original paper
Haematologica 1997; 82:318-323

RELATIONSHIP OF BLOOD TRANSFUSION, POST-OPERATIVE INFECTIONS AND IMMUNOREACTIVITY IN PATIENTS UNDERGOING SURGERY FOR GASTROINTESTINAL CANCER

LUCIA QUINTILIANI,* ANTONELLA PESCINI,* MARCO DI GIROLAMO,° PAOLA IUDICONE,* FEDERICO MARTINI,# MARINA GUGLIELMETTI*, ANNA BUZZONETTI,* SILVIA FASCIOLI^

**National Center for Blood Transfusion, Italian Red Cross, Rome; °San Giovanni Calibita Hospital, Rome; #Lazzaro Spallanzani Hospital, Rome; ^National Institute of Health, Rome, Italy*

ABSTRACT

Background and Objective. The immunosuppression induced by perioperative blood transfusion (BT) and its effect on the incidence of post-surgical infectious complications remains controversial. In this study, the relationship between BT and postoperative infections was investigated in 136 gastrointestinal cancer patients submitted to curative surgery.

Methods. Clinical and laboratory variables, data on postoperative infections, infection risk factors and types of transfusion were analyzed. Immune function was evaluated in 76 patients and compared before and after surgery.

Results. The overall postoperative infection rate was 28% for the transfused and 4.6% for the untransfused patients.

The univariate analysis of investigated variables indicated that BT, progressive cancer stage, duration of surgery, drains, all had significant association with infection. The multiple logistic regression analysis confirmed BT (p=0.0028) and advanced cancer stage (p<0.001) as significant risk factors for the postoperative infections. The results of immunological tests showed no significant differences between transfused and untransfused patient groups, after surgery. Comparing pre- and postoperative data from individual patients, an impairment of natural killer (NK) activity was observed in all patients regardless of their transfusional status; the synthesis of interleukin-2 (IL-2) and interferon-γ (IFN-γ) was also decreased respectively in the untrasfused and in the transfused patients.

Interpretation and Conclusions. These results indicate that other factors, beside BT, can induce immunosuppressive effects in these patients and thus increase their susceptibility to postoperative infections.

©1997, Ferrata Storti Foundation

Key words: blood transfusion, gastrointestinal cancer surgery, infective complications, immunomodulation

In several clinical studies blood transfusion (BT) was found to be associated, in cancer surgical patients, with detrimental effects, namely increased tumor recurrence and/or decreased survival.[1,2] More recently, perioperative BTs have been also implicated for postoperative infectious complications in patients undergoing abdominal surgery.[3-8] Similar findings were observed in orthopedic patients.[9]

It is generally believed that these findings are explained by immunosuppressive effects induced by BT.[10-13] This association was observed especially in patients receiving allogeneic BTs, while the use of autologous or filtered blood would not seem to influence the incidence of infection.[14-17] A higher frequency of these complications in transfused patients, as compared to untransfused patients or those transfused with filtered or autologous blood, was further proved by two randomized clinical studies.[17,18] These identified perioperative BT, in patients undergoing gastrointestinal cancer resection, as an independent risk factor for infection, even after adjustment for confusing variables. However, more recent studies, performed on colorectal cancer and orthopedic patients, did not confirm these results. In fact, similar incidences of infection were reported after allogeneic or autologous BTs.[19-21]

Although it seems clear that BT is associated with infection, the mechanisms by which BT adversely affects the host immune function have yet to be established.[22-24]

The present study was undertaken to investigate the relationship of BT with postoperative infections and immunoresponsiveness in patients affected by gastrointestinal cancer who underwent curative surgery.

Materials and Methods

Subjects studied

An observational study was performed on 152 patients, affected by gastrointestinal adenocarcinoma, who had curative resection at the Department of Surgery of S. Giovanni Calibita

Correspondence: Lucia Quintiliani, MD, Centro Nazionale Trasfusione Sangue - C.R.I., via Ramazzini 15, 00151 Rome, Italy. Tel./Fax International: +39.6.65741193.
Received February 14, 1997; accepted April 14, 1997.

©Ferrata Storti Foundation

Hospital, Rome. The study has been approved by the hospital ethical committee.

