

Survival of red blood cells after transfusion: a comparison between red cells concentrates of different storage periods

Marleen Luten, Bregt Roerdinkholder-Stoelwinder, Nicolaas P.M. Schaap, Willem J. de Grip, Harry J. Bos, and Giel J.C.G.M. Bosman

BACKGROUND: The use of fresh red blood cells (RBCs) is recommended for critically ill patients and patients undergoing surgery, although there is no conclusive evidence that this is beneficial. In this follow-up study, the short-term and the long-term recovery of irradiated, leukoreduced RBCs transfused after either a short storage (SS) or a long storage (LS) period were compared. By consecutive transfusion of RBCs with a SS and LS period, a direct comparison of their survival within the same patient was possible.

STUDY DESIGN AND METHODS: Ten transfusion-requiring patients each received a SS RCCs (stored 0-10 days) and a LS RCCs (stored 25-35 days) consecutively. Short-term and long-term survival of the transfused RBCs was followed by flow cytometry using natural differences in RBC antigens between donors and patients. Posttransfusion recovery (PTR) was measured at several time points after transfusion.

RESULTS: The mean 24-hour PTR of SS RBCs is 86.4 ± 17.8 percent and that of LS RBCs 73.5 ± 13.7 percent. After the first 24 hours, the mean times to reach a PTR of 50 percent of the 24-hour PTR (T50) and mean potential life spans (mPLs) of the surviving SS and LS RBCs (41 and 116 days and 41 and 114 days, respectively) do not differ.

CONCLUSIONS: The mean 24-hour PTR of both SS and LS RBCs complies with the guidelines, even in a compromised patient population. The 24-hour PTR of SS RBCs, however, is significantly higher than that of LS RBCs. The remaining population of SS and LS RBCs has a nearly identical long-term survival. Therefore, depletion of the removal-prone RBCs before transfusion may be an efficient approach for product improvement.

During storage, red blood cells (RBCs) undergo various biochemical and structural changes that impair their oxygen-delivering capacity and trigger secondary reactions, especially in transfusion-dependent patients.¹ The actual relationship between these storage lesions and RBC function and survival after transfusion is not known. Although there is no conclusive evidence that a shorter RBC storage period is beneficial,² the use of fresh RBCs has been recommended for critically ill patients and for patients undergoing surgery.³⁻⁶

Survival of at least 75 percent at 24 hours after transfusion is required to license RBC products (Table 1). Chromium-51 labeling is the classical method to evaluate the 24-hour recovery. A major disadvantage of this method is the radiation exposure. Hence, in some countries including the Netherlands, this method is not allowed. As an alternative, immunolabeling can be used with minor blood group antigens as markers. This method requires allogeneic transfusions, but the advantages are the potential to measure long-term as well as short-term

ABBREVIATIONS: BV = blood volume; LS = long storage; MPL = mean potential life span; PTR = posttransfusion recovery; SAGM = saline adenine glucose mannitol; SS = short storage; T50 = time to reach a PTR of 50 percent of the 24-hour PTR; TAC = total adenylate content.

From the Department of Research and Education, Sanquin Blood Bank Southeast Region, Nijmegen; and the Departments of Hematology, Blood Transfusion and Transplantation Immunology, and Biochemistry, Nijmegen Center for Molecular Life Sciences, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands.

Address reprint requests to: Harry Bos, Sanquin Blood Bank Southeast Region, PO Box 1013, 6501 BA Nijmegen, the Netherlands; e-mail: h.bos@sanquin.nl.

Received for publication July 30, 2007; revision received January 16, 2008, and accepted January 29, 2008.

doi: 10.1111/j.1537-2995.2008.01734.x

TRANSFUSION 2008;48:1478-1485.

TABLE 1. Product requirements for leukodepleted RBCs during storage

Variable	Requirement
Glucose*	≥5 mmol/L
ATP*	≥75% of initial level
Hemolysis*†	<0.8%*
24-hr PTR†‡§	≥75% of transfused RBCs surviving

* Dutch guidelines.⁸† European guidelines.⁷‡ In the United States, no written guideline is available but generally a limit of less than 1 percent is used.¹⁰§ AABB guidelines.⁹

survival and the ability to compare the survival of different RBC populations within the same individual.¹¹

In the past two decades, flow cytometric detection of chimerism in RBC populations has been applied for the follow-up of patients after allogeneic marrow transplantation,^{12,13} to identify illicit homologous blood transfusion in athletes,^{14,15} to detect and quantify fetal RBCs in fetomaternal hemorrhage,¹⁶ and for monitoring the survival of donor RBCs after transfusion.¹⁷ To our knowledge, no study has been reported that compares the short-term as well as the long-term survival of RBCs transfused after either a short storage (SS) or long storage (LS) period. We present the results of such a study on the posttransfusion survival by means of flow cytometric ratio quantification of transfused RBCs that were stored in saline adenine glucose mannitol (SAGM). By consecutive transfusion of RCC with a short and long shelf life, we could compare their survival within the same patient.

