: massive transfusion (MT), require blood products but not MT (Req), or no blood products required (none). MT patients are defined as patients who require greater than 10 units of RBCs. Based on admission type, patients are then assigned a priority status and blood product requirements.

Following a MCE, casualties arrive at the TC based on a probability distribution function which assigns their time of arrival. As casualties arrive, they are first triaged as a Priority 1 (P1) or Priority 2 (P2) patient. P1 patients tend to be more severely injured and have an immediate need for blood products. Priority 3 (P3) patients are not included in the model as it is assumed that they will not require blood products and will be diverted to another facility.

TABLE 1. **Model assumptions**

1. MCE generated by an explosion in an urban setting.
2. Event occurs during normal working hours, with the hospital fully staffed.
3. There are no other concurrent casualty responses occurring at the time of the MCE.
4. Trauma center is in a state of readiness and is able to respond to the MCE.
5. Once triaged, patient's priority status is not changed.
6. Only P1 and P2 patients require blood products.
7. P3 patients were transported to another facility and not treated at the level 1 trauma center.
8. All P1 and P2 casualties who require blood products have a predetermined blood product requirement that does not change with respect to time.
9. There is adequate staff to transport blood samples to blood bank.
10. No limitations in transporting blood products from blood bank to patients.
11. There is no resupply of blood products.
12. All casualties are between the ages of 15–85.

After triage, patients undergo a trauma assessment, during which their blood product requirement is determined and, if necessary, a blood sample is sent to the lab for typing. Patients who do not require blood products exit the model following their assessment. P1 patients and MT patients who require blood products receive UCM blood products until their blood type is determined. P2 patients, who do not require massive transfusion, receive only type specific blood products. The blood bank may release up to six units of RBCs, six units of plasma, and one unit of platelets (6/6/1) at a time for MT patients and 2/2/1 for Req patients until their blood product requirements are satisfied. The terms ''least demanding'' and ''most demanding'' describe how taxing the model parameters were with regards to the percentage of patients who required blood products and the percentage of patients who required massive transfusion. The percentage of patients who required blood products and the percentage of patients who required massive transfusion were the driving force behind blood product consumption. Patient triage category (P1/P2) helped to determine each entity (patient) blood product requirement based on the model parameters. Ultimately, the model was not built to be able to report the results on a per patient triage category bases. Instead, the model was built to stress how many patients the system can handle based on global blood product requirements. Details regarding timelines and blood product hierarchy can be found in the appendix (Appendix 1, http://links.lww.com/SHK/B205).

Blood product supplies were run through 90 different scenarios that varied casualty size from 20 to 200 in 20 patient increments, percentage of patients requiring blood products from 20% to 40% in 10% increments, and percentage of patients requiring massive transfusion from 6% to 10% in 2% increments. Each TC's initial blood product supplies went through 100 iterations of each scenario. If during an iteration a patient required RBCs or plasma and the blood bank was unable to fulfill the request, that patient received what products they could, and the iteration ended in failure. Platelet exhaustion was excluded as termination criteria due to its common occurrence. However, data on platelet consumption were collected and analyzed to determine when it was the limiting blood product and would have resulted in failure.

To evaluate the validity of the model, 1,000 runs of the most demanding scenario were conducted, using a blood bank of infinite supplies. The number of RBCs transfused per admitted patient, the proportion of RBCs given as UCM blood, and the percentage of RBCs, plasma, and platelets transfused to MT patients were analyzed to ensure that the model fit with historical data on blood

