Field-expedient thawing of fresh-frozen plasma

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INTRODUCTION: Frozen plasma is superior to crystalloids for hemorrhage resuscitation but remains logistically challenging in austere environments because of specialized clinical equipment for on-demand thawing. This research examines some ad hoc thawing techniques that have been implemented by military medical personnel.

METHODS: Fresh-frozen plasma (FFP) units were thawed accordingly: using a slow cooker (three temperature settings) with preheated or room temperature water; affixing flameless ration heaters from meals ready-to-eat (MREs) to FFP and submerging in water; exposing FFP to electric kettle-boiled water; incubating with a sous vide immersion circulator; or using a clinical thawer (control). Hemostatic function, thrombin generation, factor activities, and essential chemistry were measured after thawing.

RESULTS: Even at the highest temperatures, without preheated water the slow cooker doubled thawing time (62.5 min vs. control, 32.5 min; $p < 0.0001$), and the final temperature was 13.5°C versus 28.8°C in control ($p < 0.01$). When preheated, the slow cooker thawed in 31.3 minutes ($p < 0.05$), with a final temperature of 22.4°C. Kettle-boiled water thawed in 23.0 minutes with a final temperature of 25.1°C. The sous vide thawed in 28.1 minutes, with a final temperature of 20.2°C. MRE heaters were insufficient. Functional measures were similar in all conditions.

DISCUSSION: In emergencies, protracted plasma thawing is unacceptable, and slower thawing methods also produced cryoprecipitate. Although no functional changes were observed with boiled water thawing, potential negative physiological impacts must be examined. Safe, controlled thawing can be obtained with the sous vide, although optimization requires further testing.

Prehospital resuscitation is of critical importance for maximizing survivability following hemorrhage, and several studies have recognized that resuscitation with blood products is superior to using crystalloid solutions for damage control resuscitation.[1–5] While whole blood may be best to replace that which has been lost, it is difficult to maintain in sufficient quantities, and its usage is limited despite evidence suggesting its superiority to other resuscitation solutions in many instances.[6–8] Until whole blood is widely available, freeze-dried plasma, oxygen carriers, and other adjuncts may become a significant part of resuscitation strategies in austere environments. Liquid, never-frozen plasma (or prethawed plasma) is also an available asset, but its usage outside the hospital is impractical due to its 5-day shelf life. In the meantime, however, refrigerated red blood cell (RBC) concentrates and frozen plasma make up the largest bulk of available blood products in rural or forward locations.

RBC concentrates and frozen plasma are not without their own logistical complications. Frozen plasma in particular

ABBREVIATIONS: aPTT = activated partial thromboplastin time; ASBP = Armed Services Blood Program; CT = clotting time; FFP = fresh-frozen plasma; FV = factor V; FVIII = factor VIII; MCF = maximal clot firmness; MREs = meals ready-to-eat; PT = prothrombin time; ROTEM = rotational thromboelastometry; TCMC = Tactical Combat Medical Care; USAISR = US Army Institute of Surgical Research.

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requires both freezer capability for functional preservation as well as on-demand thawing, an easily overlooked but critical requirement for usage of the product. The timing of thawing is essentially bounded with upper and lower limits: excessively long thawing is adverse for the patient awaiting transfusion and detrimental to the plasma itself, as slowly thawing plasma at low temperatures creates cryoprecipitate[9]; but too rapidly thawing the plasma can also damage coagulation enzyme function, rendering the product ineffectual in its intended purpose.

In the hospital, thawing the plasma at an optimal 37°C is trivial because specially designed devices can easily accomplish this feat in 30 minutes or less. But if frozen plasma is to be used closer to the point of injury, whether that be at the scene of a severe car accident or the front lines of a war zone, more portable solutions are required. In the US military, deployed physicians and medics have frequently resorted to improvised methods of thawing plasma; several of these ad hoc methods have been collected and are taught at the US Army's Tactical Combat Medical Care (TCMC) training course (described below in "Methods"). Questions were raised by the Armed Services Blood Program (ASBP) to the Coagulation and Blood Research group at the US Army Institute of Surgical Research (USAISR) as to whether these "field-expedient" plasma thawing methods had a negative impact on the plasma function, and this paper describes the results of in vitro assays performed on plasma thawed with use of a selection of these methods.

METHODS

Plasma

Sixty-five units (250 mL) of deidentified fresh-frozen plasma (FFP) were acquired from ASBP, kept frozen during overnight shipping to USAISR, and stored at −20°C until the day of testing. Sixty FFP units were Group O, with five of those being Rh negative; and five FFP units were Group A, with one of those being Rh negative.

Clinical plasma thawer

A clinical plasma thawer (DH8, Helmer Scientific) was used as the control FFP thawing technique (n = 8). This device is designed to hold a constant water temperature even with up to 8 units of FFP in the bath (only two were thawed simultaneously in these studies). For FFP thawing, the temperature was set to a constant 37°C with automated agitation to reduce thawing time. When room temperature water was added to the bath, it required 35 min to reach 37°C.

Slow cooker

The basin of a slow cooker with 3-quart (2.84 L) capacity (model 33236, Hamilton Beach) was filled with 1.3 L of purified room-temperature water and set to one of its three settings, labeled "keep warm" (W), "low" (L), and "high" (H). FFP was added to the water immediately as described below. In a follow-up study, 1.3 L of purified water was prewarmed for 1 hour with each of the three cooker settings. Without addition of FFP, time required to reach maximum temperature was 5 hours (39°C, W), 3 hours (55°C, L), or 2.5 hours (60°C, H). These time requirements were outside of the required usage window, so alternatively, by using both room temperature and 1-hour preheated water, the scenarios of immediate need and advanced warning for plasma need were simulated. FFP was added to the water either immediately (n = 4 for each setting) or after 1 hour of preheating (n = 8 each).

