

Transition from room temperature to cold-stored platelets for the preservation of blood inventories during the COVID-19 pandemic

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Abstract

Background: The COVID-19 pandemic has placed great strain on blood resources. In an effort to extend platelet (PLT) shelf life and minimize waste, our institution transitioned room temperature to cold-stored PLTs for administration to bleeding patients.

Study Design and Methods: We describe the administrative and technical processes involved in transitioning room temperature PLTs to cold storage in April 2020. Additionally, we describe the clinical utilization of cold-stored PLTs in the first month of this practice change, with a focus on changes in PLT counts after transfusion, hemostasis, and safety outcomes.

Results: A total of 61 cold-stored PLT units were transfused to 40 bleeding patients, with a median (interquartile range [IQR]) of 1 (1-2) units per patient. The median age was 68 (59-73) years; 58% male. Median pretransfusion and posttransfusion PLTs counts were 88 (67-109) and 115 (93-145). A total of 95% of transfusions were administered in the operating room: 57% cardiac surgery, 20% vascular surgery, 8% general surgery, and 5% solid organ transplantation. Hemostasis was deemed to be adequate in all cases after transfusion. There were no transfusion reactions. One patient (3%) experienced a fever and infection within 5 days of transfusion, which was unrelated to transfusion. Median (IQR) hospital length of stay was 8.5 (6-17) days. Two patients (5%) died in the hospital of complications not related to transfusion.

Conclusion: Cold-stored PLT utilization was associated with adequate hemostasis and no overt signal for patient harm. Conversion from room temperature to cold-stored PLTs may be one method of reducing waste in times of scarce blood inventories.

KEYWORDS

COVID-19, hemostasis, platelets, surgery, transfusion

1 | INTRODUCTION

The COVID-19 pandemic has led to shortages in blood bank inventories across the globe. In the United States, the initial response to the COVID-19 pandemic led to the closure of numerous blood collection facilities, particularly mobile units, with subsequent deficiencies in the availability of both red blood cells (RBCs) and non-RBC component therapies.¹ Blood donations at open centers were also impacted by decreased donor turnout, by donor deferrals due to previous COVID-19 infection or exposure, and by staffing shortages due to employee illness or quarantine. It is also possible that blood shortages may have been exacerbated in certain regions secondary to increasing patient volumes and transfusion demand secondary to COVID-19–related illness; however, deficiencies on the supply end remain the principle driver for blood shortages. In our high-volume surgical center with robust in-house blood bank resources and a strong community-driven blood donor program that was not intimately impacted by the initial wave of US COVID-19 cases, the suspension of elective surgical procedures was associated with decreased blood product utilization and a temporary surplus of in-house blood bank inventories, particularly platelets (PLTs).

Platelets are a blood component at high risk for shortages both secondary to insufficient collections and product outdating. Regarding outdating, PLT units are typically stored at room temperature (20°C–24°C) with continuous agitation and have a shelf life of 5 days given concerns for bacterial growth with longer storage durations,² although this shelf life may be extended to 7 days in select circumstances.³ PLT unit shelf life can be further expanded through cold storage (2°C–6°C).^{4,5} Generally speaking, cold-stored PLTs are not utilized in most clinical practices given concerns with reduced circulatory half-life (1–2 days vs 7–9 days).⁶ While a reduced circulatory half-life is likely suboptimal in those with hypoproliferative thrombocytopenia, data suggest that cold-stored PLTs may have superior hemostatic efficacy in patients with acute hemorrhage.^{7–9} As such, cold-stored PLT use has expanded in military and trauma applications. Overall, however, there is limited availability of these products in most medical institutions, and when available, use is typically reserved for those with acute trauma.⁴

In response to looming COVID-19–related blood shortages and PLT outdating secondary to a substantial decrease in elective surgical volume, our institution made the decision to transition room temperature PLTs to cold storage after they reached their 5-day shelf life, with these delayed cold-stored PLT units then made available for patients with acute bleeding. In this article, we describe

the administrative, regulatory, and technical processes involved in this practice change. Additionally, we report the clinical outcomes of patients transfused with cold-stored PLTs during the first month of this practice change.