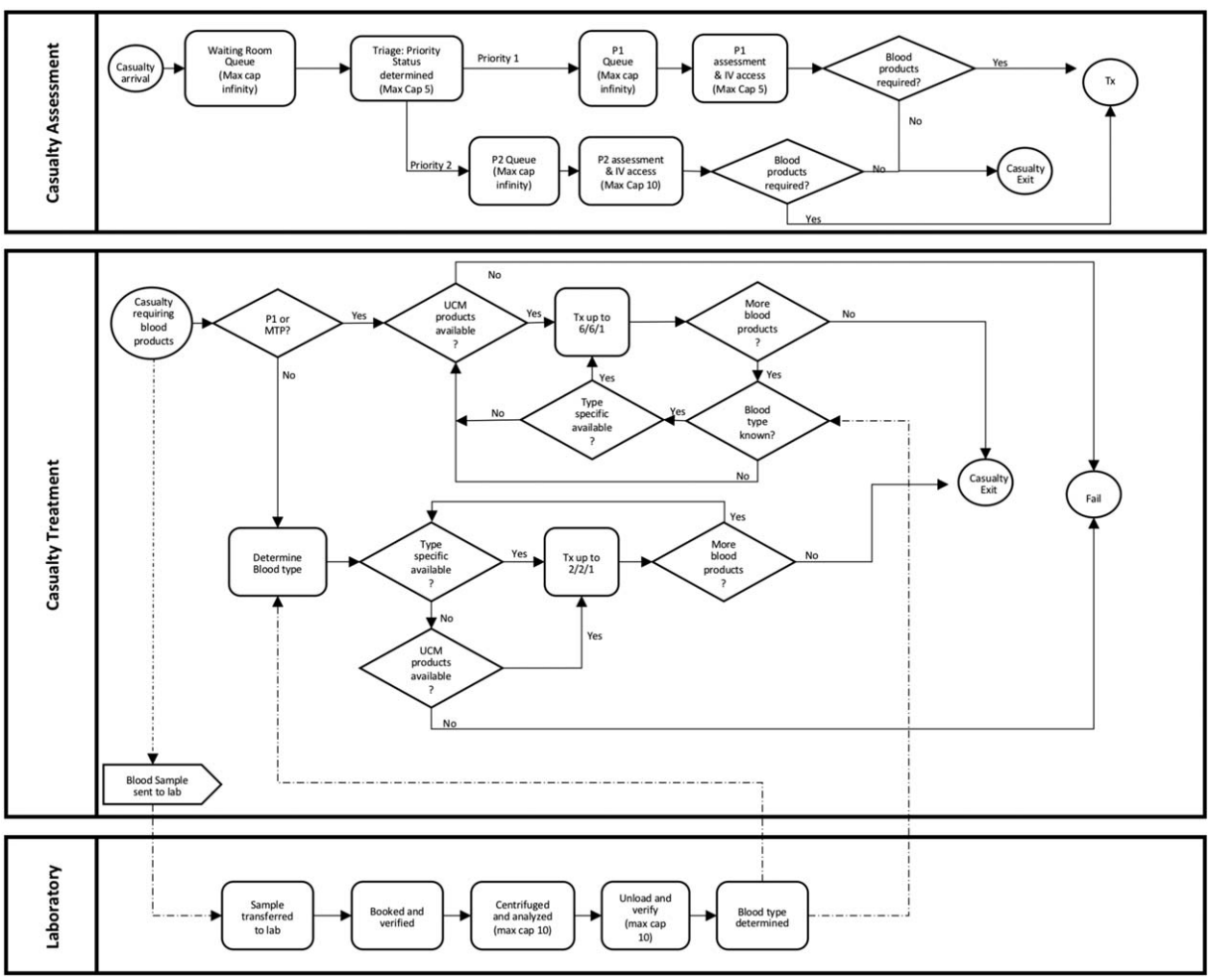

FIG. 1. **Schematic of discrete event simulation.** P1 indicates priority 1; P2, priority 2; IV, intravenous; MTP, massive transfusion protocol; Tx, treatment; UCM, universal cross-matched product.

TABLE 2. **Number of type specific blood products at responding US level-1 trauma centers.**

		Median	IQR
RBCs	O+	104	(84–200)
	O−	40	(25–70)
	A+	70	(50–115)
	A−	20	(20–28)
	B+	20	(15–30)
	B−	5	(2–8)
	AB+	2	(0–6)
	AB−	1	(0–4)
Plasma	O	50	(40–90)
	A	62	(54–130)
	B	40	(30–60)
	AB	44	(35–90)
Platelets		12	(5–25)

product consumption. We ran 1,000 iterations of the most demand scenario (200 admitted patients, 40% of admitted patients requiring blood products, and 10% of admitted patients requiring massive transfusion) were ran assuming an infinite supply of blood products. The number of RBCs transfused per admitted patient, the proportion of RBCs given as uncross-matched blood, and the percentage of RBCs, plasma, and platelets transfused to massive transfusion patients were measured. This data was then compared to historical data on blood product consumption to ensure that the model accurately reflected past events. Unfortunately there are errors with this type of validation. A significant portion of case reports regarding blood product consumption during a MCE, on which our models are based, predate the era of balanced blood product resuscitation (Appendix 1, http://links.lww.com/SHK/B205).