Electric kettle

An electric kettle (model K4097, Proctor Silex), was filled to capacity with 1.7 L of purified water and activated to boil the water. Approximately 7 minutes were required to reach temperature peak (100°C), at which time the water was poured into the same basin used for the slow cooker until half full. FFP was added to the water immediately as described below (n = 8).

Sous vide immersion circulator

A sous vide immersion circulator (EH800D51, All-Clad Metalcrafters) was placed in an 8-L plastic basin filled with 4.5 L of tap water and set to 37°C. The time required for the device to heat the water to 37°C before the addition of FFP was 5 minutes. FFP was added either simultaneously with activation of the device (n = 3) or after 7 minutes of preheating the water (n = 4).

Chemical heating element

The contents of Department of Defense–issued meals ready-to-eat (MREs; Ameriqual Packaging) were removed from the packaging and discarded, aside from the flameless ration heater. These strips contain magnesium powder that, when mixed with water, produces an exothermic reaction intended to heat the food of the MRE. Anecdotally, the MRE heaters have been used to thaw plasma. Several configurations were implemented to attempt to replicate this scenario. The empty MRE plastic outer packaging was either 1) left empty, 2) filled one-quarter, or 3) filled one-half with room-temperature water. Then, either one or two MRE chemical heating elements were placed in the bag adjacent to a single FFP unit—in the no-water scenario, the element was first dampened, and if using two elements, one was placed on either side of the FFP unit. In all cases, temperatures were monitored, but the FFP units were unable to thaw before the expiration of the MRE chemical heating element, so most runs were terminated early and no further testing was done with this method.

Temperature monitoring

For both slow cooker and electric kettle methods, 2 units of FFP were placed into the water and allowed to thaw with

manual agitation every 5 to 10 minutes. The temperature of the water bath was monitored with an alcohol thermometer (Bronwill Scientific), and the exteriors of the plasma bags were monitored with a dual-probe digital thermometer (52 II, Fluke); one lead was taped to each plasma bag to maintain consistency over the duration. The final temperature of plasma was measured by collecting a sample from the bag into a 4.5-mL tube immediately after thawing and measuring temperature directly.

Transfusion filtration

While assays were conducted on the thawed FFP directly from its original storage bag, normally plasma is filtered during the transfusion process. During thawing, some samples, particularly those obtained from using the slow cooker's lowest setting (W), had observable precipitate formation. To determine what effects filtration of the precipitate formed when thawing with the W setting would have on plasma, samples were collected before and after passing through a standard 200-µm transfusion filtration set (10010985; BD Carefusion), then subjected to the assays described below (n = 6).

Functional analysis

Thawed plasma was characterized using a variety of clinical point-of-care and research use–only assays. Essential chemistry values (including pH, bicarbonate, and lactate) were collected from thawed plasma with a handheld blood analyzer (i-STAT, CG4+ cartridges, Abbott Laboratories). Prothrombin time (PT), activated partial thromboplastin time (aPTT), factor V (FV) activity, factor VIII (FVIII) activity, and fibrinogen concentration were measured from thawed FFP with a coagulation analyzer (STA-R Evolution, Diagnostica Stago). Global coagulation function was measured by rotational thromboelastometry (ROTEM) using the EXTEM assay on the ROTEM delta (Instrumentation Laboratory). Finally, thrombin generation was measured by calibrated automated thrombogram assay by mixing

