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ORIGINAL RESEARCH

TRANSFUSION

Performance assessment of intravenous catheters for massive transfusion: A pragmatic in vitro study

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Abstract

Background: Rapid infusion of warmed blood products is the cornerstone of trauma resuscitation and treatment of surgical and obstetric massive hemorrhage. Integral to optimizing this delivery is selection of an intravenous (IV) catheter and use of a rapid infusion device (RID). We investigated which IV catheter and RID system enabled the greatest infusion rate of blood products and the governing catheter characteristics.

Study Design and Methods: The maximum flow rates of nine IV catheters were measured while infusing a mixture of packed red blood cells and fresh frozen plasma at a 1:1 ratio using a RID with and without a patient line extension. To account for IV catheters that achieved the RID's maximum 1000 ml/min, the conductance of each infusion circuit configuration was calculated.

Results: IV catheters of 7-Fr caliber or higher reached the maximum pressurized flow rate. The 9-Fr multi-lumen access catheter (MAC) achieved the greatest conductance, over sevenfold greater than the 18 g peripheral catheter (4.6 vs. 0.6 ml/min/mmHg, $p < .001$). Conductance was positively correlated with internal radius ($\beta = 1.098$, 95% CI 4.286–5.025, $p < .001$) and negatively correlated with length ($\beta = -0.495$, 95% CI −0.007 to 0.005, $p < .001$). Use of an extension line ($\beta = -0.094$, 95% CI −0.505 to −0.095, $p = .005$) was independently associated with reduced conductance in large caliber catheters.

Conclusion: Short, large-diameter catheters provided the greatest infusion rates of massive transfusion blood products for the least pressure. For patients requiring the highest transfusion flow rates, extension tubing should be avoided when possible.

KEYWORDS

intravenous catheters, large volume resuscitation, massive transfusion, rapid infusion device

1 | INTRODUCTION

A vital step in the resuscitation of patients with major hemorrhage is achieving adequate intravenous (IV) access. This refers to the insertion of a catheter capable of infusing blood products at a sufficient flow rate to reverse a volume deficit and maintain tissue perfusion despite ongoing blood loss.

The Hagen–Poiseuille law, which governs laminar flow rates in noncompressible Newtonian fluids, suggests that infusion rate should be proportional to the internal radius of the IV catheter to the fourth power and driving

pressure, but inversely proportional to the viscosity of the infusate and length of the catheter. Previous work has confirmed the impact of these catheter characteristics on flow rates achievable.[1]

In more clinically representative models, others have shown that the Hagen–Poiseuille law is a poor predictor of in vivo IV catheter performance in part because commercially available systems at typical resuscitative flows often involve multiple points along the infusion path where turbulence is introduced.[2] Adding to the difficulty in predicting catheter performance is the variation in techniques used by manufacturers to generate their stated flow rates; some use pressure bags while others utilize the hydrostatic pressure of a 100 cm head height.[3]

The majority of previous studies employed crystalloid, synthetic colloid, or packed red blood cells at room temperature, with standard administration tubing and pressurized by means of pressure bags.[1–5] However, blood viscosity is inversely proportional to temperature, and because current practice in hemostatic resuscitation of trauma patients calls for the infusion of warmed packed red blood cells and fresh frozen plasma at an approximate ratio of 1:1, these findings may not apply directly to all massive resuscitation scenarios. In addition, many major trauma centers employ the use of a rapid infusion device (RID), capable of achieving flow rates of up to 1200 ml/min, while warming to physiologic temperature. There are notable rheological differences in infusing warmed, pressurized blood products when compared to crystalloid. The viscosity of blood is not only higher than that of crystalloids, it varies with shear stress, rendering it a non-Newtonian fluid. This, together with the high probability of turbulence within infused products, reduces the applicability of the Hagen–Poiseuille law in this instance.

Rather than attempting to strictly apply the laminar flow dynamics dictated by the Hagen–Poiseuille law to the flow of blood, a non-Newtonian fluid, through a complex, turbulence-inducing tube, we aimed to clarify these concepts for clinicians involved in the management of major hemorrhage via a pragmatic in vitro assessment of the maximum flow rates achievable with different IV catheters using a resuscitation fluid consisting of a fixed ratio of warmed blood products and a commercially available RID. We hypothesized that larger-bore, shorter catheters without an extension line would afford higher flows of mixed blood products at lower pressures than smaller-bore, longer catheters with an extension line. We also used this clinically representative system and fluid to investigate factors that determined flow rates, in particular the effect of IV catheter characteristics.

