the PLASMIC score may contribute to raising awareness of the clinical/laboratory features of TTP in clinicians with no expertise in such hematologic disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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DOI 10.1111/trf.16105

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Evaluating blood product quality post expiry to mitigate blood shortages during the COVID-19 pandemic in Canada

To the Editor

During the early months of the COVID-19 pandemic blood manufacturers and transfusion services were alerted to the potential for reduced blood collections that could limit the availability of vital blood products for transfusion. Implementation of public restrictions such as physical distancing measures and stay at home orders led to decreases in blood donations in Canada in early March of 2020. Measures were taken by Canadian Blood Services to increase public awareness through advertising and social media campaigns emphasizing the continued need for blood donations and to ensure donors felt safe visiting donation centers. Strategies to reduce the strain on the blood supply, such as postponing elective surgeries, were implemented in Canada but additional options for healthcare providers to respond to a critically low blood supply were required. One potential option was the transfusion of red cell concentrates (RCCs) after regulatory approved expiry.

Canadian Blood Services produces RCCs using two different methods from CPD collected whole blood; the buffy coat derived red cell filtration (RCF) method and the whole blood filtration (WBF) method. RCCs produced from these methods are leukocyte reduced and stored in SAGM for 42 days of hypothermic storage. Regulatory approval for RCC products is heavily weighted on two criteria; RBC hemolysis (<1% USA, <0.8% Canada and Europe) and RBC in vivo survival (75% in vivo cell recovery at 24 hours post transfusion). While in vivo evaluation of RCC quality past the regulatory expiry is impractical during a pandemic, ATP content has been demonstrated to correlate with in vivo RBC survival where a concentration over 2 μmol/g of hemoglobin (Hgb) is indicative of at least 75% in vivo recovery and

TABLE 1 Influence of extended hypothermic storage on the quality of SAGM red cell concentrates

		Length of hypothermic storage post collection (d)	
Parameter	**RCC production method**	**42**	**49**
Hematocrit (%)	**RCF (n = 66)** CSA pass/fail	60 ± 2 pass	61 ± 2 pass
	WBF (n = 14) CSA pass/fail	62 ± 2 pass	63 ± 2 pass
Hgb (g/unit)	**RCF (n = 66)** CSA pass/fail	53.1 ± 5.3 pass	52.9 ± 5.1 pass
	WBF (n = 14) CSA pass/fail	59.5 ± 5.2 pass	59.0 ± 5.4 pass
MCV (fL)	**RCF (n = 66)**	95.3 ± 4.1	96.0 ± 4.1
	WBF (n = 14)	93.5 ± 5.6	94.1 ± 5.5
EI_{MAX} (elongation index)	**RCF (n = 10)**	0.612 ± 0.014	0.604 ± 0.010
	WBF (n = 10)	0.604 ± 0.010	0.599 ± 0.009
K_{EI} (membrane rigidity)	**RCF (n = 10)**	1.226 ± 0.197	1.611 ± 0.634*
	WBF (n = 10)	1.114 ± 0.202	1.119 ± 0.190*

Note: Data shown as mean ± 1 SD. Hgb = hemoglobin; RCC = red cell concentrate; RCF = red cell filtration; WBF = whole blood filtration.
*$P < 0.05$.