MATERIALS AND METHODS

Study design

We present a follow-up study with 10 patients for the determination of the posttransfusion survival of RBCs with different shelf lives, that is, a SS period (0-10 days) and a LS period (25-35 days). The study allowed direct comparison of the posttransfusion survival of SS RBCs and LS RBCs by consecutive transfusion into a single patient. Hematologic, biophysical, and biochemical measurements were performed on the samples taken from the RCCs just before transfusion. Posttransfusion survival was measured by flow cytometry using natural differences in the RBC antigen profile between donors and patients (Table 2).

The study was approved by the Committee on Research involving Human Subjects (CMO) of the Radboud University Nijmegen Medical Center, Nijmegen (pABTI-01). All patients gave written informed consent.

Subjects

Ten patients, who all required transfusions after high-dose chemotherapy, were included in the study (6 male,

4 female, age 25-59 years). Six patients suffered from multiple myeloma; the other 4 patients suffered from light-chain deposition disease, Hodgkin's disease, non-Hodgkin's lymphoma, and acute myeloid leukemia, respectively (Table 3). None of the patients had RBC alloantibodies before transfusion. The patients had either not been transfused previously or had not received a transfusion less than 6 months before the study.

One of the patients received allogeneic stem cell transplantation 2 weeks after RBC transfusion. The RBCs of the stem cell donor were positive for both the antigens that were chosen as markers for the transfused RBCs. Therefore, in the period before the appearance of allogeneic RBCs in the blood circulation, only the first three measurements (1 hr, 24 hr, and 7 days) of this patient were included in the analysis.

RCC preparation

RBCs were prepared as described previously, using standard procedures.¹¹ Briefly, 500 mL of whole blood was collected in a quadruple citrate phosphate dextrose (CPD)-SAGM top-and-bottom bag system (Composelect, Fresenius HemoCare, Emmer-Compascuum, the Netherlands) and anticoagulated with 70 mL of CPD. After cooling for at least 4 hours and centrifugation, the blood was separated into plasma, buffy coat, and RBCs using a Compomat G4 (Fresenius HemoCare). SAGM (110 mL) was transferred from the RBC storage bag to the RBCs. The RBC solution was leukodepleted by in-line filtration. The RCCs were subsequently stored at 2 to 6°C for a maximum of 35 days.

Determination of RBC antigens

RBC antigens were determined using a column technique (DiaMed ID microtyping, DiaMed-Benelux NV, Turnhout, Belgium), by direct agglutination using an autoanalyzer (Olympus PK7200, Goffin Meyvis Analytical & Medical Systems BV, Etten-Leur, the Netherlands), or by indirect agglutination using an automated blood group analyzer (ID-GelStation, DiaMed). The ABO, Rhesus, Kell, Kidd, and MNS antigens were determined using monoclonal antibodies from Sanquin Reagents (Amsterdam, the Netherlands), ImmucorGamma Benelux (Heppignies, Belgium), Ortho-Clinical Diagnostics (Tilburg, the Netherlands), and Biotest Seralec (Soest, the Netherlands). The Duffy and s antigens were determined using polyclonal antibodies from Sanquin Reagents.

Storage, sampling, and transfusion

A stock of O- RBCs was reserved to ensure a population of LS RBCs (storage time, 25-35 days). SS RBCs (storage time

TABLE 2. Blood groups and selected antigens of transfused RBC

Study patient number	SS RBCs		LS RBCs	
	Antibody used for detection	Blood group (ABO and Rh)	Antibody used for detection	Blood group (ABO and Rh)
1	Fy ^a	A-	K	O-
2	K	O+	Jk ^a	O-
5	K	AB+	Jk ^b	O-
8	K	A+	Jk ^a	O-
10	C	O-	E	O-
11	Fy ^a	A+	K	O-
12	K	A+	C	O-
13	E	O+	s	O-
14	E	A+	Jk ^b	O-
18	K	B-	E	O-

TABLE 3. Patient characteristics

Study number	Sex	Age (years)	Blood group (ABO and Rh)	Diagnosis	Transfusion order (first, second)	Symbol in figures
1	Male	45	A-	Non-Hodgkin's lymphoma	SS, LS	◆
2	Male	25	O+	Hodgkin's lymphoma	LS, SS	■
5	Female	45	AB+	Acute myeloid leukemia	LS, SS	▲
8	Female	56	A+	Multiple myeloma	SS, LS	×
10	Male	59	B-	Multiple myeloma	LS, SS	*
11	Female	50	A+	Multiple myeloma	SS, LS	●
12	Male	58	A+	Multiple myeloma	LS, SS	+
13	Female	45	O+	Light-chain deposition disease	SS, LS	○
14	Male	38	A+	Multiple myeloma	LS, SS	-
18	Male	55	B-	Multiple myeloma	LS, SS	◇

0-10 days) were selected from the regular stock when the patient's phenotype was determined. SS RBCs were ABO-compatible and Rhesus-compatible for the patient. The blood groups of the selected RCC and the antigens that were selected for simultaneous detection of transfused SS and LS RBCs are listed in Table 2. All the antigens showed a stable expression during storage (data not shown).