2 | MATERIALS AND METHODS

This is a descriptive review of the process of transitioning from room temperature to cold-stored PLTs at a large tertiary care medical center during the COVID-19 pandemic, in addition to providing a retrospective review of clinical outcomes in patients receiving transfusion of cold-stored PLTs. The study was deemed to be exempt from review by the local institutional review board given negligible patient risk. All consecutive patients receiving at least 1 unit of cold-stored PLTs between April 20, 2020, and May 31, 2020, were included. Manual chart review was performed to extract demographic, clinical, surgical, and laboratory features of transfused patients. This was performed in June 2020 after all patients had either been discharged from the hospital or died during inpatient admission. Outcomes of interest included change in pretransfusion to posttransfusion PLT count, with the pretransfusion value defined as the PLT count obtained closest to the start of the PLT transfusion (must have occurred within 24 hours of the transfusion start time) and the posttransfusion value defined as the PLT count obtained immediately after the last cold-stored PLT unit transfused (must have occurred within 24 hours of the transfusion stop time); the 72-hour (± 12 hours) post-transfusion PLT count (taking the value occurring closest to 72 hours from PLT transfusion for those with multiple values available); clinician-determined adequacy of hemostasis, as documented in clinical/surgical notes; suspected or confirmed transfusion reactions; fever or new diagnosis of infection within 5 days of the last PLT transfusion; reoperation for bleeding within 48 hours of the last PLT transfusion; hospital length of stay; and hospital mortality. Outcomes are given as frequency (%) for categorical outcomes and median (interquartile range [IQR]) for continuous outcomes.

3 | RESULTS

3.1 | Factors influencing the decision to transition to cold storage PLTs

As the COVID-19 pandemic began to gain a foothold in the United States in early 2020, contingency plans were developed in the Division of Transfusion Medicine at the Mayo

Clinic in Rochester, Minnesota, to address the potential impact on blood product inventories. It was anticipated that blood product inventories would decrease due to a decline in blood donations related to donor illness, donor deferrals due to previous COVID-19 infection or exposure, and blood collection employee illness or quarantine. The demand for blood components during the COVID-19 crisis was uncertain. It was possible that blood usage would drop related to decreases in the care of non-COVID-19 cases, such as elective surgical procedures and management of non-life-threatening diseases. It was possible, however, that the transfusion support of a subset COVID-19 patients could be extensive (eg, extracorporeal membrane oxygenation patients) in the setting of a large number of severe cases. Further, the collection of convalescent plasma from COVID-19 survivors via apheresis, which was projected to be a high priority initiative for our institution, had to be accomplished at the expense of apheresis PLT collections, which utilized the same equipment and personnel. Therefore, a plan to mitigate anticipated shortages of blood product inventories was required. This included the freezing of RBCs while blood collections were strong to help maintain support of patients during periods of low blood collections and the transition of room temperature PLTs at the end of their 5-day storage period to refrigerated storage for an additional 9 days (14-day total shelf life) to maintain inventories during the COVID-19 pandemic. It is important to note that before this transition, we were outdating approximately 27 PLT units each month from our institutional blood bank, for an expiration rate of 3.1% of all donated units. Our goal was to substantially decrease this number as part of our institutional COVID-19 response.

3.2 | Regulatory, administrative, and technical processes

On April 1, 2020, the Division of Transfusion Medicine informed the U.S. Food and Drug Administration (FDA) of its intent to change its PLT inventory management process by converting pathogen-reduced apheresis PLTs collected at the Mayo Clinic Donor Center from 5-day room temperature storage to cold-stored PLTs for 9 additional days of storage, not to exceed 14 days' total storage. This decision was based on internal projections of a marked increase in the number COVID-19 infections encountered at the Mayo Clinic and in Olmsted County, Minnesota, resulting in an increased caseload of patients; a decrease in the number of donors due to illness or other unavailability related to COVID-19; and the probability of significant impact on the workforce involved in the collection, processing, testing, and administration of

blood components. This step was taken to safely preserve PLT inventories throughout the COVID-19 crisis for as long as possible.

