Survival rate changes with transfusion of blood products during liver transplantation

[Le taux de survie change avec la transfusion de produits sanguins pendant la transplantation hépatique]

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Purpose: To determine whether red blood cell (RBC) or plasma transfusion is associated with the one-year survival rate variation previously detected in liver transplantation.

Methods: A retrospective study of 206 consecutive liver transplantations was undertaken. Intraoperative transfusions of blood products were identified. Twenty-seven variables were studied using univariate and multivariate analyses to identify factors that were associated significantly with survival rate. For analysis of one-year survival, the cases were studied according to the transfused blood products. Patients were stratified according to the degree of RBC and plasma transfusion into four groups: more than four units of RBC, one to four units of RBC, plasma transfusion only, and no plasma or RBC transfusions.

Results: Patients received an average of 2.8 ± 3.5 units of RBC and 4.1 ± 4.1 units of plasma. Thirty-two percent of the patients did not receive any RBC transfusion and 19.4% did not receive any blood products. The one-year survival rate was 81.9% for all patients and 97.4% for patients without any transfusions. Of the 27 variables evaluated, only RBC and plasma transfusions were associated with significant decrease in the one-year survival rate, which was seen in the group who received only plasma (76.9%, $P = 0.014$) and the group who received more than four units of RBC (62.5%, $P < 0.0001$).

Conclusion: Although we cannot demonstrate causality, our analysis shows that our one-year survival rate following liver transplantation decreased significantly with the intraoperative transfusion of any amount of plasma or more than four units of RBC.

Objectif : *Déterminer si la transfusion de globules rouges (GR) ou de plasma est associée à la variation du taux de survie d'un an déjà détectée pour une transplantation hépatique.*

Méthode: *Une étude rétrospective de 206 transplantations hépatiques consécutives a été menée. Les transfusions peropératoires de produits sanguins ont été recensées. Nous avons étudié 27 variables par des d'analyses à une ou plusieurs variables pour repérer les facteurs associés de façon significative au taux de survie. Pour l'analyse du taux de survie d'un an a été faite selon les produits sanguins transfusés. Les patients ont été stratifiés en quatre groupes d'après le degré de transfusion de GR et de plasma : plus de quatre unités de GR, de une à quatre unités, transfusion de plasma seulement et aucune transfusion.*

Résultats: *Les patients ont reçu en moyenne 2,8 ± 3,5 unités de GR et 4,1 ± 4,1 unités de plasma. Trente-deux pour cent n'ont reçu aucune transfusion de GR et 19,4 % aucun produit sanguin. Le taux de survie d'un an a été de 81,9 % pour tous les patients et de 97,4 % pour ceux qui n'ont eu aucune transfusion. Des 27 variables évaluées, seules les transfusions de Gr et de plasma ont été associées à une baisse significative du taux de survie d'un an, notée chez les patients qui ont reçu du plasma seulement (76,9 %, $P = 0,014$) ou plus de quatre unités de GR (62,5 %, $P < 0,0001$).*

Conclusion : *Sans pouvoir établir de causalité, notre analyse montre que le taux de survie d'un an après une transplantation hépatique diminue significativement avec la transfusion peropératoire de toute quantité de plasma ou de plus de quatre unités de GR.*

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LIVER transplantation is a surgical procedure that can be associated with massive blood loss and the need for allogenic blood product transfusion.[1–4] Transfusion may contribute to morbidity and mortality.[5–9] Improvements in surgical and anesthetic techniques have decreased the number of blood products transfused.[5–11] Cacciarelli *et al.*[5] and Ramos *et al.*[9] reported a decrease of the one-year survival rate associated with intraoperative transfusion of more than four or six units of red blood cells (RBC) respectively.

The St-Luc Hospital of the Centre Hospitalier de l'Université de Montréal (CHUM) performs more than 50 liver transplantations annually. The purpose of this study was to assess the relationship between one-year survival rate and intraoperative RBC or plasma transfusion.

Methods

With the approval of the CHUM Ethics Committee, a retrospective study was undertaken of all liver transplantations performed between 1998 and 2002.