2 | MATERIALS AND METHODS

2.1 | General

This in vitro study was exempt from requiring institutional review board approval.

2.2 | IV catheters

Catheters were selected based on their availability at our level-one trauma center and likelihood of encountering them during a massive transfusion situation. Physical

TABLE 1 Intravenous catheters characteristics and manufacturers

Catheter	Description	Manufacturer	Material	ID (mm)	TL (mm)
PVC 18 g	Introcan Safety IV Catheter	B. Braun Medical (Bethlehem, PA, USA)	FEP	0.84	32
PVC 16 g	Introcan Safety IV Catheter	B. Braun Medical (Bethlehem, PA, USA)	FEP	1.19	32
PVC 14 g	Introcan Safety IV Catheter	B. Braun Medical (Bethlehem, PA, USA)	FEP	1.60	50
CVC	ARROWguard Blue PLUS Two-Lumen Central Venous Catheter	Teleflex (Wayne, PA, USA)	PU	1.60	300
Trialysis	Short Term Dialysis 15 cm Straight Catheter	Bard (Covington, GA, USA)	PU	2.16	250
7-Fr RIC	Arrow Rapid Infusion Catheter	Teleflex (Wayne, PA, USA)	PU	2.33	50
9-Fr Sheath	Arrow sheath Introducer	Teleflex (Wayne, PA, USA)	PU	3.20	300
9-Fr MAC	ARROWguard Blue PLUS Multi-lumen Access Catheter	Teleflex (Wayne, PA, USA)	PU	3.00[a]	215

Abbreviations: PVC, peripheral venous catheter; CVC, central venous catheter; RIC, rapid infusion catheter; MAC, multi-lumen access catheter; ID, internal diameter; TL, total length; FEP, fluorinated ethylene propylene; PU, polyurethane.

[a]Oval-shaped lumen is 9-Fr per manufacturer.

characteristics and manufacturer details of the IV catheters assessed are provided in Table 1. Per the manufacturers of the French scale catheters, French refers to the inside diameter. The Teleflex (Wayne, PA, USA) 9-Fr sheath has a 3.20 mm inside diameter per the manufacturer; this measurement was used in calculations. For all other French-sized catheters, internal diameter (ID) was converted to mm using the following calculation: mm = Fr/3.

2.3 | Infusion circuit

An infusion circuit (Figure 1) was assembled using the Belmont FMS 2000 rapid infusion device (RID) and a 3-L reservoir with a 5-spike connector set (Belmont Instrument Corporation, Billerica, MA, USA). The standard 54-inch patient line was employed for all assessments and the 54-inch patient line extension tubing (Belmont Instrument Corporation, Billerica, MA, USA) was added where indicated. To minimize the volume of blood products required, the infusate was recirculated into the 3-L reservoir by cutting the single spike tubing and inserting each of the various IV catheters into the lumen of the tubing such that the tip hung freely inside the reservoir. Two catheters (the 9-Fr multi-lumen access catheter [MAC] and Trialysis catheters) were too wide for the spike tubing lumen and in this instance the infusate was collected in an empty normal saline (NS) bag prior to disposal. To minimize variation in hydrostatic pressure within the infusion circuit, the IV catheters' tips were set at the same height during each trial.

2.4 | Infusion fluids

Performance of the IV catheters was assessed using NS (Baxter, Deerfield, IL, USA) and a mixture of expired packed red blood cells (RBCs) and fresh frozen plasma (FFP) units at a ratio of 1:1 (R + F [1:1 mixture of RBCs and FFP]). The mean hematocrit of RBC units was 55% (personal communication, Esensten, J., Department of Laboratory Medicine, ZSFG). The mean (standard deviation) number of days beyond expiration date of the R + F was 4.83 (2.72) for RBCs and 9.17 (4.68) for FFP.

2.5 | Conduct of trials

The maximum flow rate achievable with each IV catheter and the pressure required to achieve them were measured using the RID's integral sensors. In catheters with two lumens of equal caliber, both lumens were assessed, otherwise only the largest bore lumen was assessed. All RIDs were within the service period, and the manufacturer has indicated that the device does not require regular calibration.