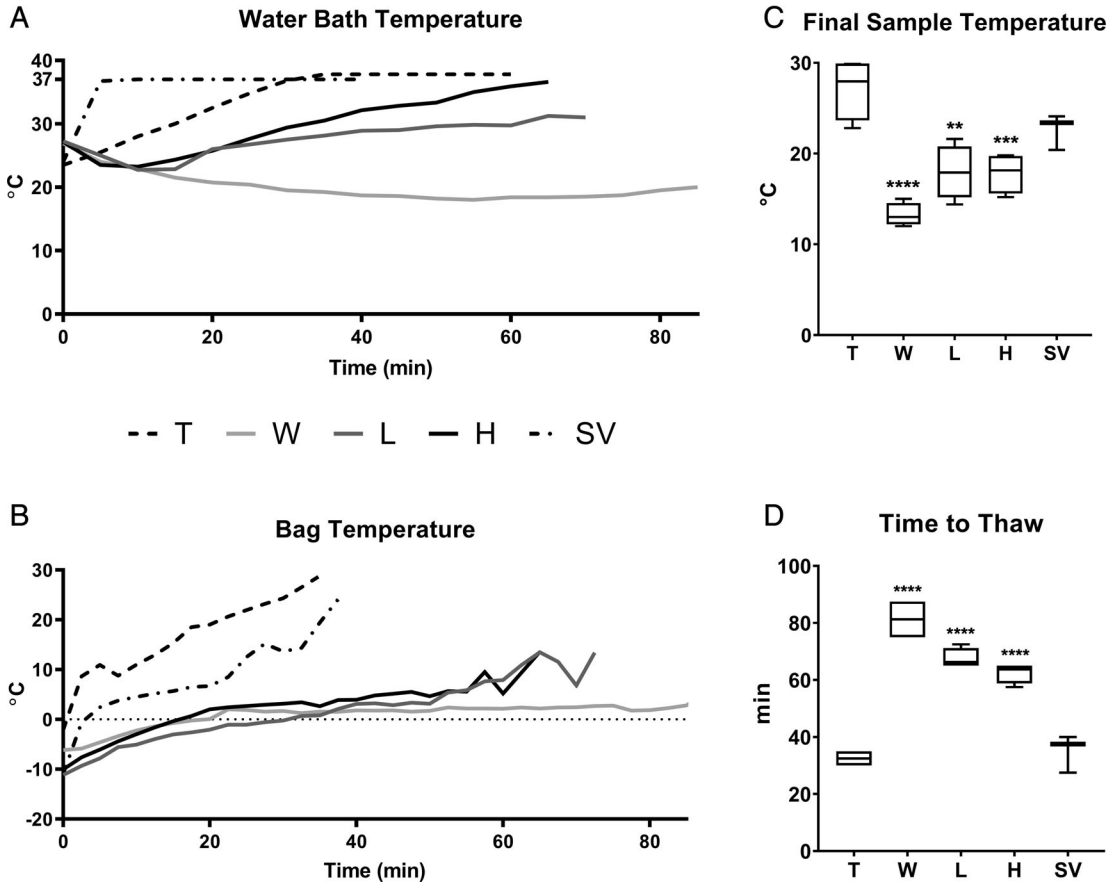

Fig. 1. Temperature kinetics in tests without prewarmed water. Room-temperature water was exposed to heat and two FFP units simultaneously. (A) Water temperature and (B) FFP bag exterior temperature were monitored over the duration of thawing. Means are shown in both cases. (C) Final temperatures of the plasma after thawing and extraction showed that the slow cooker could not reach the same temperature as the clinical thawer at any setting. (D) The time to thaw with the slow cooker, regardless of setting, was significantly longer than the clinical thawer. H = slow cooker high; L = slow cooker low; SV = sous vide; T = clinical thawer; W = slow cooker keep warm. **p < 0.01 versus control (T); ****p < 0.0001 versus T.

samples with platelet-poor plasma–low reagent and FluCa buffer (Diagnostica Stago) and collecting thrombograms on a microplate fluoremeter (Fluorskan Ascent FL, Thermo-Fisher Scientific), which were analyzed using computer software (Thrombinoscope BV).

Statistical analysis

One-way analysis of variance with Tukey's multiple comparisons test was used to determine significance of difference between groups. Paired t tests were used to determine the significance of differences in filtered and unfiltered samples.

RESULTS

Thawing kinetics: no prewarming

The first set of studies started with FFP units submerged in room-temperature water together when heating began (Fig. 1). The temperature of the water in the clinical thawer increased steadily, requiring the same 35-minute time period to reach 37°C as it did without the FFP present, while water temperature in the slow cooker bath initially declined with the introduction of FFP (analogous to a large block of ice) before increasing more gradually (Fig. 1A). The sous vide raised the water temperature more rapidly, requiring only 5 minutes to reach 37°C.

Exterior bag temperature of the FFP was initially −7.3 ± 4.1°C (Fig. 1B). With the clinical thawer, this temperature reached 28.8 ± 3.3°C after 35 minutes. With the W setting, a nearly steady-state temperature between 1.5 and 2.5°C on the FFP exterior was reached by 25 minutes and maintained until the 80 minutes mark, while the FFP bag temperature increased to 13.5 ± 5.3°C by 65 minutes with both L and H settings. Using the sous vide immersion circulator, the bag temperature was 24.1 ± 4.0°C after 35 minutes. After thawing was complete (no noticeable solid), final plasma temperatures were recorded as 27.2 ± 3.4°C (T), 13.3 ± 1.3°C (W), 18.0 ± 3.0°C (L), 17.8 ± 2.2°C (H), and 22.6 ± 2.0°C (SV); all three slow cooker values were statistically significantly different from the clinical thawer (Fig. 1C). Mean required times to thaw