Surgery

Four surgeons were involved during the study period. Two of these surgeons were present during each transplant procedure. The different transplantation procedures were all similar. Neither veno-venous shunts nor any piggyback technique were utilized. All livers were from ABO-Rh compatible, cadaveric donors and there were no reduced-sized grafts.

Anesthesia

Twelve anesthesiologists participated in the liver transplant team. In all cases, vascular access and invasive and non-invasive monitoring techniques were identical. The anesthetics were comparable. Induction consisted of propofol, sufentanil or fentanyl as the narcotic of choice, and usually rocuronium as the muscle relaxant. Anesthesia was maintained with either isoflurane or desflurane in oxygen. There was no standardized protocol pertaining to blood product transfusion. All the transfused RBC and plasma were ABO-Rh compatible. The decision to transfuse was an individual one based on the measured hemoglobin (Hb) level and the evaluation of the ongoing blood loss. Aprotinin was given to every patient according to the Hammersmith protocol except in patients with Budd-Chiari syndrome. Isovolemic hemodilution was not used. A cell saver device was used in one patient. The main laboratory test used was arterial blood gas analysis, which also included Hb, potassium, and ionized calcium levels. The arterial blood gas analyses were done on an "as needed" basis dictated by the clinical situation. All these tests were done in the hospital's central biochemical testing facilities.

Statistical analysis

Twenty-seven variables (Tables I–III) were analyzed by univariate and multivariate methods. Patients were divided into four groups (more than four units of RBC, one to four units of RBC, plasma only, no blood products) to analyze the influence of RBC transfusion practice on patient survival based upon the same parameters used by the Stanford group.[5] The influence of plasma transfusion on patient survival was analyzed by stratifying the patients into four plasma transfusion groups: no blood products, RBC only, one to four units of plasma, and more than four units of plasma.

Distributions were examined to ensure proper statistical evaluation. Parametric and non-parametric statistical tests were used as appropriate. For the univariate analysis, continuous variables were also analyzed as categorical variables using the median and the

TABLE I Demographics and health characteristics of the 206 patients and the four subgroups of RBC transfused

Variables	*206 patients*	*40 patients no blood product*	*26 patients plasma only*	*97 patients 1–4 RBC*	*43 patients > 4 RBC*
Gender (male)	62.6%	60.0%	61.5%	61.9%	67.4 %
Age (yr)	52 ± 11	50 ± 12	49 ± 12	53 ± 10	52 ± 11
Weight (kg)	73 ± 17	72 ± 14	82 ± 22	71 ± 15	74 ± 20
Height (cm)	167 ± 9	166 ± 8	168 ± 9	167 ± 9	166 ± 11
Starting Hb value ($g \cdot L^{-1}$)	105 ± 22	125 ± 16	123 ± 15	98 ± 18	91 ± 22
Starting INR value	1.8 ± 0.9	1.3 ± 0.5	1.7 ± 0.6	1.7 ± 0.7	2.3 ± 1.3
Starting platelet count (10^9 platelet$\cdot L^{-1}$)	102 ± 68	125 ± 85	104 ± 73	100 ± 60	78 ± 52
Starting creatinine value ($\mu mol \cdot L^{-1}$)	107 ± 72	83 ± 44	85 ± 48	108 ± 66	147 ± 102
Pugh's score	10 ± 2	8 ± 2	11 ± 2	11 ± 2	11 ± 2
MELD score	17 ± 10	11 ± 7	19 ± 10	18 ± 8	25 ± 11

RBC = red blood cells; Hb = hemoglobin; INR = international normalized ratio. With the exception of gender, all values are expressed as mean ± SD.