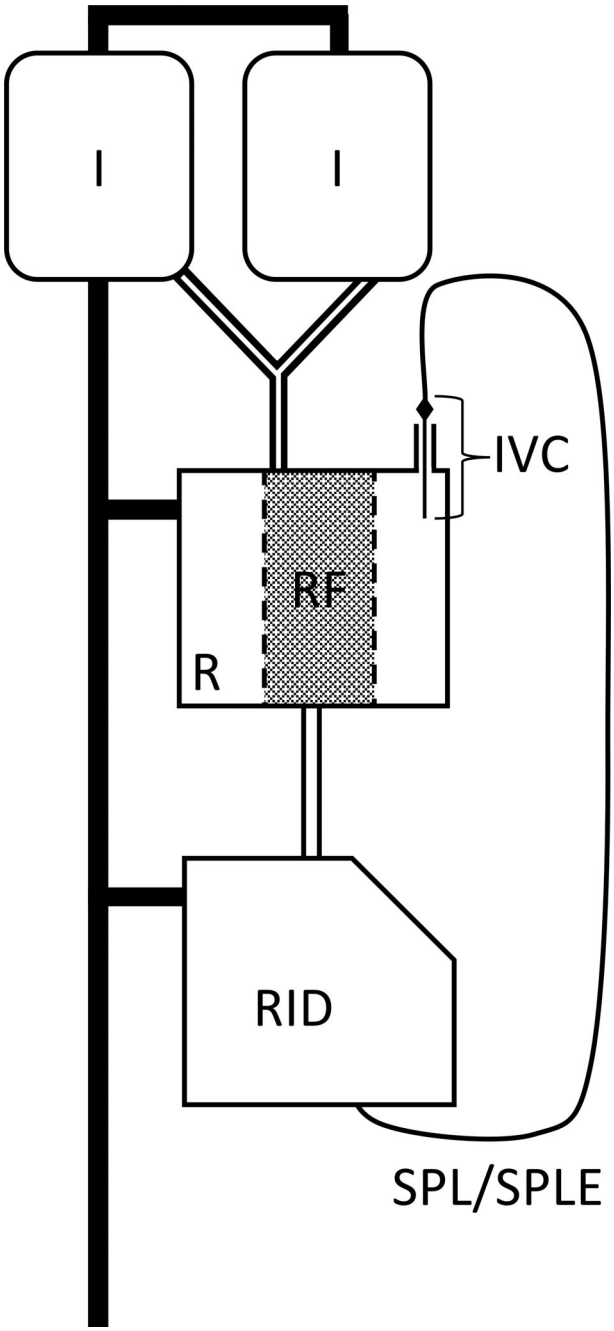

FIGURE 1 Schematic representation of infusion circuit (not to scale). I, infusate; IVC, intravenous catheter; R, 3-liter reservoir; RF, reservoir filter; RID, rapid infusion device; SPL, standard patient line; SPLE, standard patient line with extension

The sequence of trials was as follows: all catheters using NS and standard patient line (SPL) (NS group); all catheters using R + F and SPL (R + F group); all catheters using R + F, SPL, and patient line extension (R + F + E [R + F with patient line extension] group). This sequence was repeated on three different RIDs, using new infusate, reservoir, and patient lines each time.