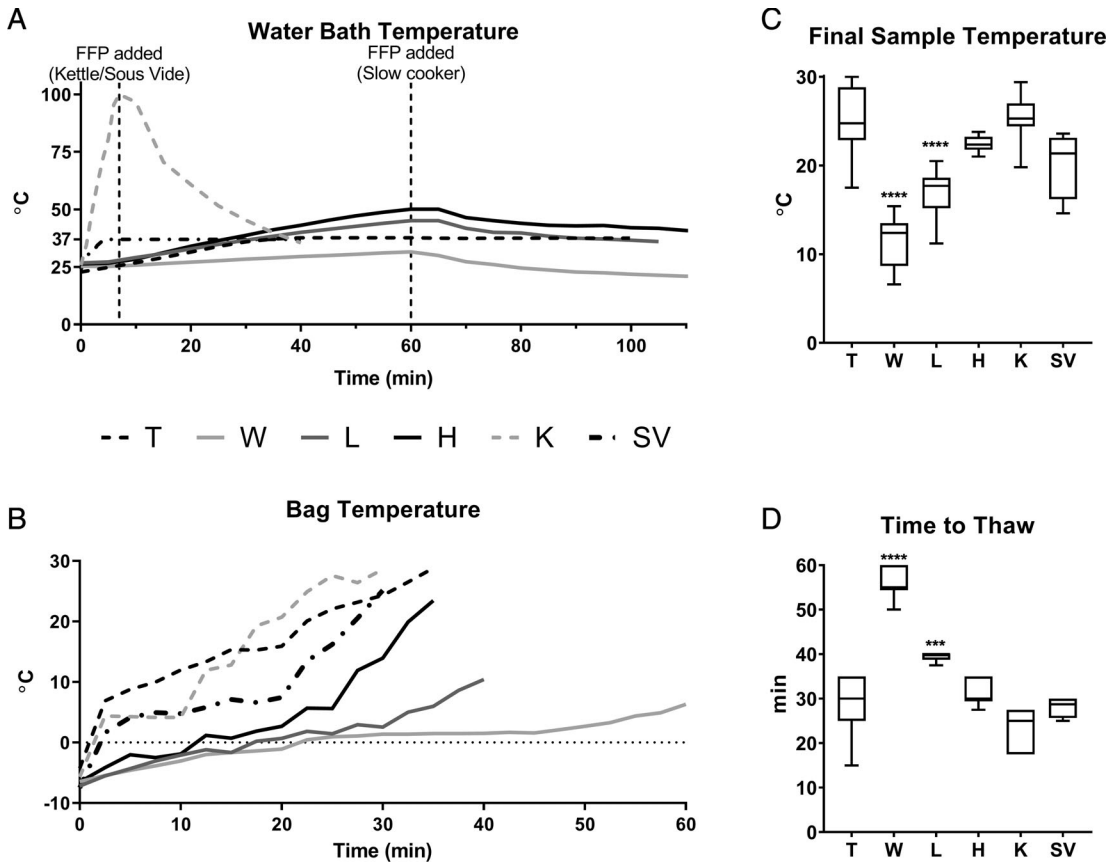

Fig. 2. Temperature kinetics were measured in tests where clinical thawer and slow cooker were preheated for 1 hour and electric kettle water was heated to boiling over 7 minutes. (A) Mean water temperatures are shown with indicators of FFP addition. (B) Mean FFP bag exterior temperature was measured beginning from FFP addition. (C) Final temperatures of plasma were significantly lower in the W and L thawed FFP, but H and K were able to reach temperatures similar to T. (D) Thawing time was also significantly slower in the W and L. H = slow cooker high; K = electric kettle; L = slow cooker low; SV = sous vide; T = clinical thawer; W = slow cooker keep warm. ***p < 0.001 versus T; ****p < 0.0001 versus T.

were 32.5 ± 2.9 minutes (T), 81.3 ± 7.2 minutes (W), 67.5 ± 3.5 minutes (L), 62.5 ± 3.5 min (H), and 35.0 ± 6.6 minutes (SV); again, the slow cooker times were significantly different from the clinical device (Fig. 1D).

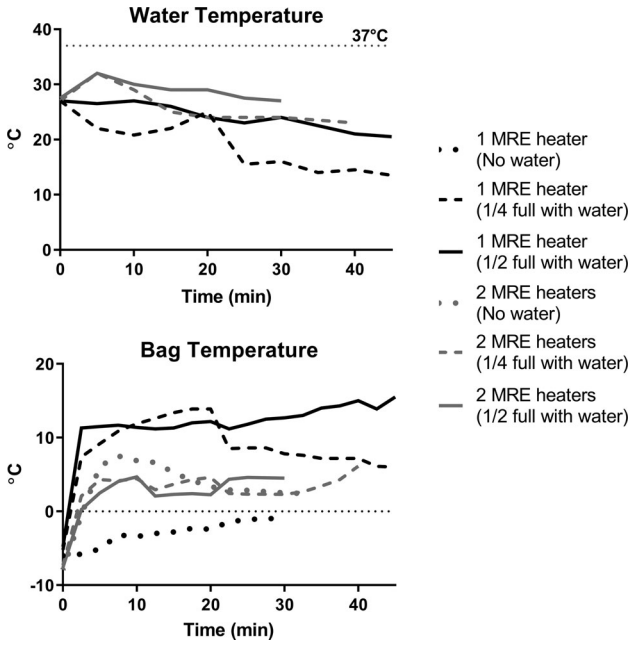

Fig. 3. MRE heaters were activated with water and placed on one or both sides of the FFP unit within the MRE outer packaging, with or without water also in the packaging. Temperatures of both water and bag exterior were measured when possible. Means at each time point are shown.

Thawing kinetics: prewarmed water

Follow-up studies used water preheated for up to 1 hour prior to the addition of FFP for thawing (Fig. 2). The clinical plasma thawer was already at target temperature, but the slow cooker temperatures were still increasing. FFP was added to the sous vide water bath after it reached temperature in approximately 4.5 minutes. The electric kettle's water was poured into the bath immediately after boiling (requiring only 7 min instead of 1 hour) and FFP was added without delay (Fig. 2A). With the clinical thawer and sous vide, water temperature remained constant (37°C) throughout the thawing process. However, with the slow cooker (regardless of setting), the water temperature dropped throughout thawing, limiting the rate of thawing. With the kettle, there was a precipitous drop in water temperature immediately after adding the FFP, but it remained above 37°C until thawing was completed.

Exterior FFP bag temperatures steadily increased over thawing, although the slow cooker–thawed samples that used the W setting produced a similar pattern as was observed without prewarming, with a nearly steady-state temperature between 1.3 and 1.6°C over the period between 30 and 45 minutes (Fig. 2B). Conversely, the exterior FFP bag temperature continued to rise after the 25-minute mark when using the L and H settings in the slow cooker due to higher starting water temperatures. The clinical thawer and water from the kettle both produced similar temperature curves (paired t test: p = 0.97). Final plasma temperatures were 24.8 ± 4.0°C (T), 11.3 ± 3.1°C (W), 16.9 ± 2.9°C (L), 22.4 ± 0.9°C (H), 25.1 ± 2.7°C (K), and 20.2 ± 3.9°C (SV); both W and L settings produced final FFP temperatures that were significantly lower versus those in the clinical thawer (Fig. 2C). The mean required times to thaw were 27.9 ± 7.0 minutes (T),