TABLE II Surgical characteristics and survival rate of the 206 patients and the four subgroups of RBC transfused

Variables	*206 patients*	*40 patients no blood product*	*26 patients plasma only*	*97 patients 1–4 RBC*	*43 patients > 4 RBC*
RBC transfused (units/patient)	2.8 ± 3.5	0	0	2.6 ± 1.0	7.7 ± 4.4
Plasma transfused (units/patient)	4.1 ± 4.1	0	4.9 ± 2.7*	3.6 ± 3.0*	8.6 ± 4.2
Platelet transfused (units/patient)	0.4 ± 1.9	0	0	0.4 ± 1.8	2.1 ± 4.0
Albumin 25% 100 mL (units/patient)	1.3 ± 1.6	0	0	1.1 ± 1.6	1.8 ± 2.1
Final Hb value ($g \cdot L^{-1}$)	87.3 ± 13.9	101.7 ± 14.8	87.8 ± 14.8	84.2 ± 11.8	78.1 ± 14.1
CVP (mmHg) before the anhepatic phase	9 ± 5	10 ± 5	8 ± 3	8 ± 5	11 ± 6
Temperature (°C) at the end of surgery	36.4 ± 0.7	36.5 ± 0.7	36.4 ± 0.6	36.2 ± 0.7	36.5 ± 0.8
Duration of surgery (min)	258 ± 68	230 ± 54	256 ± 77	251 ± 60	299 ± 75
Clamping time (min)	44 ± 11	41 ± 8	47 ± 15	43 ± 11	47 ± 13
Cold ischemia (min)	535 ± 187	495 ± 176	493 ± 174	557 ± 180	530 ± 205
Volume of crystalloid administered (mL)	5122 ± 2105	4751 ± 1614	4964 ± 1866	4929 ± 2011	5667 ± 2861
Diuresis (mL)	621 ± 430	664 ± 432	648 ± 373	622 ± 502	567 ± 539
Survival rate (%)	81.9	97.4†‡	76.9	86.6§¶	62.5

RBC = red blood cells; Hb = hemoglobin; CVP = central venous pressure. With the exception of survival rate, all values are expressed as mean ± SD. Each unit of RBC was 300 mL. Units were leukoreduced since June 1999. Each unit of fresh frozen plasma was 175 to 225 mL until October 1999 and was 200 mL since October 1999. Each unit of pooled platelet concentrate was 50 mL and contained 55×10^9 platelets$\cdot L^{-1}$. *$P = 0.0475$; †$P = 0.014$ for comparison of no blood product *vs* plasma only; ‡$P < 0.0001$ for comparison of no blood product *vs* > four units of RBC; §$P = 0.034$ for comparison of one to four units of RBC *vs* plasma only; ¶$P = 0.002$ for comparison of one to four units of RBC *vs* > four units of RBC.

TABLE III Univariate analysis of independent variables with respect to survival rate

Independent continuous variables	*Dead (35 patients)*	*Alive (167 patients)*	*Value*	*P*
Age (yr)	53 ± 11	51 ± 11	-1.223	NS
Weight (kg)	77 ± 23	73 ± 16	-0.757	NS
Height (cm)	168 ± 10	166 ± 9	-1.008	NS
Starting Hb value ($g \cdot L^{-1}$)	100.9 ± 24.4	106.1 ± 22.0	-1.006	NS
Starting INR value	1.9 ± 1.2	1.7 ± 0.8	-1.317	NS
Starting platelet count (10^9 platelet$\cdot L^{-1}$)	89 ± 50	104 ± 70	-0.389	NS
RBC transfused (units/patient)	5.0 ± 5.0	2.4 ± 2.9	-3.123	0.002
Plasma transfused (units/patient)	5.9 ± 4.0	3.8 ± 4.0	-3.033	0.002
Platelet transfused (units/patient)	0.5 ± 1.5	0.4 ± 2.0	-0.023	NS
Albumin transfused (units/patient)	0.87 ± 1.3	1.3 ± 1.7	-0.033	NS
Starting creatinine value ($\mu mol \cdot L^{-1}$)	110 ± 62	106 ± 58	-1.200	NS
Pugh's score	10.1 ± 2.1	9.9 ± 2.3	-0.604	NS
MELD score	20 ± 11	17 ± 10	-1.037	NS
CVP just before anhepatic phase (mmHg)	10.2 ± 6.2	9.0 ± 4.6	-0.278	NS
Temperature at the end of the surgery (°C)	36.2 ± 0.6	36.4 ± 0.7	-1.163	NS
Duration of surgery (min)	285 ± 66	253 ± 68	-2.279	0.023
Clamping time (min)	46 ± 16	44 ± 10	-0.425	NS
Cold ischemia (min)	558 ± 182	525 ± 178	-0.016	NS
Crystalloid transfused (mL)	5185 ± 1893	5119 ± 2149	-0.033	NS
Urine output (mL)	657 ± 424	615 ± 432	-0.640	NS
Independent categorical variables				
Gender (male; %)	58	63	0.009	NS
History of previous abdominal surgery			2.492	NS
Previous transplantation			0.978	NS
Surgeon work shift			1.736	NS
Diagnosis			22.261	NS
Surgeon			3.823	NS
Anesthesiologist			7.066	NS