RESULTS

Cross-sectional survey results for available blood products can be seen in Table 2. One TC's data is included in the survey results but was not evaluated via the DES, due to being a late submission.

This study ran 9,000 simulations on each TC's initial on-hand blood products to evaluate its ability to respond to a MCE as the number of admitted patients increased, the percentage of patients requiring blood products increased, and the percentage of patients requiring massive transfusion increased. Each TC's blood bank was evaluated on three parameters. The first was the ability to meet the blood product requirements of admitted patients following a MCE using a MTP for massive transfusion patients. A TC was considered able to meet the blood product requirements if it was successful in ≥80% of the iterations at the specified scenario parameters.

Under the *least* demanding MCE, 20% of patients requiring blood products and 6% requiring massive transfusion, more than half of the TCs evaluated failed to meet the blood product requirements for a MCE with 100 admitted patients, excluding platelets. The median size MCE that resulted in failure was 80 admitted patients (IQR 60–120), excluding platelets. Considering platelets with the same blood product requirements, more than half of the TCs failed at a MCE of 60 admitted patients, with a median of 50 admitted patients (IQR 20–90). Figures 2 and 3 show the percentage of successful runs for all 16 TCs excluding and including platelets under the least demanding MCE parameters, respectively.

Under the *most* demanding MCE, 40% of patients requiring blood products and 10% requiring massive transfusion, more than half of the TCs failed at a 60-admitted-patient sized MCE. The median size was 60 admitted patients (IQR 40–85), not considering platelets. Considering platelets, more than half of the TCs failed at 40-admitted-patient sized MCE with a median of 30 admitted patients (IQR 20–45). Figures 4 and 5 show the percentage of successful model runs for all 16 TCs under the most demanding MCE parameters, excluding and including platelets respectively.

The second parameter each TC's blood bank was evaluated on was the maximum number of MT patients treated. TCs were analyzed across all scenarios assuming 200 admitted patients. MT patients were considered treated if their blood product requirement was satisfied prior to the iteration ending. For the *least* demanding MCE, not considering platelets, more than half of TCs were unable to treat four MT patients. The median number of treated MT patients was 3.56 (IQR 1.91–6.97).