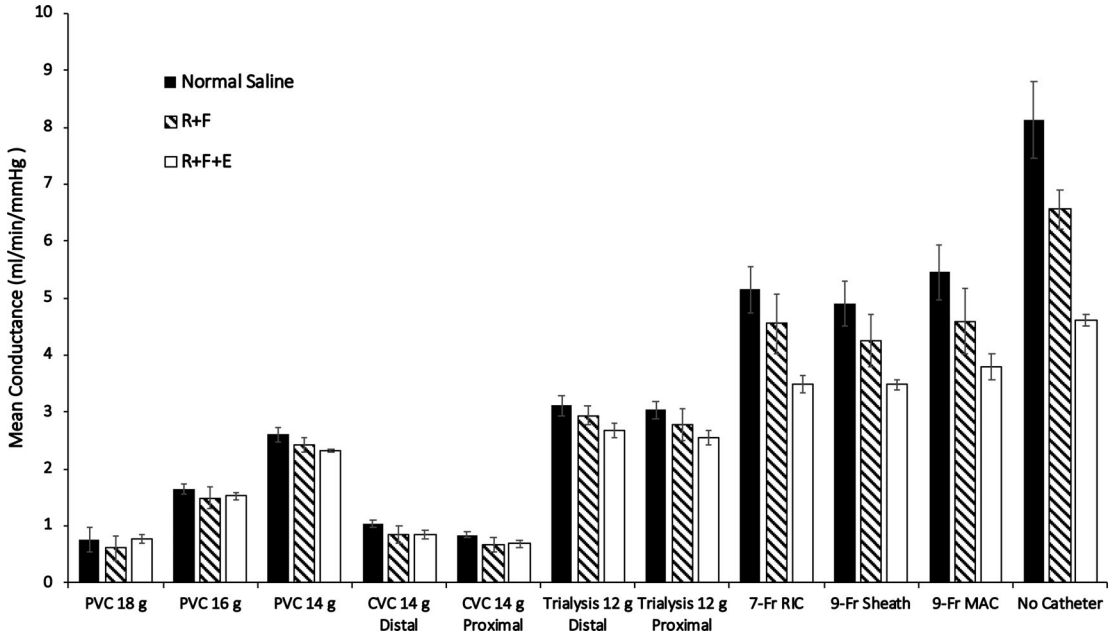

FIGURE 2 Mean conductance of each intravenous catheter using normal saline (NS), 1:1 mixture of RBCs and FFP (R + F), and R + F with patient line extension (R + F + E). Error bars indicate standard deviation. CVC, central venous catheter; MAC, multi-lumen access catheter; PVC, peripheral venous catheter; RIC, rapid infusion catheter; R + F, 1:1 mixture of RBCs and FFP; R + F + E, R + F with patient line extension

2.6 | Calculation of conductance

Several infusion circuit configurations achieved the RID's maximum flow rate of 1000 ml/min. Consequently, to normalize the data for analysis, the system conductance (ml/min/mmHg) was calculated as maximum flow (ml/min)/pressure at maximum flow (mmHg), in accord with previous work.[6]

2.7 | Statistics

Continuous data are presented as mean with standard deviation. Data analysis was performed with SPSS v23 (IBM, Endicott, USA). Analysis of variance tests were used for univariate analysis. The relationship between the infusion circuit configurations and conductance was assessed by multiple linear regression analysis. All independent variables were included in the model. All *p* values are two-tailed with an α level of .05. To ensure our inclusion of NS in the model did not affect potential relationships between catheter characteristics and conductance, linear regression was repeated with infusion circuits only using R + F as a sensitivity analysis.

3 | RESULTS

The addition of any catheter to the rapid infusion device (RID) reduced the maximum flow capabilities of the infusion circuit (Figure 2) and ranged from 4.6 ml/min/mmHg with the 9-Fr MAC to 0.6 ml/min/mmHg with the peripheral venous catheter (PVC) 18 g. Table 2 outlines the mean maximum flow rates and the pressures at which these were achieved for each configuration of the infusion circuit. Catheters with ID of 7-Fr or greater reached the 1000 ml/min maximum flow rate of the RID; all other catheters' maximum flow rates were restricted by the RID's integral pressure limitation of 300 mmHg. The conductance of R + F compared to NS was approximately 15% reduced in the larger bore catheters, whereas the difference was minimal in the smaller bore catheters.

The percentage increase in conductance due to increasing the ID of the IV catheter is illustrated by Table 3, using as a reference the PVC 18 g infusing R + F via a standard patient line without extension. Conductance was approximately sevenfold higher with the 7-Fr rapid infusion catheter (RIC) and 9-Fr catheters compared to the PVC 18 g. The only catheter that did not render a significant increase in flow capability was the proximal lumen of the central venous catheter (CVC) 14 g catheter.

In general, the addition of the patient line extension caused a reduction in conductance in the larger bore catheters of approximately 20% (Table 3); this reached statistical significance with the 9-Fr sheath and the 7-Fr RIC, but not the 9-Fr MAC. No significant difference was observed in conductance between NS and R + F infusions for any catheter tested.