The treating physician ordered RBCs in accordance with the hospital guidelines (Radboud University Nijmegen Medical Center; hemoglobin [Hb] < 5.0 mmol/L). Before transfusion, the RCCs were irradiated with 25 Gy⁸ and mixed gently by inversion for approximately 5 minutes before a sample was taken. Approximately, 30 mL of RBCs was collected by a sterile sampling device for the in vitro analyses.

RCCs were transfused in a random order (Table 3) within 1 to 2 hours after each other, and subsequently blood samples (10 mL) were collected after transfusion (1 and 24 hr and 7, 28, 56, 84, and 126 days) for flow cytometric determination of posttransfusion survival. None of the patients received another RBC transfusion within 24 hours after the transfusion of the study units. If an additional transfusion was necessary within the study period, patients received RCCs that were negative for the antigens used for the survival studies.

In vitro analyses

In vitro analyses were performed as described before.¹⁸ Briefly, RBC counts and total Hb concentration were measured with a hematology analyzer (Sysmex XT1800i, Sysmex Corporation, Kobe, Japan). Extracellular Hb concentration was determined by a colorimetric assay on a clinical chemistry analyzer (Aeroset, Abbott Diagnostics, Abbott Park, IL). The percentage of hemolysis was estimated from the extracellular Hb concentration using the formula

$$\text{hemolysis} = 100 \text{ percent} \times \left(\frac{(1 - \text{Hct}) \times \text{extracellular (Hb)}}{\text{total (Hb)}} \right)^{19,20}$$

The pO₂, pCO₂, pH, bicarbonate, extracellular sodium, glucose, and lactate were determined with a blood gas analyzer (Chiron 860/865, Bayer Diagnostics, Tarrytown, NY).

Lactate dehydrogenase (LDH) and potassium levels were measured in the extracellular fluid after centrifugation using the clinical chemistry analyzer (Aeroset, Abbott Diagnostics). Adenine nucleotides were quantitated by anion-exchange high-performance liquid chromatography,^{21,22} and the intracellular 2,3-diphosphoglycerate acid (2,3-DPG) concentration was determined with a commercial assay (Kit 148334 UV, Roche Diagnostics, Penzberg, Germany).

Flow cytometric determination of survival

RBC isolation from patient blood samples

Before labeling, white cells were removed by Ficoll-Paque centrifugation (Amersham Biosciences, Uppsala, Sweden). For this purpose, 1 vol of blood was mixed with 1 vol of phosphate-buffered saline containing 0.1 percent bovine serum albumin (PBS-BSA). This mixture was layered on 2 mL of Ficoll-Paque and centrifuged (400 × g, 35 min, room temperature), and the RBC pellet was washed three times with 0.1 percent PBS-BSA. A RBC suspension containing 1.25×10^8 cells per mL was prepared.

Labeling and analysis

Human serum samples containing immunoglobulin G (IgG) antibodies against E, c, C, K, and Fy^a were obtained from Sanquin reagents. A polyclonal antibody against s was obtained from Ortho-Clinical Diagnostics. The Kidd antigens (Jk^a and Jk^b) were detected using polyclonal antibodies from Biotest Seralc.

RBCs were labeled by adding 50 μL of the appropriate antiserum to 200 μL of RBC suspension. Anti-K was diluted 1:8 with 0.1 percent PBS-BSA. The other antibodies were used undiluted. After 1 hour at 37°C, the RBCs were washed three times with 0.1 percent PBS-BSA to remove unbound antibodies. Subsequently, 7.5×10^5 RBCs were pelleted in round-bottomed 96-well microtiter plates and resuspended in 70 μL of 1:128 diluted fluorescein isothiocyanate-conjugated goat Fab fragment to human IgG (MP Biomedicals, Aurora, CO). RBCs were incubated for 30 minutes at room temperature in the dark and subsequently washed three times with 0.1 percent PBS-BSA. After being washed, the RBCs were resuspended in 1 mL of 0.1 percent PBS-BSA. The number of antigen-positive RBCs was calculated from appropriate marker regions in a histogram obtained with a flow cytometer (Cytomics FC 500, Beckman Coulter, Fullerton, CA). Positive and negative controls (RBCs from antigen-positive or antigen-negative donors) were included in each measurement. As determined previously,^{11,23} a sensitivity of at least 0.1 percent was achieved.