TABLE 1. Hemostasis and chemistry parameters of thawed FFP

		T	W	L	H	K	SV
PT (sec)	I	14.7 ± 0.3	13.8 ± 0.6	14.5 ± 0.8	14.0 ± 0.5		14.7 ± 0.7
	P	14.9 ± 0.5	15.0 ± 1.5	14.5 ± 1.0	14.5 ± 0.7	15.2 ± 1.5	14.9 ± 0.5
aPTT (sec)	I	34.7 ± 2.1	38.1 ± 5.0	36.2 ± 3.0	36.0 ± 2.1		31.8 ± 1.1
	P	35.7 ± 1.8	35.7 ± 4.3	36.0 ± 4.8	35.9 ± 5.1	37.9 ± 4.4	32.6 ± 2.3
Fibrinogen (mg/dL)	I	298.3 ± 30.7	260.3 ± 34.2	242.3 ± 37.5	262.3 ± 46.2		266.0 ± 30.0
	P	264.9 ± 48.8	236.0 ± 43.1	278.9 ± 59.6	246.5 ± 52.4	237.4 ± 24.7	289.0 ± 32.3
FV (%)	I	72.8 ± 20.8	101.5 ± 10.7	74.0 ± 18.8	79.5 ± 7.2		87.5 ± 14.3
	P	72.4 ± 13.9	84.1 ± 15.6	87.8 ± 20.5	90.3 ± 13.9	71.8 ± 14.2	77.7 ± 16.1
FVIII (%)	I	89.3 ± 18.9	56.8 ± 21.8	68.5 ± 24.5	64.8 ± 21.4		76.8 ± 13.4
	P	85.5 ± 15.1	69.5 ± 28.6	73.6 ± 28.6	77.4 ± 20.1	65.6 ± 21.5	97.8 ± 30.2
pH	I	7.3 ± 0.0	7.4 ± 0.0**	7.4 ± 0.0*	7.3 ± 0.0		7.5 ± 0.1
	P	7.3 ± 0.0	7.3 ± 0.1	7.4 ± 0.1	7.4 ± 0.0	7.41 ± 0.1	7.4 ± 0.1
HCO_3 (mM)	I	21.8 ± 1.7	20.8 ± 2.3	20.9 ± 0.7	22.8 ± 2.0		20.0 ± 2.6
	P	20.5 ± 2.5	20.2 ± 2.4	19.7 ± 2.0	19.4 ± 1.2	18.0 ± 0.8	20.6 ± 1.0
Lactate (mM)	I	3.8 ± 1.2	1.6 ± 0.6**	2.6 ± 0.5	3.1 ± 0.6	2.84 ± 0.7	4.24 ± 1.0
	P	3.6 ± 1.0	3.9 ± 0.7	3.4 ± 0.6	3.0 ± 0.7		5.3 ± 1.1**

* p < 0.05, ** p < 0.01 (vs. matched value thawed in T).
aPTT = activated partial thromboplastin time; FFP = fresh-frozen plasma; FV = factor V; FVIII = factor VIII; H = slow cooker high; I = immediate thawing; K = electric kettle; L = slow cooker low; P = prewarmed before thawing; PT = prothrombin time; SV = sous vide immersion circulator; T = clinical thawer; W = slow cooker keep warm.

56.0 ± 3.4 minutes (W), 39.5 ± 1.1 minutes (L), 31.3 ± 3.1 minutes (H), 23.0 ± 4.4 minutes (K), and 28.1 ± 2.4 minutes (SV); both W and L settings took significantly longer to thaw than the clinical thawer (Fig. 2D).

MRE chemical heating elements

When a single MRE chemical heating element was used inside the MRE outer packaging, the water temperature declined from an initial peak of 27.0°C linearly over the duration of the element; with two elements, the temperature increased over the first 5 minutes to a peak of 32.0°C before declining linearly over the remaining heating period (Fig. 3). The temperature declined less rapidly with the larger water volume (half-filled bag vs. quarter-filled) regardless of whether one or two elements were used. The maximum exterior FFP bag temperature (measured between heating element and the frozen bag) was 15.5°C (Fig. 3), and the FFP never sufficiently thawed for further analysis.

Thawed plasma function

Samples thawed by clinical plasma thawer, slow cooker (all settings), and electric kettle were subjected to a set of assays to determine functional performance. The hematology analyzer measured no significant differences in PT, aPTT, FV, or FVIII activity in FFP samples thawed in the clinical thawer or slow cooker (at all settings) without prewarming, but the pH values of W (7.4 ± 0.02; $p < 0.01$) and L (7.4 ± 0.04; $p < 0.05$) thawed samples were slightly but significantly different than the control (7.3 ± 0.04), as was the lactate level in W thawed samples (1.6 ± 0.6 mM vs. 3.8 ± 1.2 mM in control; $p < 0.01$) (Table 1). In samples placed in prewarmed baths, there were no significant differences measured in PT, aPTT, FV, FVIII, fibrinogen, pH, or bicarbonate between any of the samples, but the lactate in the sous vide (5.3 ± 1.1 mM) was significantly different than in the control thawer (3.6 ± 1.0 mM; $p < 0.01$). The clinical significance of this lactate level difference is unknown. Additionally, no differences in these values were observed