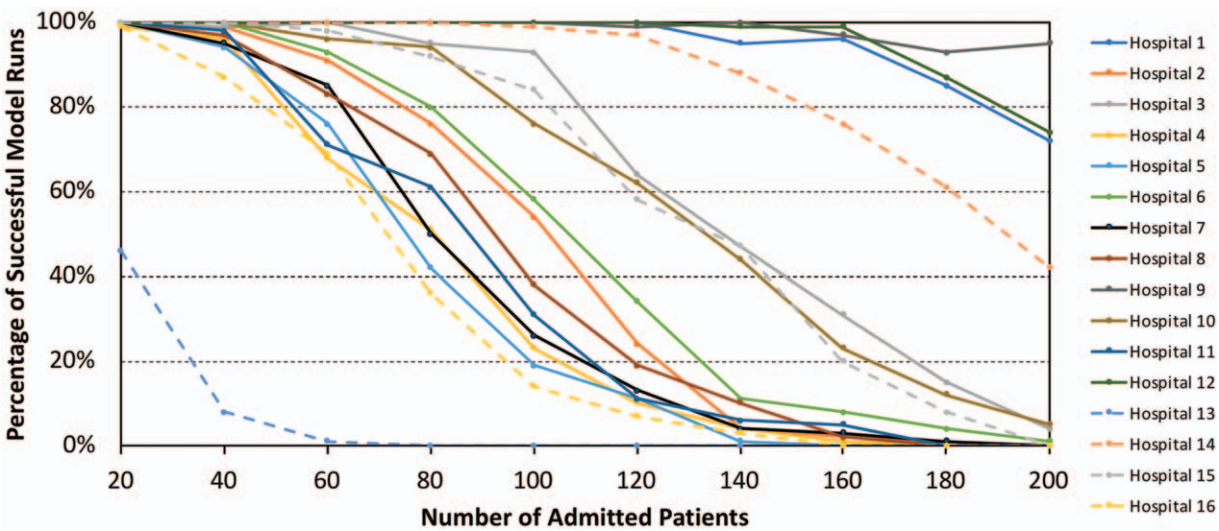

FIG. 2. **Percentage of successful model runs across all 16 trauma centers when 20% of admitted patients require blood products and 6% require massive transfusion, excluding platelets.**

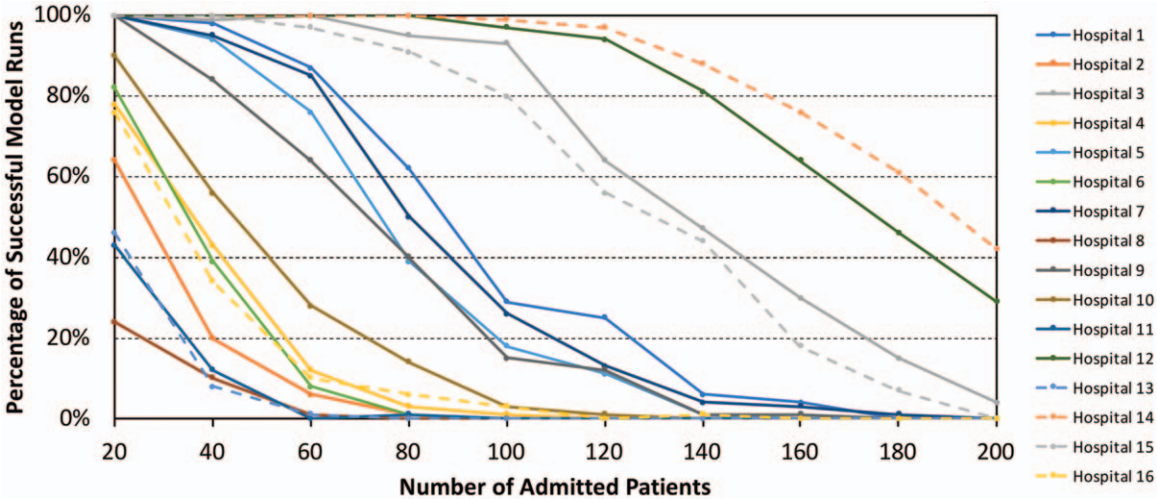

FIG. 3. **Percentage of successful model runs across all 16 trauma centers when 20% of admitted patients require blood products and 6% require massive transfusion, including platelets.**