This decision was based on multiple factors. First, as part of a variance request for cold-stored PLTs submitted to the FDA, we compared bacterial contamination of 10 pathogen-reduced apheresis double units (ie, 20 total units) after 14 days' storage either at room temperature ($n = 10$) or refrigerated ($1-6^{\circ}\text{C}$; $n = 10$) and found no evidence of bacterial growth in either storage condition (unpublished data). Therefore, from a risk perspective, it was concluded that storage of pathogen-reduced room temperature PLTs for 5 days followed by 9 days at refrigerated temperature would be unlikely to pose a significant threat of bacterial contamination. Second, there was literature supporting the quality of PLTs placed in refrigerated storage after room temperature storage.¹⁰ Finally, on February 21, 2020, the FDA granted South Texas Blood & Tissue Center approval to manufacture and distribute cold-stored PLTs with a shelf life of 14 days, so there was a precedent for the use of 14-day cold-stored PLTs in the United States. However, it should be noted that this approval was for PLT units to be stored at refrigerated temperatures for the entirety of the 14-day storage duration rather than transitioning to cold storage after 5 days of storage at room temperature.

Starting on April 20, 2020, cold-stored PLTs were provided to fill appropriate PLT orders when such components were available. Cold-stored PLTs were used preferentially for patients with acute bleeding, including those in surgery, the emergency department, and the intensive care unit and during massive blood transfusion activation. All cold-stored PLTs were collected by the Mayo Clinic Donor Center and were subjected to an FDA-approved pathogen reduction process. The process would involve the conversion to cold-stored PLTs in the late evening before the midnight outdate of room temperature PLTs. After conversion, the product codes of the cold-stored PLTs were changed, the expiration date was extended, and they were placed in refrigerated storage ($1^{\circ}\text{C}-6^{\circ}\text{C}$ without agitation). Much like RBCs, cold-stored PLTs were issued in a cooler or a red biotransport bag (to impede warming) for transport to the bedside. A tie tag was added as a visual reminder that the component should be kept in the transport container until the time of transfusion.

3.3 | Clinical review

A total of 61 room temperature PLT units were transitioned to cold storage between April 20 and May

29, 2020, after they reached their 5-day shelf life. These 61 cold-stored PLT units were subsequently transfused to 40 non-COVID-positive patients between April 21 and May 31, 2020, with a median (IQR) of 1 (1-2) units transfused per patient. The median (IQR) total storage duration of the cold-stored units was 6 (6-7) days with a maximum of 9 days (inclusive of room temperature storage time). No cold-stored PLT units were wasted. The median (IQR) age of recipients was 68 (59-73) years, of which 58% were male (Table 1). Two pediatric patients under the age of 18 years (2 and 6 years, respectively) received cold-stored PLTs. Thirty-nine of 40 (97.5%) patients had available pretransfusion and posttransfusion PLT count values. Median (IQR) pretransfusion and posttransfusion PLTs counts for the cohort were 87 (67-106) and $115 (93-145) \times 10^9/L$, with a median (IQR) PLT increment of $25 (7-51) \times 10^9/L$. The median (IQR) PLT count 72 hours after transfusion was $97 (68-129) \times 10^9/L$. A total of 95% of transfusions were administered in the operating room; of these 57% occurred in cardiac surgery, 20% in vascular surgery, 8% in general surgery, and 5% in

TABLE 1 Demographic and clinical characteristics of transfused patients (n = 40)

Variable	Median (IQR) or n (%)
Age (years)	68 (59-73)
Sex	
Female	17 (42)
Male	23 (58)
Comorbidities	
Coronary artery disease	19 (47.5)
Hypertension	27 (67.5)
Diabetes mellitus type 2	12 (30)
Stroke	5 (12.5)
Chronic kidney disease	8 (20)
Transfusion location	
Emergency department	1 (2.5)
Operating room	38 (95)
Intensive care unit	1 (2.5)
Surgery type (n = 38)	
Cardiac	23 (58)
General surgery	3 (7.5)
Vascular	8 (20)
Transplant	2 (5)
Other	4 (10)
Pretransfusion PLT count ($\times 10^9/L$) ^a	87 (67-106)
Posttransfusion PLT count ($\times 10^9/L$) ^a	115 (93-145)

^aAvailable for 39 (97.5%) patients.