TABLE 2 Mean maximum flow rate and required pressure for each infusion circuit configuration. Data expressed as mean (standard deviation)

	NS		R + F		R + F + E	
Catheter	Flow (ml/min)	Pressure (mmHg)	Flow (ml/min)	Pressure (mmHg)	Flow (ml/min)	Pressure (mmHg)
PVC 18 g	226 (65)	300 (0.00)	183 (63.31)	300 (0.00)	231 (22)	300 (0.00)
PVC 16 g	495 (30)	300 (0.00)	448 (57.52)	300 (0.00)	458 (20)	300 (0.00)
PVC 14 g	785 (37)	300 (0.00)	728 (41.63)	300 (0.00)	698 (7)	300 (0.00)
CVC 14 g Distal	311 (16)	300 (0.00)	253 (47.52)	300 (0.00)	255 (21)	300 (0.00)
CVC 14 g Proximal	251 (15)	300 (0.00)	198 (37.53)	300 (0.00)	205 (18)	300 (0.00)
Trialysis 12 g Distal	935 (55)	300 (0.00)	880 (50.00)	300 (0.00)	799 (38)	300 (0.00)
Trialysis 12 g Proximal	913 (45)	300 (0.00)	833 (83.12)	300 (0.00)	765 (35)	300 (0.00)
7-Fr RIC	1000 (0.00)	195 (15)	1000 (0.00)	221 (24)	1000 (0.00)	287 (12)
9-Fr Sheath	1000 (0.00)	204 (16)	1000 (0.00)	237 (24)	1000 (0.00)	287 (7)
9-Fr MAC	1000 (0.00)	184 (16)	1000 (0.00)	220 (27)	1000 (0.00)	264 (14)
No Catheter	1000 (0.00)	123 (10)	1000 (0.00)	152 (8)	1000 (0.00)	217 (4)

Abbreviations: NS, normal saline; R + F, 1:1 mixture of RBCs and FFP; R + F + E, R + F with patient line extension; PVC, peripheral venous catheter; CVC, central venous catheter; RIC, rapid infusion catheter; MAC, multi-lumen access catheter.

TABLE 3 Percentage difference in mean conductance with changes in catheter (compared with reference [PVC 18 g using R + F and standard patient line]), infusate (R + F vs. NS), and patient line extension (R + F vs. R + F with patient line extension)

	Catheter (%)	*p* value[a]	Infusate (%)	*p* value	Patient line extension (%)	*p* value
PVC 18 g	Reference		81	.455	127	.281
PVC 16 g	245	<.001	91	.281	102	.790
PVC 14 g	398	<.001	93	.156	96	.287
CVC 14 g Distal	138	.015	81	.116	101	.959
CVC 14 g Proximal	108	.833	79	.085	104	.791
Trialysis 12 g Distal	481	<.001	94	.269	91	.910
Trialysis 12 g Proximal	455	<.001	91	.217	92	.261
7-Fr RIC	746	<.001	88	.191	77	.029
9-Fr Sheath	697	<.001	87	.131	82	.044
9-Fr MAC	753	<.001	84	.116	83	.087

Abbreviations: NS, normal saline; R + F, 1:1 mixture of RBCs and FFP; R + F + E, R + F with patient line extension; PVC, peripheral venous catheter; CVC, central venous catheter; RIC, rapid infusion catheter; MAC, multi-lumen access catheter.
[a]*p* values from one-way ANOVA.

Multiple linear regression revealed a significant positive relationship between the internal radius of the catheter and conductance ($\beta = 1.098$, 95% CI 4.286–5.025, $p < .001$); this variable was the most predictive of conductance within the circuit (Table 4). Increasing catheter length was a significant independent predictor of reduced conductance ($\beta = -0.495$, 95% CI −0.007 to −0.005, $p = .001$). Use of R + F was associated with reduced conductance as compared to NS ($\beta = -0.107$, 95% CI −0.548 to −0.137, $p = .001$), as was the addition of the patient line extension ($\beta = -0.094$, 95% CI −0.505 to −0.095, $p = .005$). Neither use of a proximal port nor catheter material were significant predictors of conductance.