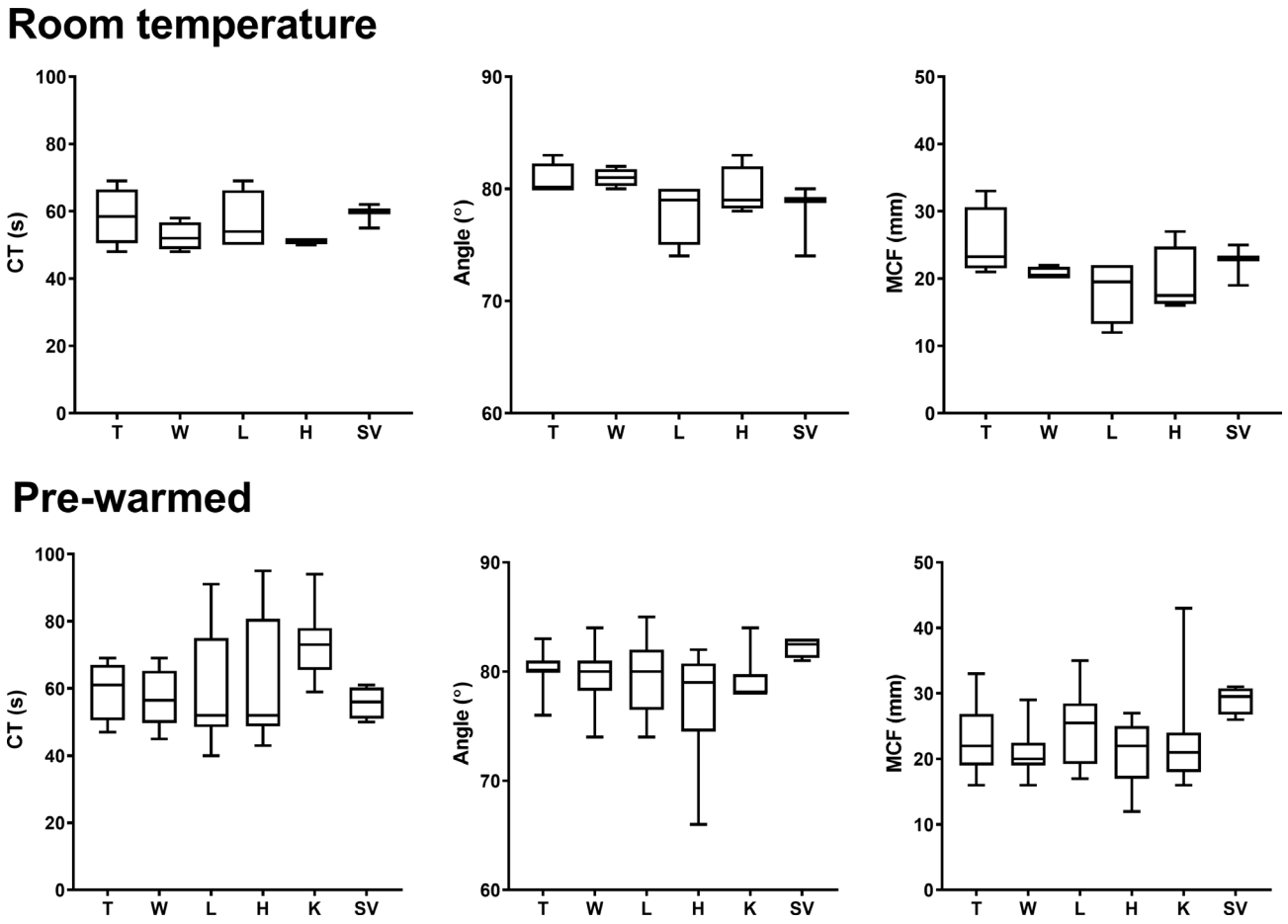

Fig. 4. ROTEM coagulation function of thawed FFP. No statistically significant differences were observed regardless of whether samples were thawed without prewarming (top) or with water that had been prewarmed for up to 1 hour before addition of FFP (bottom). CT = clotting time; H = slow cooker high; K = electric kettle; L = slow cooker low; MCF = maximal clot firmness; SV = sous vide; T = clinical thawer; W = slow cooker keep warm.