NS = not significant; Hb = hemoglobin; INR = international normalized ratio; CVP = central venous pressure. Unless specified, all values are expressed as mean ± SD. All continous variables were analyzed using the Mann-Whitney test. Gender was analyzed using Fisher's exact test; all other categorical variables were analyzed using the Pearson chi-square test.

mean to separate the categories. The Mann-Whitney test was used to analyze independent continuous variables. Previous liver transplantation, the history of previous abdominal surgery, the work shift, the diagnosis, the surgeon, and the anesthesiologist were analyzed using the Pearson chi-square test. The Fisher's exact test was used to study the other independent categorical variables. A *P*-value > 0.05 was considered not significant. To assess subgroup differences, we used a Pearson chi-squared test. A forward logistic regression model was used to analyze the data in a multivariate fashion. The statistical programs SPSS 10 (SPSS Inc., Chicago, IL, USA) and Statview 5 (SAS Institute Inc, Cary, NC, USA) were used.

Results

Demographic and perioperative data for 206 cases are presented in Tables I and II. No transplant patients were excluded from the study. Patient's age ranged from 17 to 68 yr. Two hundred and six liver transplantations were performed on 193 patients. Ten patients had two liver transplantations and one patient required four transplantations. Four patients had a previous liver transplantation before the study period.

Patients received an average 2.8 ± 3.5 units of RBC (median 2.0 units, maximum 25 units) and an average of 4.1 ± 4.1 units of plasma (median 4.0 units, maximum 24 units). Cryoprecipitate was not used; platelets and albumin were rarely given (Table II). A time-based review of laboratory data showed that intraoperative RBC transfusions were started when the average Hb level was 68.2 ± 12.8 $g \cdot L^{-1}$ and the final Hb value was 87.3 ± 13.9 $g \cdot L^{-1}$. Analysis of the pattern of transfusion practice revealed that 43 patients (20.9%) received more than four units of RBC, 97 patients (47.1%) received between one and four units of RBC, 26 patients (12.6%) received only plasma, and 40 patients (19.4%) received no blood products (Table I). Sixty-six patients (32.0 %) did not receive any RBC.

Survival

There were no intraoperative deaths. The overall one-year survival rate was 81.9%. Four of the deceased patients had received two liver transplantations each. Mortality was mostly due to multiple organ failure at a mean of 31 ± 24 days post-transplantation.

Univariate analyses (Table III) showed that three variables were associated significantly with the one-year survival rate: the number of RBC units transfused (P = 0.002), the number of plasma units transfused (P = 0.002), and the length of surgery (P = 0.023). The association between RBC or plasma transfusion and one-year survival rate was significant whether the independent variables were studied as categories (mean, median, or subgroups of RBC and plasma (low *vs* high) transfusion) or as continuous variables. These three variables were entered as continuous and categorical variables in a logistic regression model. Increased RBC or plasma transfusions were associated with decreased survival. However, the colinearity was too strong for these variables to be analyzed separately hence we created a new variable, low *vs* high transfusion. Table IV summarizes the logistic regression model. Although identified as a confounding variable, multivariate analysis showed that the length of surgery did not modify the relationship between the survival rate and RBC or plasma transfusion. All other study variables did not influence the one-year survival rate (Table III).