Calculation of survival

The percentage of surviving donor RBCs was determined at several time points after transfusion. From these data the posttransfusion recovery (PTR) could be calculated (Equation 1), taking into account the patient's blood volume (BV; Equation 2) and RBC count and the RBC count and volume of the transfused RCCs.

$$\text{PTR}(\%) = 100 \times \left(\frac{\text{BV patient} \times \text{RBC count patient} \times \% \text{ donor RBCs}}{\text{Vol RCC} \times \text{RBC count RCC}} \right) \quad (1)$$

The volume of the transfused RCCs was determined by dividing the net weight by the density of the RCCs

$$((1.100 \times \text{Hct}) + (1.004 \times (1 - \text{Hct})))$$

The percentage of donor RBCs was determined by flow cytometry.

Patient's BV was calculated according to the formula of Lauermaann and colleagues:²⁴

$$\begin{aligned} \text{Male: BV(mL)} &= \exp[7.0506 + 0.724 \times (0.00718 \times \\ &\quad \text{height (cm)}^{0.725} \times \text{weight (kg)}^{0.425})] \\ \text{Female: BV(mL)} &= \exp[6.9870 + 0.724 \times (0.00718 \times \\ &\quad \text{height (cm)}^{0.725} \times \text{weight (kg)}^{0.425})]. \end{aligned} \quad (2)$$

Two other characteristics of RBC survival were calculated from the survival data: 1) mean potential life span (MPL) and 2) time to reach a PTR of 50 percent of the 24-hour PTR (T50).

Long-term survival of RBCs (T50 and MPL) was calculated using the equation of the regression line on the basis of samples collected 24 hours after transfusion until 126 days after transfusion, with all data recalculated relative to a 24-hour PTR set at 100 percent. The equation of the regression line follows the general exponential equation of

$$y = ax^2 + bx + c,$$

where a, b, and c were determined for each patient separately. The mean correlation coefficient for the regression lines was 0.9796 (range, 0.9352-0.9999) for the SS RBCs and 0.9758 (range 0.9257-0.9946) for the LS RBCs.

Statistical analyses

Comparison of means were made with the paired t test or Wilcoxon signed-ranks test. The correlations were calculated by the Pearson method. p Values of less than 0.05 were considered significant.

RESULTS

Characteristics of transfused RCC

The mean storage time of the SS RCC was 5 ± 2 days (mean ± SD) with a minimum of 2 days and a maximum of 9 days. The LS RCC had a mean storage time of 30 ± 3 days (mean ± SD) with a range of 21 to 33 days.

The degree of hemolysis, the extracellular bicarbonate, potassium, lactate, and LDH level of SS RCC were all significantly lower than those of the LS RCC (Table 4). The extracellular pH, sodium, and glucose concentrations; the intracellular ATP and 2,3-DPG concentrations; and the cellular adenylate energy charge of LS RCCs were all significantly lower than those of the SS RCCs.

PTR

A relatively large portion of SS and LS RBCs has already disappeared from the circulation within 1 hour after

transfusion, especially of the LS RBCs. The 1-hour PTR of SS RBCs (91.2 ± 15.8) is significantly higher than that of LS RBCs (77.5 ± 10.3 ; $p = 0.002$).

In all patients, the 24-hour PTR of LS RBCs is lower than the 24-hour PTR of SS RBCs (Fig. 1). Both the SS RBCs and the LS RBCs have a mean 24-hour PTR that is statistically within the required limit of 75 percent (Table 5). Six of 10 LS RCCs, however, and 3 of 10 SS RCCs have a 24-hour PTR of less than 75 percent (Fig. 1). On average, the 24-hour PTR of SS RBCs is significantly higher than that of LS RBCs (Table 5).

Both SS and LS RCCs show a curvilinear survival (Fig. 2). The T50 and MPL are calculated from the equa-

tions for the regression lines (Fig. 2B) based on the 24-hour recovery, that is, after setting the 24-hour PTR at 100 percent. The mean T50 and MPL of SS RBCs (41 and 116 days) and LS RBCs (41 and 114 days) are almost identical (Table 5; Fig. 3).

Correlations between in vitro variables and PTR

When the SS and LS RBCs are taken together, the 24-hour PTR and the various storage variables (Table 4) show only a significant correlation for the Na^+ level ($r = 0.524$, $p < 0.05$). When the data of the SS and LS RBCs are analyzed separately, a significant correlation ($r = 0.796$) is found between the 24-hour PTR and the lactate concentration for the SS RBCs ($p < 0.05$). Analysis of the data of the LS RBCs shows significant correlations ($p < 0.05$) between the 24-hour PTR and pO_2 ($r = 0.721$), ATP ($r = 0.758$), and total adenylate content (TAC; $r = 0.636$).