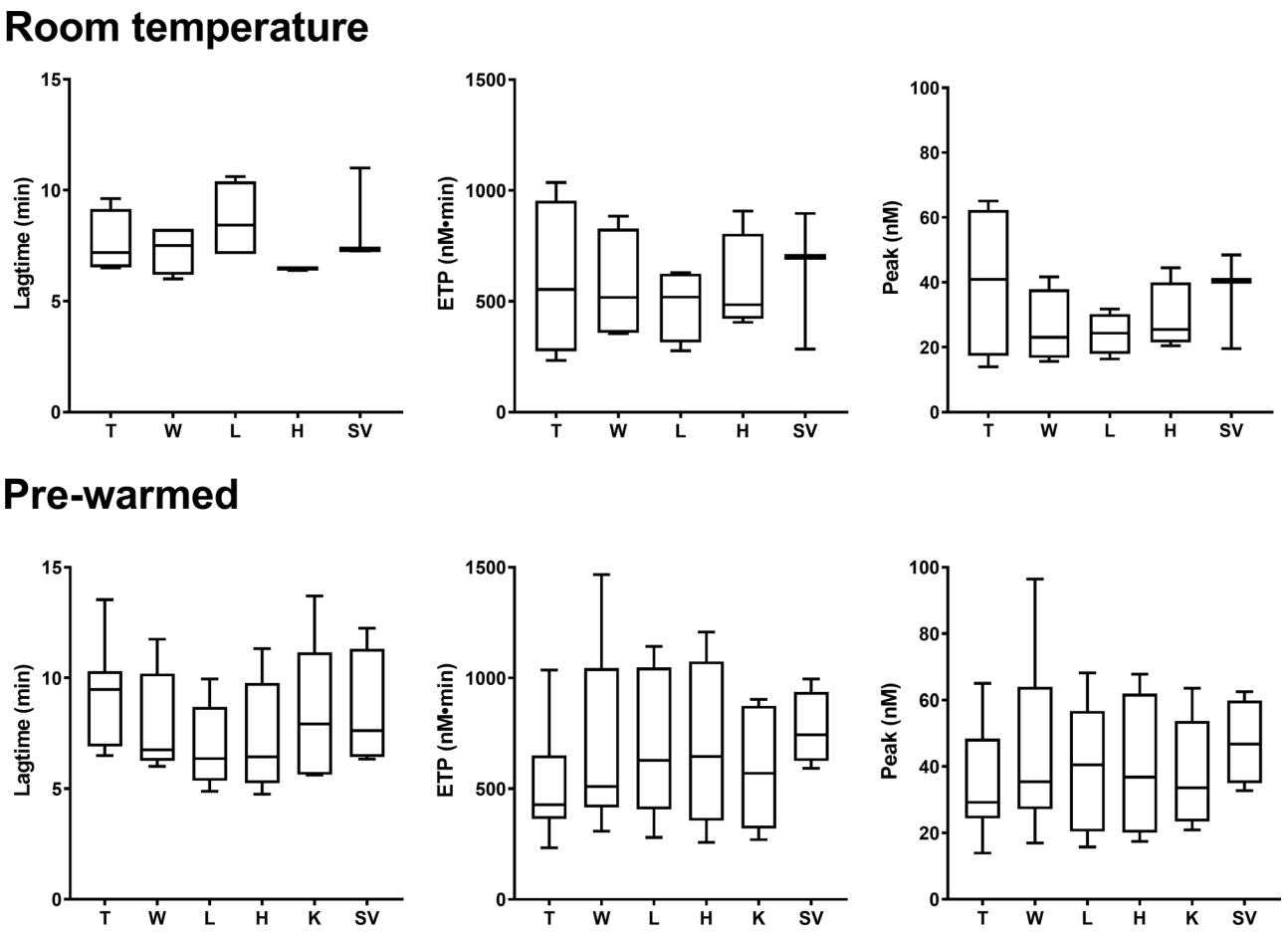

Fig. 5. Thrombin generation tests on thawed FFP. No statistically significant differences were observed regardless of whether samples were thawed without prewarming (top) or with water that had been prewarmed for up to 1 hour prior to addition of FFP (bottom). ETP = endogenous thrombin potential; H = slow cooker high; K = electric kettle; L = slow cooker low; SV = sous vide; T = clinical thawer; W = slow cooker keep warm.

between immediate thawing and prewarmed thawing in any given thawing method.

With respect to clot formation, no significant differences were observed in ROTEM clotting time (CT), rate of clot formation (angle), or maximal clot firmness (MCF) for samples without prewarming or samples with prewarming of the water in any of the thawing methods (Fig. 4).

There were no statistically significant differences in thrombin generation test parameters between thawing conditions, regardless of prewarming (Fig. 5).

Filtration effects

Standard transfusion filtration of the precipitate observed following thawing at the W setting on the slow cooker showed only minor changes in the results of assays (Table 2). Only the aPTT assay showed a significant difference between filtered and unfiltered samples, and it was not a clinically relevant distinction (38.8 ± 5.5 sec unfiltered vs. 41.1 ± 4.6 sec filtered; p = 0.03). PT, fibrinogen, FV, FVIII, pH, bicarbonate, lactate, and ROTEM CT, MCF, and alpha angle values were not statistically different between filtered and unfiltered samples.

TABLE 2. Pre- and postfiltration differences of W setting thawed plasma

	Unfiltered	Filtered
CT (sec)	69.5 ± 10.6	70.3 ± 13.5
MCF (mm)	20.3 ± 4.9	19.2 ± 1.5
Angle (degrees)	78.7 ± 3.8	77.8 ± 4.5
PT (sec)	15.6 ± 0.7	15.8 ± 0.6
aPTT (sec)	38.8 ± 5.5	41.1 ± 4.6*
Fibrinogen (mg/dL)	250.0 ± 60.8	229.7 ± 31.3
FV (%)	63.0 ± 10.4	62.3 ± 9.5
FVIII (%)	87.5 ± 51.6	64.7 ± 37.6
pH	7.5 ± 0.1	7.5 ± 0.1
HCO_3 (mM)	17.0 ± 1.7	17.0 ± 1.9
Lactate (mM)	3.1 ± 0.5	3.09 ± 0.5

aPTT = activated partial thromboplastin time; CT = clotting time; FV = factor V; FVIII = factor VIII; MCF = maximal clot firmness; PT = prothrombin time; W = slow cooker keep warm.
* $p < 0.05$.