The model accounted for 93% of the variance observed in conductance (adjusted $R^2 = 0.931$) and assessment of the residuals confirmed normality and homoscedasticity and excluded multicollinearity. With the exception of catheter material, all independent significant predictors of conductance in the original model remained significant after excluding NS. The changes in

TABLE 4 Multiple linear regression of factors affecting conductance

	Unstandardized coefficients		Standardized coefficients			
Catheter	**B**	**SE**	***β***	**Lower 95% CI**	**Upper 95% CI**	***p* value**
Internal radius	4.656	0.186	1.098	4.286	5.025	<.001
Catheter length	-0.007	0.001	−0.540	−0.008	−0.006	<.001
Catheter lumen	−0.051	0.131	−0.014	−0.210	0.312	.697
Infusate	−0.343	0.107	−0.107	−0.556	−0.130	.002
Extension line	−0.300	0.107	−0.094	−0.513	−0.087	.006
Catheter material	0.254	0.165	0.067	−0.078	0.587	.132

Note: Reference categories for categorical variables were distal lumen for catheter lumen, normal saline (NS) for Infusate, no patient line extension for extension line, and fluorinated ethylene propylene (FEP) for catheter material.

catheter internal radius retained the strongest effect on conductance ($\beta = 1.113$, 95% CI 4.003–4.6876, $p < .001$).

4 | DISCUSSION

The flow capabilities of the IV catheters tested using R + F were predominantly governed by their internal radius. Catheter length was also an important determinant and likely accounts for the smaller bore 7-Fr RIC performing equal to the 9-Fr sheath; however, an additional potentially contributing factor is the turbulence-inducing 90-degree turn built into the sheath. These data support the widespread practice of inserting short, wide catheters for massive transfusions in surgical, obstetric, and trauma patients and underscore the unsuitability of standard CVCs for large volume resuscitations.

The addition of the patient line extension had a significant effect on the conductance of large bore catheters, in accord with previous work.[7] In smaller catheters, the flow was likely restricted to such a degree by the inner catheter diameter that additional resistance from increased path length had little relative impact on the overall resistance within the infusion circuit, as previously hypothesized.[8] The conductance of wider bore catheters was reduced by approximately 20% by adding the patient line extension, and this could have notable clinical implications for centers that include the patient line extension in their standard massive transfusion system. Additionally, the lower flows afforded by the patient line extension likely caused the infusate to cool, therefore increasing viscosity and further decreasing flow. While not tested in our study, Y-shaped extension tubing that can connect a RID to two IV catheters is commercially available. A system such as this would likely increase flow and/or reduce driving pressure.

As anticipated, the rheological differences of R + F reduced the flow capabilities of our infusion circuit as compared to NS; however, the impact was clinically significant only in large bore catheters. A previous model incorporating NS, RBCs, and a Level 1 RID to assess pediatric IV catheters achieved equivalent maximum flow rates to those observed in the current study when NS was infused through comparable cannulae.[9] However, the flow rates attained in our study using R + F (approximate hematocrit of 27.5%) were higher than theirs using RBCs (reported hematocrit of 70%), likely due to the proportional effect of hematocrit on viscosity.[10] A clinical correlate to this point would be the order in which blood products are administered during hemostatic resuscitation. In many centers, massive transfusion blood products are delivered in approximately a 1:1 ratio of FFP and RBCs; as such it may be beneficial to maximum achievable flow rates to add these in an alternating fashion to the RID reservoir, rather than sequentially.

A decrease in temperature from 36.5°C to 22.0°C has been shown to increase viscosity by 26.13% in blood.[11] Beebe *et al*[9] documented a temperature of 27.1°C in their infused RBCs using a Level 1 brand RID. The Belmont RID used in this study affords greater efficiency at warming fluids to physiologic temperatures at high flow rates,[12] potentially contributing to the higher flow rates achieved here.

Due to its ability to influence the laminarity of flow, catheter material has been suggested to affect flow rates[2]; therefore, the lack of an independent association between material and conductance was surprising. Fluorinated ethylene propylene (FEP) has a lower coefficient of friction than polyurethane (PU),[1] so in theory it should achieve greater flows. This may be attributable to confounding because the catheters composed of PU were also the wider bore catheters.