DISCUSSION

The study design and the potential to quantitate the ratio of different populations of transfused RBCs by flow cytometry have allowed us to investigate the recovery of SS and LS RBCs in one and the same patient and to monitor the short-term as well as the long-term recovery. This study was performed strictly with patients who clinically required a transfusion. This avoids deliberate transfusion of healthy subjects with antigen-mismatched RBCs, which carries the risk of antibody formation. On the other hand, mismatches in minor blood groups occur inevitably in each RBC transfusion.¹⁷

The simultaneous transfusion of SS and LS RBCs in the same patient excludes any effect of the underlying disease and treatment of the patient, the calculated BV, the sex and age of the patient, and the effect of menstrual blood loss on determination and calculation of the recovery of SS and LS RBCs.

European as well as Dutch guidelines^{7,8} prescribe several in vitro requirements for stored RCCs and one in vivo requirement, that is, a PTR of at least 75 percent at 24 hours after transfusion. The results of this study show that the 24-hour PTR of both the SS and the LS RBCs complies statistically with the guidelines ($p > 0.05$), but that only 4 of 10 LS RCCs and 7 of 10 SS RCCs have a 24-hour PTR of at least 75 percent. The underlying disease and treatment might provide the explanation for the observations that the variation between patients was higher than observed with

Variable	SS	LS
Volume RCC (mL)	261 \pm 23	261 \pm 19
Mean cell volume (fL)	88.1 \pm 5.3	92.6 \pm 6.4
Total Hb content (g)	52.1 \pm 6.9	53.0 \pm 6.0
Hemolysis (%)	0.11 \pm 0.03	0.22 \pm 0.13†
LDH (U/L)	84 \pm 36	153 \pm 66†
pH	6.81 \pm 0.03	6.47 \pm 0.05†
pO_2 (kPa)	10.9 \pm 3.5	17.9 \pm 12.6
pCO_2 (kPa)	8.9 \pm 0.7	13.3 \pm 2.0†
Na^+ (mmol/L)	126 \pm 7	110 \pm 6†
K^+ (mmol/L)	22 \pm 8	48 \pm 7†
Glucose (mmol/L)	25.5 \pm 1.8	17.7 \pm 2.9†
Lactate (mmol/L)	8.1 \pm 1.5	21.0 \pm 3.7†
ATP ($\mu\text{mol/g}$ Hb)	5.08 \pm 0.85	3.94 \pm 0.46†
TAC ($\mu\text{mol/g}$ Hb)	5.81 \pm 0.93	5.76 \pm 0.51
Adenylate energy charge	0.93 \pm 0.02	0.80 \pm 0.03†
2,3-DPG ($\mu\text{mol/g}$ Hb)	8.32 \pm 5.42	0.47 \pm 0.37†

* n = 10 for both SS and LS RBCs; data are mean \pm SD.
† Significantly different from SS RBCs, $p < 0.05$.

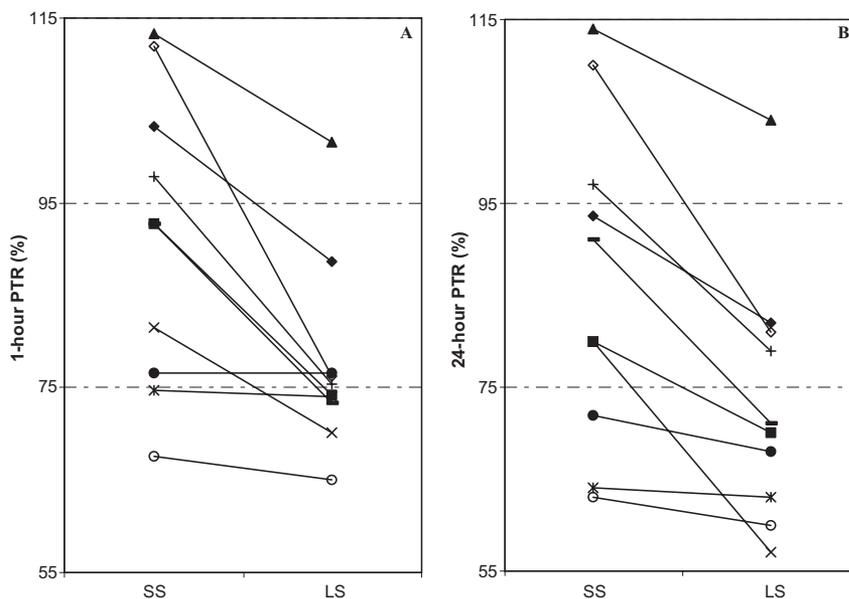


Fig. 1. Individual 1-hour PTR (A) and 24-hour PTR (B) of SS and LS RBCs. SS and LS RBCs that have been transfused into the same patient are connected to each other. Each symbol represents a patient.