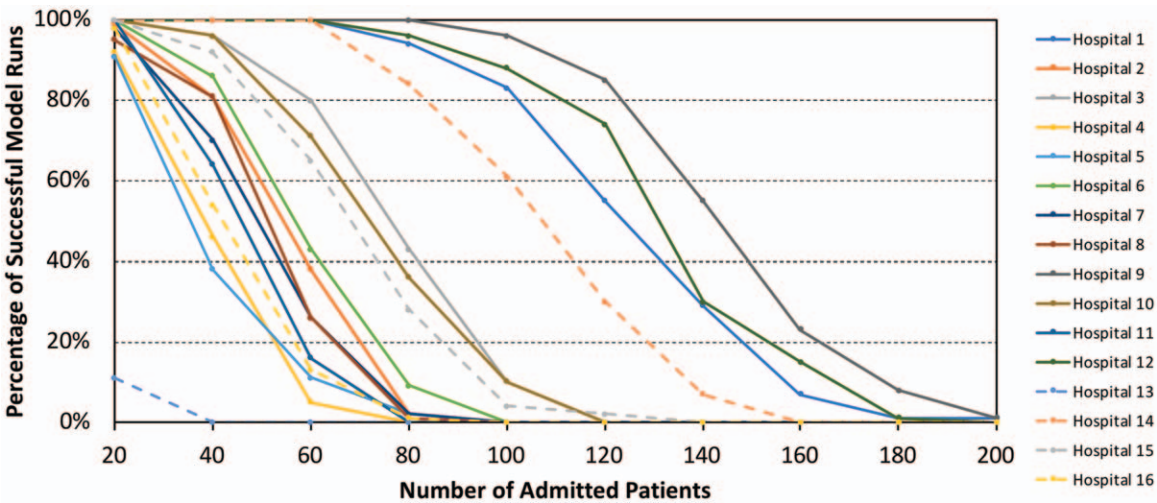

FIG. 4. **Percentage of successful model runs across all 16 trauma centers when 40% of admitted patients require blood products and 10% require massive transfusion, excluding platelets.**

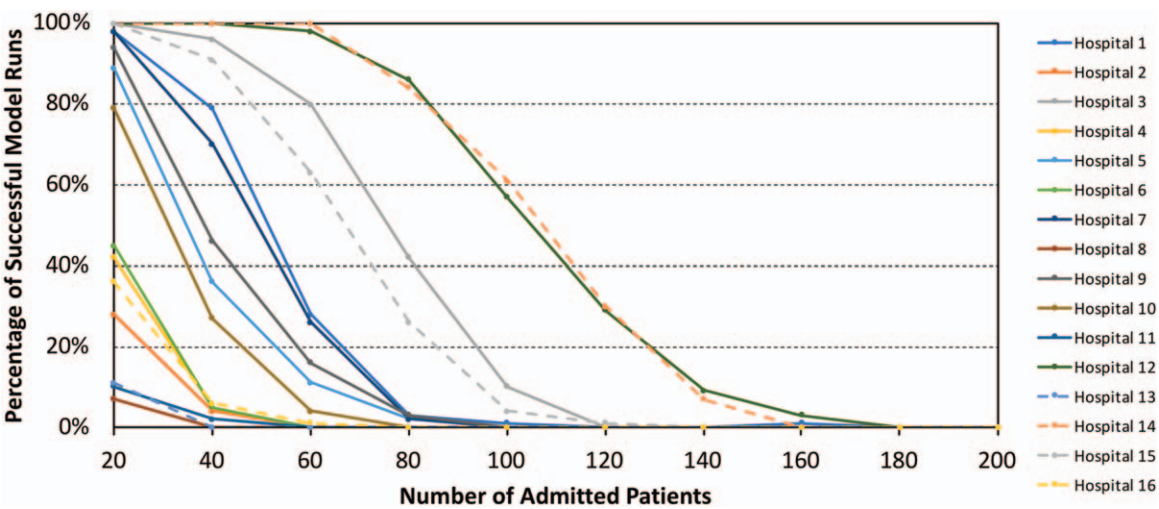

FIG. 5. **Percentage of successful model runs across all 16 trauma centers when 40% of admitted patients require blood products and 10% require massive transfusion, including platelets.**

Considering platelets, more than half of the TCs were unable to adequately treat two MT patients. The median number of MT patients treated was 1.34 (IQR 0.45–3.97).

Under the *most* demanding MCE, not considering platelets, more than half of the TCs were unable to treat three MT patients. The median number of treated MT patients was 2.26 patients (IQR 1.22–4.92). Considering platelets, more than half of the TCs were unable to adequately treat two MT patients. The median number of MT treated was 0.97 (IQR 0.34–3.14).

Lastly, each TC's blood bank was evaluated to determine which type specific blood product tends to be exhausted first. Of the 16 TCs, 10 exhaust their platelet supply first. Disregarding platelets, five TCs exhausted their O− RBC prior to AB plasma, six exhausted AB plasma first, and five had a mixed exhaustion picture. TCs with an O+ and O− RBCs to type A and AB plasma ratio less than 1 exhausted their supply of RBCs first. Those with a ratio greater than 1.5 tended to exhaust plasma first. Those with a ratio between 1 and 1.5 had a mixed exhaustion profile (Fig. 6).