Analysis of the four RBC transfusion groups revealed the following results (Table II). One-year survival in patients receiving no blood products was 97.4%. In comparison, the one-year survival rate declined to 86.6% when one to four units of RBC were transfused, 76.9% with plasma transfusion only (P = 0.014), and a nadir of 62.5% when more than four units of RBC were transfused (P < 0.0001).

Analysis of the pattern of plasma administration revealed that 40 patients received no blood products, 28 patients received RBC (mean 2.3 ± 1.1 units) but no plasma, 49 patients received between one and four units of plasma (mean 3.1 ± 0.9 units of plasma and 2.1 ± 1.6 units of RBC), and 89 patients received more than four units of plasma (mean 7.8 ± 4.3 units of plasma and 4.7 ± 4.3 units of RBC). The one-year survival rate was significantly decreased to 81.6% in patients receiving one to four units of plasma (P =

TABLE IV Summary of the logistic regression model

	Beta	*SE*	*Wald*	*Df*	*Sig*	*Exp(Beta)*
Duration of surgery	.004	.003	1.538	1	.215	1.004
Low *vs* high transfusion	1.513	.452	11.203	1	.001	4.538
Constant	-3.175	.818	15.049	1	.000	0.42

SE = standard error; Df = degrees of freedom; Sig = statistical significance. High transfusion group was defined as more than four units of RBC + more or equal to one unit of plasma; low transfusion group was defined as four units of RBC or no plasma.

TABLE V Stratification of one-year survival rate by RBC and plasma transfusions

	No plasma transfusion Survival		*Plasma transfusion Survival*	
	Proportion	*%*	*Proportion*	*%*
No RBC transfusion	38/39	97.4	20/26	76.9
RBC transfusion	24/28	85.7	85/109	78.0

With the exception of the comparison between no red blood cells (RBC) and no plasma transfusion *vs* plasma transfusion without RBC transfusion ($P = 0.014$), all other comparisons were not significant.

0.038) and 75.6% in patients receiving more than four units of plasma ($P = 0.002$).

Table V shows the stratification of the one-year survival rate according to the RBC and plasma transfusion in order to determine if one of the two variables is more strongly associated with a decrease in survival. Survival was decreased significantly in the presence of plasma transfusion in patients receiving no RBC units. In contrast, survival is not decreased in a significant fashion in those patients who received RBC with or without plasma. Survival decreased to 60.0% in patients receiving greater than four units of both RBC and plasma.

The risk of dying within a year was 4.2 times higher [95% confidence interval (CI) 1.8–9.7] in patients transfused with more than four units of RBC compared to those who received four or less units of RBC. Patients who received one or more units of plasma had a risk 5.1 times higher (95% CI 1.5–17.5) than those receiving no plasma. In patients receiving more than four units of RBC, the risk was 4.4 times higher (95% CI 1.9–10.2) in patients who also received plasma. The risk further increased to 5.3 times greater (95% CI 2.3–12.4) in patients receiving greater than four units of both RBC and plasma compared to patients receiving four or less units of both RBC and plasma.

Table VI shows the survival rate and the number of patients according to each diagnosis. The survival rate did not change after the adoption of leukoreduction of all allogenic blood products in June 1999 (80.0 % *vs* 83.8 %, P = NS).

Discussion

Our overall one-year survival rate of 81.9% is comparable to other studies,[9,12–14] but is lower than the 90% reported by the Stanford group.[5] Compared to our study, the Stanford study excluded repeated transplantations.[5] It is possible that we had a sicker patient cohort. In part this could be due to the fact that public and universal health care in the province of Québec may preclude selection bias. Furthermore, cadaveric organ procurement is less common in Québec (18.4 donors per million people per year) than in certain American states (e.g., 33 donors per million people in Pennsylvania).[15] Consequently liver transplant recipients might incur both a longer pre-transplant waiting period and an increased pre-transplant morbidity. Other potential explanations for our lower survival rate may be due to the different immunosuppressive medications in our cohort. Different immunosuppressive regimens vary in survival rates.[14] We do not know the immunosuppressive therapy used by the Stanford group.