Survival*†	SS	LS
24-hr PTR (%)	86.4 ± 17.8‡	73.5 ± 13.7
T50 (days)	41 ± 21	41 ± 18
MPL (days)	116 ± 16	114 ± 16

* n = 10 for 24-hour PTR; n = 9 for T50 and MPL. Data are mean ± SD.
 † T50 and MPL are the values of the RBCs surviving the first 24 hours after transfusion.
 ‡ Significantly different from LS RBCs, p < 0.01.

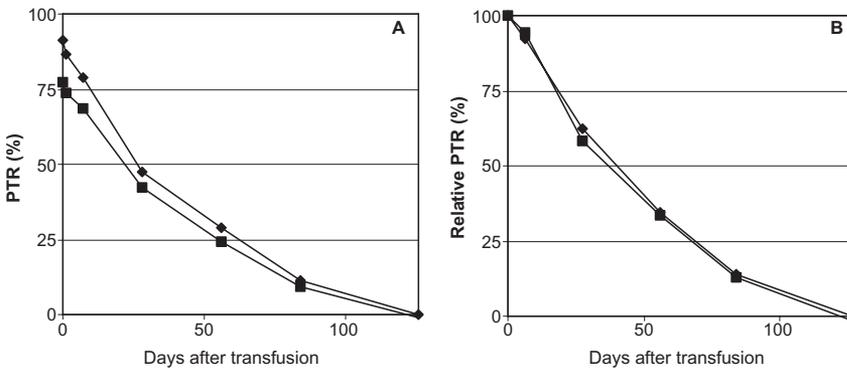


Fig. 2. Mean PTR (A) and relative PTR (B) of SS and LS RBCs at several time points after transfusion (1 and 24 hr and 7, 28, 56, 84, and 126 days). The relative PTR is the recovery of RBCs after setting the 24-hour PTR at 100 percent. (◆) SS RBCs; (■) LS RBCs.

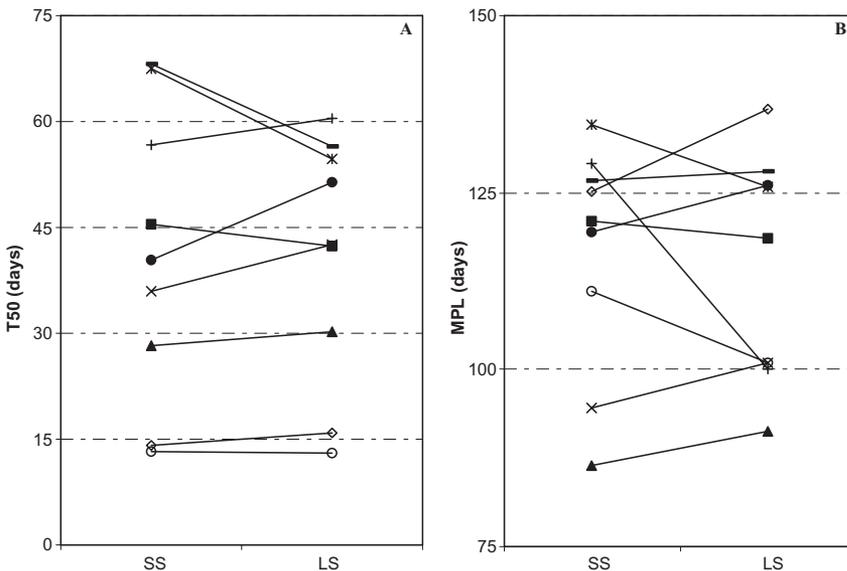


Fig. 3. Individual T50 (A) and MPL (B) of SS and LS RBCs. SS and LS RBCs that have been transfused into the same patient are connected to each other. Each symbol represents a patient.

healthy volunteers¹¹ and that the 24-hour PTR found in this study is lower. This is supported by comparable data from a study with oncologic patients using the same PTR method,¹⁷ indicating that the 24-hour PTR is lower in critically ill patients and emphasizing the need for more clinical transfusion studies.

The PTR is calculated using multiple measured as well as calculated variables, which is the likely cause of the considerable variation in the PTRs and may result in values of more than 100 percent. The formula for the BV may not be appropriate for transfusion-dependent patients. Nevertheless, since the 24-hour PTRs of SS and LS RBCs are determined after their consecutive transfusion into one and the same patient, the differences in their values are not affected by the underlying disease and treatment nor by a deviating outcome of calculated variables, allowing a direct comparison.

Thanks to our study design, we can directly compare the individual and mean PTR of SS RBCs and LS RBCs. SS RBCs have a significantly higher 24-hour PTR than LS RBCs (Fig. 1, Table 5). The SS and LS RBCs surviving the first 24 hours, however, show similar survival characteristics (Fig. 2B vs. Fig. 2A).