DISCUSSION

Because minutes matter in hemorrhage, rapid resuscitation is critical. In a hospital setting, plasma can begin thawing as soon as the emergency department is notified of an incoming patient; however, with traumatic hemorrhage, waiting to reach the hospital to begin resuscitation can be catastrophic. Point of injury and en route care resuscitation have traditionally consisted of crystalloid or colloid solutions designed to maintain blood pressure, but modern damage control resuscitation seeks to begin resuscitation that will promote hemostasis and prevent coagulopathy as early as possible. Waiting 30 minutes or longer for plasma to thaw at the point of injury is unacceptable, and the clinical devices used to thaw plasma are unavailable in the field regardless. Alternatives to frozen product exist (or are on the horizon), including liquid, never-frozen plasma, dried plasma, and whole blood, but FFP remains the most commonly available version due to its cost effectiveness and long shelf life. Additionally, multiple alternatives to water bath thawing have been developed or are under investigation for clinical usage.[10–12] It remains to be seen if any of these will present as superior solutions for austere environments, but it should be noted that, even as far back as the 1970s, microwave ovens were investigated as possible rapid thawing alternatives with only minor denaturing effects observed.[13–15]

This study was based on the premise that frozen plasma should be made available as soon as possible and thawed using limited resources. The described methods are currently taught by US Army TCMC and employed by medical personnel in theater, but no studies have been conducted to determine the impact of these nonstandard thawing techniques on plasma condition and function. Aside from the three temperature settings on the slow cooker, two approaches were examined with this device: beginning with room-temperature water to simulate usage in an emergency scenario with no forewarning, or having prewarmed water available to simulate foreknowledge of incoming casualties at Roles of Care 2 and 3. Similarly, the sous vide immersion circulator was also tested with and without prewarming of the water, and the efficiency of this device at bringing the water to the desired temperature was noteworthy, requiring only 5 minutes to reach 37°C even in the presence of FFP. The MRE chemical heating element and electric kettle have no need to prewarm the water, so these methods were examined in only one modality.

It was shown that plasma would thaw given sufficient time in the aptly named slow cooker at all three available settings, but frequently the thawing process took much longer than many clinical situations would allow, especially if the water was not prewarmed. Because time of thawing is one of the primary targeted parameters, this was not ideal. Even worse, slower thawing also had the unintended effect of producing cryoprecipitate (which is commercially produced by allowing frozen plasma to thaw at temperatures between 1 and 6°C).[9] Because of both of these factors, using the slow cooker at the lower settings should be avoided.

The boiling water from the electric kettle took only a small amount of preparation time and thawed the plasma approximately as rapidly as the clinical thawer. The time savings, while critically important, might come at the expense of damage to sensitive plasma proteins from heat exposure. Undoubtedly, there were small pockets within the FFP bag that experienced potentially damaging temperatures (and small amounts of precipitate forming in some of the thawed units), but the bulk effect was negligible, as measured by the FFP bag surface temperature. However, while these initial in vitro studies showed no significant changes to coagulation function in FFP thawed this way, a more thorough in vivo evaluation will be required to determine if there are negative effects from using high heat–exposed plasma. One previous study showed that using a constant 56°C water bath would reduce the thawing time by one-half with no significant impact to multiple enzymes and proteins.[16]

However, the superior solution with respect to timing was the sous vide immersion circulator, requiring the shortest amount of time to prepare the water and an amount of time to thaw similar to the clinical thawer. This device maintained bath temperature as accurately as the clinical thawer as well, even after adding in the 2 units of FFP, and avoided the potentially damaging temperatures of the kettle-boiled water.

The final temperature of the plasma after thawing is another important factor; approximating body temperature will prevent aggravation of the hypothermia that occurs following rapid blood loss. While fluid warmers are used where available to perform this function for plasma or other intravenous fluids, current-generation products are aimed at increasing temperature from ambient room (20-25°C) to near body (35-37°C) temperatures. Several of the tested thawing methods resulted in final plasma temperature below the room-temperature range, which would affect the ability of fluid warmers to efficiently perform their function and may require multiple warming steps to achieve the end goal. Both the kettle and sous vide (with or without prewarming) methods produced final temperatures similar to the clinical thawer.

There were some limitations to this study. Despite a single or double MRE heating element configuration being insufficient to properly thaw FFP, we did not test reapplication of additional heaters to maintain heating for longer periods of time. Water from the electric kettle was not reapplied as the bath temperature declined. Only two simultaneously thawing units were tested in the slow cooker, electric kettle, and sous vide methods; rate and efficiency of thawing would certainly change if fewer or more units were required. Only one model of slow cooker, electric kettle, and sous vide immersion circulator was tested based on user community input; different models may offer different heating kinetics and capacities. Only one temperature setting on the sous vide unit was tested; a slightly higher setting of 40 to 42°C (perhaps even as high as

the aforementioned 56 °C) might allow for more rapid thawing without risking protein denaturation. Other field-expedient thawing methods currently in use, including usage of a hypothermia blanket, personnel body heat, and hot surfaces, were not evaluated. Finally, the physiological impact of plasma thawed with these methods can only be presumed based on the assay results.

CONCLUSIONS

While the MRE chemical heating elements were insufficient to properly thaw FFP, the slow cooker, electric kettle, and sous vide immersion circulator thawing methods resulted in plasma with hemostatic characteristics comparable to those measured in FFP thawed with the clinical standard plasma thawer. The most significant differences were the speed of thawing and the final temperature of the thawed product. Because of the similarity in assay results, the thawing method among those tested that provides the most ideal thaw and gets closest to body temperature should be selected—the sous vide immersion circulator, whose capability was not dependent on prewarming the water. The electric kettle provided a similar thawing profile, and while exposure of plasma proteins to temperatures near 100°C will undoubtedly result in some denaturation and functional loss, the bulk exterior temperature of the FFP units never approached 40°C. The assay results suggest that little or no negative impact on plasma function was inflicted by the boiled water. Thus, in the absence of a standard clinical thawing device, the use of a low-power-requirement sous vide immersion circulator or electric kettle provides thawing with the least setup time and the fastest product available for transfusion. Development of a portable, low- or no-power thawing device or method would be a valuable research goal for the future.

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CONFLICTS OF INTEREST

The authors have disclosed no conflicts of interest.

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