In a preliminary study, we determined that intraoperative plasma transfusion was the variable most closely associated with the need for RBC transfusion in liver transplantation surgery. Plasma was transfused to correct prolonged international normalized ratios (INRs). A great disparity was noted in the plasma transfusion rate between anesthesiologists, indicating a liberal plasma transfusion practice. For RBC transfusion the threshold did not differ significantly amongst anesthesiologists (67.6 ± 12.5 g·L^{-1} to 69.8 ± 10.7 g·L^{-1}). In the present study, univariate analysis showed no decrease in one-year survival in the presence of an elevated initial INR (Table III).

In the Stanford study,[5] patients receiving more than four units of RBC had a significant decrease in their one-year survival rate. Multivariate analysis, in their study, showed that gender and pre-transplant morbidity ultimately influenced the survival rate rather than RBC transfusion. The Stanford study and Ramos *et al.*[9] did not report the amount of plasma transfused. Our univariate and multivariate analyses showed that only the number of transfused RBC units and the number of transfused plasma units were significantly associated with a decrease in the one-year survival rate. The starting Hb value, the starting platelet count, the cause of the liver failure, the starting creatinine value, the Pugh's score, the MELD score, a history of previous high abdominal surgery, and previous liver transplantation were not associated with a decrease in the one-year survival rate. This correlates with the observation by Deschênes *et al.*[16] that the severity of cirrhosis was a poor predictor of the six-months survival rate. We calculated that, to obtain a difference of 25% in the mean values of these variables, in the surviving patients, with an alpha error of 0.05 and a power (1-beta) over 80%, we needed the number of deaths to be between three and 30, which was lower than the actual number (35 deaths) observed in our study.

Van de Watering *et al.*[17] demonstrated a decreased mortality with transfusion of leukoreduced RBC dur-

TABLE VI One-year survival rate by etiology of hepatic failure

	Number of patients	*Percentage of all patients*	*Survival rate (%)*
Alcoholic cirrhosis	44	21.4	84.1
Hepatocarcinoma secondary to cirrhosis C	21	10.2	85.7
Cirrhosis C	21	10.2	80.1
Sclerosing cholangitis	18	8.7	88.9
Primary biliary cirrhosis	17	8.3	100
Cirrhosis B	16	7.8	87.5
Fulminant hepatitis "X"	13	6.3	84.6
Non-alcoholic steato hepatitis (NASH)	13	6.3	53.9
Cryptogenic cirrhosis	12	5.8	63.6
Autoimmune hepatitis	12	5.8	100.0
Fulminant hepatitis B	9	4.4	55.6
α_1–anti-trypsin deficiency	3	1.5	100
Budd-Chiari syndrome	2	1.0	50.0
Hepatocarcinoma secondary to cirrhosis B	2	1.0	100
Nodular hyperplasy	1	0.5	100
Wilson disease	1	0.5	100
Intrahepatic lithiasis	1	0.5	100
Total	206	100	

ing cardiac surgery. In our centre, allogenic blood products have been leukoreduced since June 14th, 1999. We did not detect an improvement of our survival rate after this date.

Our data seem to suggest that plasma transfusion may be more deleterious than RBC transfusion (Table V). For RBC transfusion, the number of administered units influenced the survival rate. The group receiving one to four units of RBC had a better one-year survival (86.6%) than those receiving more than four units of RBC (62.5%; $P = 0.002$) or those receiving plasma only (76.9%; $P = 0.034$). The group receiving only plasma received 1.3 units more plasma (mean 4.9 units) than the group receiving one to four units of RBC (mean 3.6 units) despite the fact that the former group may have been healthier on the basis of starting Hb value (Table I). The absolute presence, rather than the quantity, of plasma administered was significantly associated with a lower survival rate. This was seen most markedly in the patients receiving either no RBC or more than four units of RBC. If plasma has a deleterious effect, it could be that there is a harmful factor that is inconsistently present in plasma or whose effects are manifest inconsistently. It seems that transfusion of four or less units of RBC confers a protective effect in the presence of plasma transfusion. Furthermore, the total amount of blood products given during the whole hospitalization was also looked at, from one month prior the surgery till three months after. Patients that received few transfusions intraoperatively had the same profile in the perioperative period. The converse was also true. In the group that only received plasma, a mean of 9.2 units of plasma was transfused in the perioperative period. Patients who died in this group received even more plasma (mean 13.2 units) during their hospitalization.