DISCUSSION

MCEs, while becoming more frequent, are still rare. The majority of MCEs to occur in the recent past have been predominately in major metropolitan areas with robust health care and government resources enabling blood products to be reshuffled amongst responding facilities. However, with over 30 million US residents and greater than 70% of the geographical US living outside of a 1-h transit time to a level-1 or level-2 TC, it is important for not only large metropolitan TCs to understand the limitations of their blood product supply, but also for smaller hospitals and TCs as well (19). Understanding blood product supply limitations is also applicable to hospitals in the developing world, many of whom lack the robust resources and governmental support enjoyed by developed countries. Computer simulation modeling is one way in which centers can reasonably evaluate the limitations of on-hand blood product supplies.

Using a DES model, the objective of this study was to evaluate US level-1 TCs' ability to adequately meet the blood product needs of MCE patients based solely on their initial supply of blood products while using a 1:1:1 ratio of blood products for patients requiring massive transfusion. Similar to the model proposed by Glasgow et al., a significant portion of surveyed TCs were unable to adequately treat the number of admitted patients generated by smaller MCEs (<60 patients). This was primarily due to limitations of platelet supplies and not RBCs or plasma.

Based on our simulation, current on-hand platelet supplies at the majority of surveyed TCs allow for less than two MT patients to be treated using a MTP during a MCE. This is particularly troublesome given recent research that shows early administration of platelets is associated with decreased 24-h and 30-day mortality (20). Potentially further compounding this problem is the steady decrease in blood product donors since 2011, despite the fact that the use of platelets in critical care has increased (21). In 2013, 10% hospital respondents to an American Association of Blood Banks (AABB) survey reported having to postpone elective cases due to a shortage in available platelets (22). The availability of on-hand platelets may be the critical vulnerability to a hospital's ability to provide standard of care to massive transfusion patients.

To address the supply limitations of blood products, TCs could increase stocks of UCM blood products. However, maintaining increased stocks of blood products is likely to be both costly and wasteful. Instead, TCs could maintain an emergency stock of non-traditional blood products with a longer shelf life. Freeze dried plasma has a significantly longer