The fraction that is removed in the first 24 hours after transfusion (15%-30%) probably consists of irreversibly damaged and/or damage-susceptible RBCs. This is in agreement with our observation that this removal already largely occurs in the first hour after transfusion. The damage to these RBCs may have occurred during the entire period from the moment of collection until transfusion into the patient. A longer storage period is likely to result in more damaging insults, which would explain why a much larger fraction of LS RBCs perishes in the first 24 hours.

We postulate that this removal-prone fraction, which disappears from the circulation within the first 24 hours, is mainly responsible for transfusion side effects. Especially in transfusion-dependent patients these side effects may entail damaging consequences such as iron accumulation, inflammation, and adverse (auto)immune reactions.^{25,26} Therefore, we propose that transfusion with SS RBCs will be beneficial in transfusion-dependent patients. Pretransfusion depletion of the

removal-prone RBCs, however, or improvement of preservative solutions to prevent their generation, might be more effective alternatives. This also would eliminate any limitation on using both LS and SS RBCs for this patient category. Although the recovery of RBCs that had been stored after irradiation has been shown to be comparable to that of untreated RBCs,²⁷ we cannot exclude the fact that the irradiation procedure has contributed to the differences between the SS and LS RBCs.

The T50 and the MPL of SS and LS RBCs that have survived the first 24 hours are not significantly different. In this context, we can draw the remarkable conclusion that the surviving LS RBCs have a maximal life span of approximately 144 days instead of the alleged 110 to 120 days, namely, 30 days of storage plus 114 days in the circulation. Apparently, storage of RBCs under blood bank conditions slows the physiologic aging process of the RBCs up to a certain stage. Past this stage they are removed in the first 24 hours after transfusion.

Several *in vitro* variables, such as sodium, lactate, ATP, and TAC, are correlated with the 24-hour PTR of RBCs. All these variables are direct or indirect indicators of the energy content of RBCs. Because of the relatively low correlation coefficients, the predictive value of these *in vitro* variables for the 24-hour PTR is minor. Taken together, however, these variables indicate that the 24-hour PTR of RBCs is correlated with the energy content of RBCs and that the energy content has a higher predictive value than the hemolysis. This requires further investigation.

In conclusion, the design of the study reported here enables the determination of both short-term and long-term survival after transfusion of two different RBC products simultaneously. The most important results are as follows: 1) the mean 24-hour PTR of both SS and LS RBCs complies with the guidelines, even in a compromised patient population; 2) most of the RBCs that do not survive the first 24 hours after transfusion are removed from the circulation within the first hours after transfusion; 3) the 24-hour PTR of SS RBCs is higher than the 24-hour PTR of LS RBCs (however, the post-24-hour survival is identical for the remaining population of SS and LS RBCs); and 4) none of the current variables that are commonly used for quality control *in vitro* is a reliable predictor of the PTR.

ACKNOWLEDGMENTS

We thank the nurses of the Department of Hematology and the Department of Blood Transfusion and Transplantation Immunology of the Radboud University Nijmegen Medical Center and the Department of Blood Distribution of the Sanquin Blood Bank Southeast region, without whom this study could not have been performed. We thank Dr Joyce Curvers, Department of Research and Education at Sanquin Blood Bank Southeast Region, for her

assistance with designing the study protocol. We acknowledge the Department of Blood Cell Research at Sanquin Research, Amsterdam, the Netherlands, for the measurement of the nucleotides and 2,3-DPG.