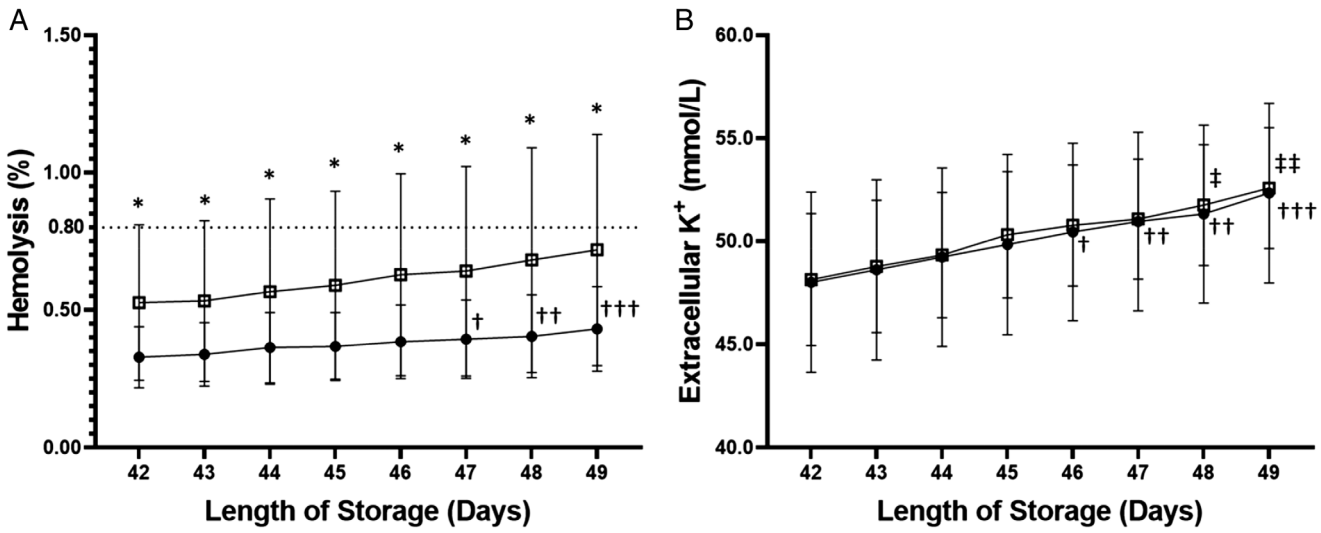

FIGURE 1 Results for RBC hemolysis (A) using a modified Drabkin's method and extracellular potassium (B) measured on a clinical chemistry analyzer. Statistical differences between the RCF method (●, n = 66) and the WBF method (□, n = 14) on the same storage day are indicated by (*) $P < 0.05$. Statistical differences for comparisons within RCC method type for all post expiry storage days compared to day 42 (expiry) are indicated for RCF RCCs by (†) $P < 0.05$, (††) $P < .01$, (†††) $P < 0.001$; and WBF RCCs by (‡) $P < 0.05$ and (‡‡) $P < 0.01$). The dotted line on a indicates the CSA standard for maximum hemolysis of <0.8% required in 95% of units tested

can be used to predict in vivo RBC survival with noted limitations.[1–3]

To inform regulatory agencies and healthcare professionals on the quality of expired RCCs, 66 RCF and 14 WBF RCCs were obtained from inventory at expiry and tested for product quality parameters from day 42 to day 49 of hypothermic storage to identify a potential failure point. In Canada, the Canadian Standards Association (CSA) sets the limits for hematocrit (≤80% in 90% of units), hemoglobin content (≥35 g/unit in 100% of units, ≥40 g/unit in 90% of units), and RBC hemolysis (<0.8% in 95% of units).[4] These parameters were examined in addition to mean cell volume (MCV), RBC deformability (EI_{MAX} - elongation index, K_{EI} - membrane rigidity) and ATP content.[5–7]

In the case of RCCs manufactured by the RCF method, all CSA standards were met at each post expiry testing point up to day 49 (Table 1, Figure 1). However, RCCs manufactured with the WBF method met both standards for hematocrit and hemoglobin content, but not RBC hemolysis with only 79% of units tested passing the requirement (Figure 1). As expected, as RBC

hemolysis increased over the storage period, similar increases were reflected in extracellular potassium (Figure 1). Additionally, during the seven extra days of storage no differences were detected in the RBCs membrane's ability to elongate compared to that of day 42 RBCs; however, a statistical difference was detected between the two production methods on day 49 of storage in regards to membrane rigidity (K_{EI}, $P = 0.0393$) indicating that the RBCs in RCF units may have a decreased ability to deform. Finally, ATP concentration, measured on day 49, was 1.807 ± 0.609 μmol/g Hgb (RCF RCCs, n = 10) and 1.690 ± 0.395 μmol/g Hgb (WBF RCCs n = 10). This data was compared to previously collected day 42 data on RCCs produced using the same methods. No statistical differences were detected between day 49 data in this study compared to previously collected day 42 data on similar RCC products (2.074 ± 0.486 μmol/g Hgb RCF, n = 88; 1.910 ± 0.495 μmol/g Hgb, WBF, n = 64). This comparison demonstrates that a continued slow decline in ATP concentration is present during the additional 7 days of storage, but ATP concentrations present in RCF RCCs are likely to still meet the in vivo recovery requirements whereas WBF RCCs may not.

In the event of a critical blood supply shortage due to an interruption in donations, the data collected here supports healthcare professionals and regulatory agencies in making informed decisions about transfusing RCCs past expiry for patients in dire need in Canada. Our study demonstrates that leukocyte reduced CPD/SAGM RCCs produced by the buffy coat derived red cell filtration method would meet the Canadian regulatory standards from day 42 to 49 of hypothermic storage and have the potential to meet the 75% in vivo cell recovery at 24-hours post transfusion allowing this specific product to be further evaluated for post expiry transfusion in times of need.

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