Prior studies have shown that RBC transfusion is an independent predictor of morbidity.[6–9,18–20] In the last three referenced studies,[18–20] RBC or whole blood transfusions increased the incidence of multiple organ failure associated with trauma or major abdominal surgery. Mortality during coronary artery bypass grafting (CABG) also increased.[19] However these studies did not differentiate between whole blood and RBC transfusions nor did they mention the amount of plasma transfused.

With transfusion of unwashed RBC some plasma is automatically transfused. If many units of RBC are transfused, eventually an appreciable quantity of plasma is also transfused. If the plasma is the culprit, this may explain a decrease in the one-year survival rate. When plasma units are transfused, a large amount of plasma is given and the survival rate decreases. This might be due to the debilitated and immunosuppressed status of the patients.

Moore *et al.*[18] and Murphy *et al.*[19] suggested that transfusion of allogenic blood could decrease immunity and lead to postoperative infections and multiple organ failure. Another hypothesis was banked blood could activate neutrophils (polymorphonuclear leukocytes) that would be part of the inflammatory cascade present in tissue damage, ischemia, or reperfusion.

The authors did not specify which blood product was the culprit.

Vamvakas *et al.*[21] could not demonstrate whether pneumonia or wound infections were increased with allogenic plasma transfusion during CABG. Allogenic plasma transfusion immunomodulation could not be proved in this study. Our patients who received plasma had a decreased one-year survival rate. It could be hypothesized that the correction of the coagulation dysfunction leads to vascular thrombosis at the graft level and hence shortens its survival; however, correction of the coagulation defects with transfusion of plasma was not measured.

Although our findings meet several criteria for causality (biological plausibility, the presence of temporal association, a dose-effect relationship, consistency, specificity, and strength of association),[22] one should be cautious in concluding that there is a direct relationship between plasma or RBC transfusion and decreased one-year survival. Unfortunately, plasma or RBC transfusions are not the only variables that can affect the survival rate. In some other institutions, immunosuppressants like tacrolimus and cyclosporine are used separately and tacrolimus is associated with superior survival.[14] In our cohort, drugs were associated in different ratios according to three different immunosuppressive research protocols; thus, it was possible for a given patient to have received as many as five different immunosuppressive medications (prednisone, azathioprine, tacrolimus, cyclosporine, and basiliximab). Therefore, no conclusions can be drawn from our data with respect to the relationship between a specific immunosuppressive program and the one-year survival rate.

The retrospective nature of this study has other inherent weaknesses. For example, there was no blood transfusion protocol in place. However, looking back raised the question of whether patients could be identified as having received blood products without absolute necessity. Another weakness was the relatively few patients in this study. Since this study, we have looked at the one-year survival rate of liver transplantations in the five-year period (January 1993 to December 1997) before this study. There were 183 liver transplantations and the one-year survival rate did decrease in the groups receiving only plasma or more than four units of RBC.

In conclusion, in our series of 206 consecutive liver transplantations done at the St Luc Hospital of the CHUM, patients received an average of 2.8 units of RBC and 4.1 units of plasma. Univariate and multivariate analyses of 27 variables showed that RBC and plasma transfusions were associated significantly with a decrease in the one-year survival rate following liver transplantation. One-year survival rate following liver transplantation decreased significantly in association with the intraoperative administration of any amount of plasma or the administration of more than four units of RBC. Plasma transfusion appeared to be more deleterious than RBC transfusion. A direct causal relationship between plasma or RBC transfusion and outcome could not be verified by our study. Despite this limitation, we feel that the result of this study is another call for prudent risk-benefit analysis in transfusion decision-making.

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