REFERENCES

- Hess JR. An update on solutions for red cell storage. *Vox Sang* 2006;91:13-9.
- van de Watering L, Lorinser J, Versteegh M, Westendorp R, Brand A. Effects of storage time of red blood cell transfusions on the prognosis of coronary artery bypass graft patients. *Transfusion* 2006;46:1712-8.
- Ho J, Sibbald WJ, Chin-Yee IH. Effects of storage on efficacy of red cell transfusion: when is it not safe? *Crit Care Med* 2003;31:S687-S697.
- Solheim BG, Flesland O, Seghatchian J, Brosstad F. Clinical implications of red blood cell and platelet storage lesions: an overview. *Transfus Apher Sci* 2004;31:185-9.
- McLellan SA, McClelland DB, Walsh TS. Anaemia and red blood cell transfusion in the critically ill patient. *Blood Rev* 2003;17:195-208.
- McLellan SA, Walsh TS, McClelland DB. Should we demand fresh red blood cells for perioperative and critically ill patients? *Br J Anaesth* 2002;89:537-9.
- Guide to preparation use and quality assurance of blood components. 11th ed. Strasbourg: Council of Europe Publishing; 2005.
- Richtlijn Bloedproducten. PT009.RL.SQ_002. Amsterdam: Stichting Sanquin Bloedvoorziening; 2005.
- Brecher ME, editor. Technical manual, 14th ed. Bethesda: American Association of Blood Banks; 2002.
- de Korte D, Verhoeven AJ. Quality determinants of erythrocyte destined for transfusion. *Cell Mol Biol* 2004;50:187-95.
- Luten M, Roerdinkholder-Stoelwinder B, Bos HJ, Bosman GJ. Survival of the fittest?—Survival of stored red blood cells after transfusion. *Cell Mol Biol* 2004;50:197-203.
- Hendriks EC, de Man AJ, van Berkel YC, Stienstra S, de Witte T. Flow cytometric method for the routine follow-up of red cell populations after bone marrow transplantation. *Br J Haematol* 1997;97:141-5.
- Blanchard D, Bruneau V, Bernard D, Germond-Arnoult F, Gourbil A, David B, Muller JY. Flow cytometric analysis of dual red blood cell populations after bone marrow transplantation. *Br J Haematol* 1995;89:741-7.
- Nelson M, Ashenden M, Langshaw M, Popp H. Detection of homologous blood transfusion by flow cytometry: a deterrent against blood doping. *Haematologica* 2002;87:881-2.
- Neslon M, Popp H, Sharpe K, Ashenden M. Proof of homologous blood transfusion through quantification of blood group antigens. *Haematologica* 2003;88:1284-95.
- Kumpel BM, MacDonald AP. Quantitation and phenotyping of fetal RBCs in maternal blood by flow cytometry. *Transfusion* 2003;43:416-7.

17. Zeiler T, Muller JT, Kretschmer V. Flow-cytometric determination of survival time and 24-hour recovery of transfused red blood cells. *Transfus Med Hemother* 2003, 2008; 30:14-9.
18. Luten M, Roerdinkholder-Stoelwinder B, Rombout-Sestrienkova E, de Grip WJ, Bos HJ, Bosman GJ. Red cell concentrates of hemochromatosis patients comply with the storage guidelines for transfusion purposes. *Transfusion* 2008;48:436-41.
19. Gyongyosst-Issa MI, Weiss SL, Sowemimo-Coker SO, Garcez RB, Devine DV. Prestorage leukoreduction and low-temperature filtration reduce hemolysis of stored red cell concentrates. *Transfusion* 2005;45:90-6.
20. Rapaille A, Moore G, Siquet J, Flament J, Sondag-Thull D. Prestorage leukocyte reduction with in-line filtration of whole blood: evaluation of red cells and plasma storage. *Vox Sang* 1997;73:28-35.
21. de Korte D, Haverkort WA, van Gennip AH, Roos D. Nucleotide profiles of normal human blood cells determined by high-performance liquid chromatography. *Anal Biochem* 1985;147:197-209.
22. de Korte D, Haverkort WA, Roos D, van Gennip AH. Anion-exchange high performance liquid chromatography method for the quantitation of nucleotides in human blood cells. *Clin Chim Acta* 1985;148:185-96.
23. Luten M, Klaarenbeek JM, Bos HJ. Detection of the in vivo survival of transfused RBCs. *Vox Sang* 2002;83:211.
24. Lauer mann I, Hecker H, Kirchner E. Erstellung von blutvolumenreferenzwerten für erythrozytenmarkierende indikatorverdunnungsmethoden anhand von literaturdaten. *Infusionsther Transfusionsmed* 1999;26:360-6.
25. Harmatz P, Butensky E, Quirolo K, Williams R, Ferrell L, Moyer T, Golden D, Neumayr L, Vichinsky E. Severity of iron overload in patients with sickle cell disease receiving chronic red blood cell transfusion therapy. *Blood* 2000;96: 76-9.
26. Singer ST, Wu V, Mignacca R, Kuypers FA, Morel P, Vichinsky EP. Alloimmunization and erythrocyte autoimmunization in transfusion-dependent thalassemia patients of predominantly Asian descent. *Blood* 2000;96:3369-73.
27. Moroff G, Holme S, AuBuchon JP, Heaton WA, Sweeney JD, Friedman LI. Viability and in vitro properties of AS-1 red cells after gamma irradiation. *Transfusion* 1999;39: 128-34. ■



本文献由“学霸图书馆-文献云下载”收集自网络，仅供学习交流使用。

学霸图书馆（www.xuebalib.com）是一个“整合众多图书馆数据库资源，提供一站式文献检索和下载服务”的24小时在线不限IP图书馆。

图书馆致力于便利、促进学习与科研，提供最强文献下载服务。

图书馆导航：

[图书馆首页](#) [文献云下载](#) [图书馆入口](#) [外文数据库大全](#) [疑难文献辅助工具](#)