TABLE 2 Clinical outcomes after cold-stored PLT transfusion to 40 patients

Outcome	Median (IQR) or n (%)
Posttransfusion PLT increment ($\times 10^9/L$) ^a	25 (7-51)
Adequate posttransfusion hemostasis	40 (100)
Fever/sepsis within 5 days of PLT transfusion ^b	1 (2.5)
Return to operating room for bleeding within 48 hours	0 (0)
Hospital length of stay (days)	8.5 (6-17)
Hospital mortality ^b	2 (5)

^aAvailable for 39 (97.5%) patients.

^bFever/sepsis and hospital mortality were not related to PLT transfusion.

solid organ transplantation. The remaining 5% of transfusions were administered to hemorrhaging patients in the emergency department (2.5%) and intensive care unit (2.5%).

Clinical outcomes are displayed in Table 2. Surgical hemostasis was deemed to be adequate in all cases. No patients required return to the operating room for bleeding in the first 48 hours after PLT administration. Regarding safety, there were no documented or suspected transfusion reactions. One patient (3%) experienced a fever and infection within 5 days of PLT transfusion, which was deemed to be secondary to a right middle lobe pneumonia (blood culture negative) and exacerbation of chronic obstructive pulmonary disease rather than related to the PLT transfusion. All patients had either been discharged from the hospital (95%) or died (5%) at the time of data analysis. Median (IQR) length of stay was 8.5 (6-17) days. Two patients (5%) died in the hospital of complications not related to transfusion. The first died secondary to portal vein thrombosis and decompensated liver disease occurring 30 days after the cold storage PLT transfusion. The second patient was admitted for acute hypoxemic respiratory failure in the setting of end-stage multiple myeloma and was ultimately transitioned to hospice cares.

4 | DISCUSSION

The transition from room temperature (5-day shelf-life) to cold-stored PLTs (14-day shelf life) in a large tertiary care medical center prevented wastage of 61 units in the first month of implementation. Cold-stored PLT units were administered to acutely bleeding patients of varying clinical profiles, including administration to two pediatric

patients. Hemostasis was deemed to be adequate after transfusion and hemorrhage control in all cases. There were no transfusion-related adverse events, including no PLT-related bacterial infections.

Cold-stored PLTs are not commonly used outside of military and trauma applications despite evidence for improved hemostatic efficacy over room temperature products.^{7–9} Challenges to broader cold-stored PLT utilization are largely related to the infrastructure and resources required to maintain dual PLT inventories, as room temperature PLTs are likely to remain the standard treatment for severe hypoproliferative thrombocytopenia given their longer circulatory half-life.⁶ However, in times of low blood inventories or when room temperature PLT units are at risk of expiration, the transition to cold storage (ie, delayed cold storage) is one way to reduce wastage and maintain adequate PLT supplies for patients with acute life-threatening hemorrhage.

In this study, two pediatric patients were transfused with cold-stored PLTs with no adverse events. To our knowledge, there are no prior reports of cold-stored PLT transfusion in children, although pediatric trauma patients have received cold-stored whole blood with preserved posttransfusion PLT function and no apparent complications.¹¹ Similar to adults, further research is clearly needed to assess the safety and efficacy of cold-stored PLT transfusion in pediatric patients.

There are limitations to this report, which provides the experience of a single institution with a large in-house blood bank and a robust patient blood management program. First, data were retrospectively ascertained without a control group, which introduces concerns with data completeness and bias. Second, extrapolation of our experience to other practice environments is not guaranteed. Third, presented clinical outcomes are representative of only a limited number of patients, and no PLT units were transfused beyond 9 days of storage. Hence, these limited data are insufficient to conclude that delayed cold storage is safe. Fourth, posttransfusion PLT count increments for several patients were assessed after more than 1 PLT unit had been transfused, which represents the reality of clinical practice during active hemorrhage management and is very distinct from PLT transfusions administered for non-bleeding indications (ie, hypoproliferative thrombocytopenia). Finally, comparative efficacy of cold-stored against room temperature PLTs cannot be assessed through this study design. Future investigations are warranted to further explore the efficacy and safety of cold-stored PLT units for bleeding patients outside of trauma and military applications.

In summary, the transition from room temperature to cold-stored PLTs during COVID-19–related blood

shortages prevented the outdating of more than 60 units of PLTs over the first month of implementation. Delayed cold-stored PLT administration to a diverse group of patients was associated with adequate hemostasis and no signal for patient harm. In times of blood bank shortages, it is critical that we examine ways to conserve limited blood bank resources.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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