A limitation of our in vitro model was our inability to account for downstream pressure at the point at which infused fluids enter the venous system of the patient. The differential between the driving pressure generated by the RID and downstream pressure is what generates flow, and in our model this was at atmospheric pressure. A previous study employed the use of a standing water

column at 10 cm H_2O to represent this pressure,[2] but our access to blood products was limited and this would have prevented us from employing our recirculation technique. Other models calculated flow by measuring the volume infused over 30 s.[9] This method would lead to an underestimation of maximum flow rates using the Belmont as it accelerates flow until the desired rate has been reached or it becomes restricted by pressure limitation. Again, this would also have precluded our recirculation technique. Previous studies also compared their findings with the manufacturer's quoted maximum flow rates[4]; however, our use of the RID and wide bore tubing render this comparison less meaningful.

Early work noted a pressure of approximately 8 mmHg in superficial veins of the median cubital fossa.[13] Experience and physiological first principles suggest that in the volume-depleted patient this would be much reduced; however, peripheral venous pressure may be higher than anticipated during hypovolemic shock due to segmental constriction of the veins.[14] The 7-Fr RIC achieved the second highest conductance of the lines assessed, greater than the 9-Fr sheath or the Trialysis catheter. However, given that the RIC is inserted peripherally and the others centrally, it is possible that it would be subjected to greater back pressure in vivo and as such our model may have overestimated its flow rate relative to the other catheters. With many of the wide bore catheters achieving the maximum flow rates the RID could deliver, the conversion to conductance served a useful function as it permitted ranking of the catheters. While variations in pressure required to achieve 1000 ml/min may not be clinically significant, once downstream pressure is encountered in vivo they may become so. Nonetheless, the short 7-Fr RIC catheter may provide an equivalent flow rate to a wide-bore central venous catheter in patients with conditions associated with vasodilation undergoing procedures with a high risk of major hemorrhage, such as obstetric patients or liver transplant recipients.

Our study builds upon recent work performed by Berman *et al*[5] who analyzed the flow of blood products through similar catheters. While this group arrived at similar conclusions to ours, individual blood products at room temperature were employed. The use of warmed, mixed blood products, via a RID in the current study may better represent the clinical conditions encountered during massive transfusions.

Our RIDs were up to date in servicing and the manufacturer notes that no regular calibration is required. Nonetheless, we analyzed each configuration of the infusion circuit on three separate RIDs. While this should have minimized the potential for experimental error and the effect of any imprecisions in the flow, pressure, or temperature sensors of the RIDs, independent measurements of these parameters were not performed. Therefore, we are unable to rule out internal inaccuracies caused by variation in RID function. Likewise, independent measurements of catheter ID were not performed. Thus, we cannot rule out inaccuracies in the manufacturer-stated inside diameter, which may have affected our calculation of conductance.

Use of expired blood products and their recirculation back into the RID reservoir enabled us to perform this trial efficiently, with no wastage of a valuable resource. Although the storage lesion present in products of this age is likely to have affected the membranes of our RBCs and the biochemical constituency of the suspending solution,[15] it is unclear how this would impact the rheology of our products. Studies have shown a negative effect of older RBCs on in vivo blood flow through alterations in microvascular structure[16] but there are no data on the ex vivo hemorheology of expired products. Lastly, we cannot rule out the occurrence of cell lysis during the recirculation experiment because assessment of RBC stability, such as serial hematocrit measurements, was not performed.

We evaluated a commercially available RID and wide catheter selection using a commonly transfused ratio of RBCs and FFP in our study. However, our findings may not directly apply to centers using different devices, different blood product processing methods, or favoring a transfusion ratio other than 1:1 RBC:FFP. In addition, we did not study the limitations to flow that would be predicted by insertion of catheters or central pressure monitors into the 9-Fr sheath or 9-Fr MAC catheters. We anticipate that future studies utilizing alternative systems will produce different flows and/or pressures that will be consistent with our findings overall.

To our knowledge, there are no other studies evaluating IV catheter performance using blood products in ratios typically seen during massive transfusion in trauma, obstetric, or surgical resuscitation. Data presented here may help clinicians deliver optimal hemostatic resuscitation of critically bleeding patients by maximizing the achievable blood product flow rate.

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CONFLICT OF INTEREST

Milne (None); Teng (None); Vargas (None); Markley (None); Collins (None).

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