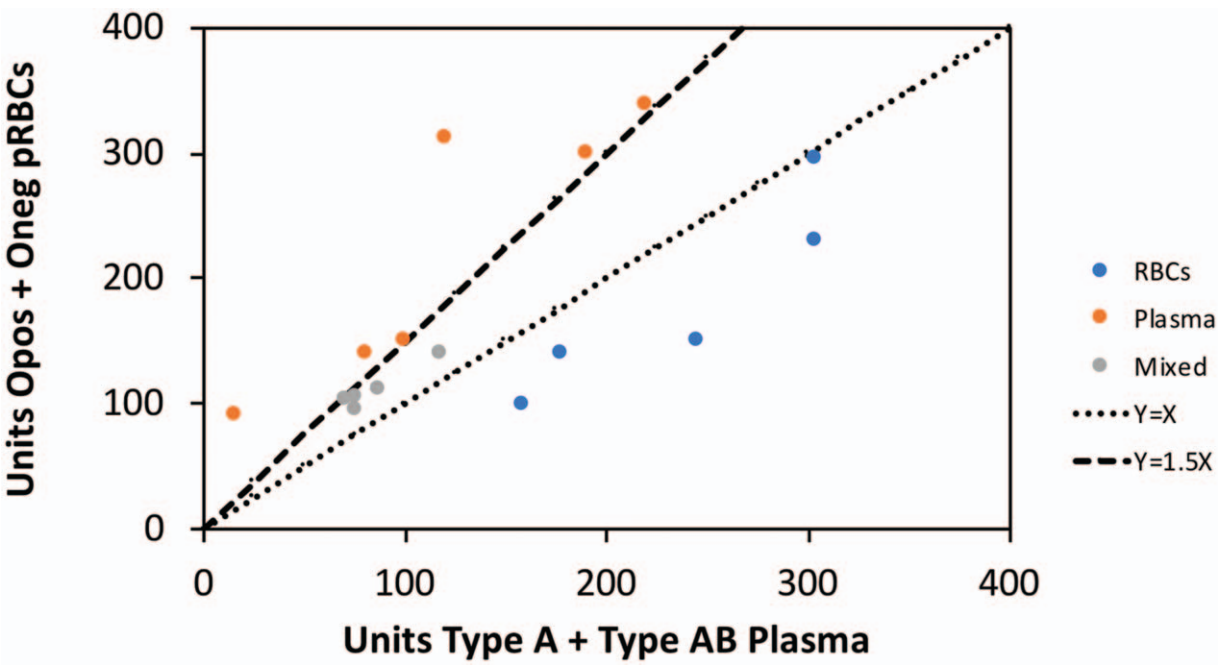

FIG. 6. **Ratio of type O+ and O− red blood cells to type A and AB plasma.** RBCs indicates red blood cells.

shelf life than fresh frozen plasma, and has equal efficacy in treating hemorrhage shock (23). Cryopreserving RBCs extend the shelf life from 42 days to 10 years without decreasing efficacy (24, 25). Though the complexity involved in manipulating frozen RBCs for use in urgent conditions may make them irrelevant during a MCE. Likewise, advances in platelet storage techniques may also extend shelf life without compromising efficacy (26, 27). In fact, cold stored platelets may have increased hemostatic potential for treating traumatic hemorrhage when compared to current platelet storage techniques (26, 27). With the exception of freeze-dried plasma, none of the above-mentioned extended shelf life products have FDA approval for use in trauma. For TCs exhausting their RBCs first, there is no benefit in switching to a lower transfusion ratio, as RBCs will still be the limiting product. Most TCs may also be able to extend their platelet supplies by lowering the ratio of platelets to RBCs for MTPs during a MCE; though this would be less than ideal given the benefit of early platelet administration.

The current gold standard for disaster planning with regards to blood products is the AABB disaster operations handbook. Last updated in 2008 this handbook does not reflect the adoption of MTPs at most medical centers (28). It is antiquated in this regard. It suggests that the need for blood products is likely to occur in phases, with RBCs primarily being needed within the first 24 h and RBCs and platelets being needed within the first 1 to 10 days while failing to mention plasma (29). Additionally, it recommends estimating three units of RBCs for each admitted patient in a disaster (29). However, as our model has shown, RBCs are not necessary the limiting blood product for most TCs; platelets are. While it does provide a guideline how to transport blood products in a timely manner, it is not unreasonable to believe that logistical constraints may arise as roads become congested and air resources are limited in availability. These constraints may prolong the resupply of blood products outside of the 6-h window when the early administration of component products has been shown to be beneficial (14). There has been no study to date examining the timeline on the consumption of blood products during a MCE, comparing the time of transfusion between initially available blood products and resupplied blood products. Further analysis is needed to see whether or not resupplied blood products are delivered to patients in a timely manner. Potential logistical constraints and geographical austerity make it all the more important that hospitals have an understanding of their blood product supply limitations prior to a MCE occurring.

When interpreting the results of this study there are several limitations that should be considered. First, this study was conducted using a model, which is based on historic blood product consumption during MCEs; the majority of which predates modern MTPs and focuses primarily on RBC consumption. Second, this model assumes blood product requirements do not vary with time. Additionally, this model evaluated all TCs using a 1:1:1 ratio of blood products for MTP in treating MT patients, in accordance with the most appropriate standard of care (4). Lastly, this model assumes blood products stocks are the limiting factor in patient care. There are likely other logistical or personnel constraints that need to be considered when assessing a TC's surge capacity during a MCE.

CONCLUSION

Assuming a TC's ability to treat patients is limited only by their supply of blood products, this simulation study demonstrates that US level-1 TCs lack the on-hand blood products required to meet the requirements of patients following a MCE when using a MTP. TCs may be better suited to respond to a MCE by stocking non-traditional blood products with extended shelf lives for emergency use. Additionally, TCs should evaluate their blood product supply limitations to revise their MTPs during MCEs to optimize blood product supplies.

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