Sixteen patients were excluded from the study: four patients for preexisting infections and four for previous transfusional therapy; two patients had diagnosis of gastrointestinal lymphoma and one had a recent surgical operation; in five patients curative resection was not possible because of extended carcinoma.

The remaining 136 patients, 68 men (mean age 66) and 68 women (mean age 67) were suitable for the study. All patients received prophylactic perioperative antibiotics, generally a long-acting i.v. cephalosporin, associated with an i.m. aminoglicoside. Antibiotics were continued for 24 hours postoperatively.

The following characteristics of the patients and of the operations were collected: *anatomic location of tumor* (1. stomach, 2. cecum, ascending colon, flexures and transverse colon, 3. descending colon and sigmoid, 4. rectosigmoid and rectum); *staging of tumor* (Dukes' classification); operative procedures (1. total or subtotal gastrectomy, 2. right emicolectomy, 3. transverse colectomy, left emicolectomy, sigmoid resection, 4. Hartmann's operation, 5. anterior rectum resection with colostomy and abdominoperineal excision); *presence of drains*; *enteral and parenteral nutrition*. Other data collected included: age, gender, time elapsed from the onset of symptoms to admission, hemoglobin level, total white blood cell count (WBC), total serum proteins, duration of surgery.

The transfusions were given during the intraoperative or postoperative period (up to 12 days after operation); the type (1. whole blood or red blood cells, buffy coat not depleted, +fresh frozen plasma and 2. fresh frozen plasma alone) and unit number were reported.

Attending surgeons were the same for all patients.

Postoperative complications were those that occurred within 20 days of operation or until discharge from the hospital. Postoperative fever was defined as a temperature of more than 38°C for at least three days. Fever alone, without an identified infection, was not recorded.

Infective complications were defined as follows:

- pneumonia infection: fever, leukocytosis, clinical and radiological signs of chest infiltrate;
- urinary tract infection: leukocyturia in sediment with clinical signs and symptoms of UTI leading to treatment with antibiotics and/or positive urine culture;
- intra-abdominal or perineal abscess: intraperitoneal or pelvic collection of pus, diagnosed by ultrasonography or spontaneous discharge;
- wound infection: erythema and a purulent exudate from the wound.

The immune status of the last 76 consecutive patients was assessed before and 8-10 days after surgery evaluating the natural killer (NK) activity, the *in vitro* lymphokine syntesis by peripheral blood mononuclear cells (PBMC) and the *in vivo* and *in vitro* synthesis of prostaglandin E2 (PGE_2).

Lymphokine synthesis and assay

10^6 PBMC/mL, isolated by centrifugation on ficoll-hypaque, were cultured in RPMI 1640 supplemented with 20 mM HEPES buffer, penicillin, streptomycin, L-glutamine, sodium bicarbonate and 10% fetal calf serum (complete medium, CM), in presence of phytohemagglutinin (PHA 2 μg/mL) for 48 h. The supernatants were separated by centrifugation and stored at –30°C until lymphokine quantification was carried out. The levels of interleukin-2 (IL-2), interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α) were measured in the culture supernatants by using immunoradiometric assay (Medgenix-Fleurus, Belgium) according to the manufacturer's instructions.

Cytotoxicity assay

2×10^6 target cells (K-562 erythroleukemia cell line) were incubated for 1h with 50 μCi ^{51}Cr (Amersham International Plc., UK) at 37°C. After washing, the target cells were incubated again for 30 min, washed twice and plated in 96 V-well plates at 10^4 cells/well. PBMC were added to achieve the effector/target (E:T) ratios of 50:1, 25:1, 12.5:1. After 18h incubation, the supernatants were harvested and the ^{51}Cr release was measured by a γ-counter.

Prostaglandin production and assay

2.5×10^6 PBMC/mL were cultured in CM with and without 25 mg/μL of lipopolysaccharides (LPS) (Sigma-Aldrich, Milan, Italy) for 48 h. After centrifugation, the supernatants were separated and stored at –30°C.

The serum was separated from the blood, collected in tubes containing indomethacin (1% w/v), and processed within 1h of collection. PGE_2 levels were evaluated either in the sera or in the supernatants of unstimulated and stimulated cultures, by using PGE_2 (^{125}I) Assay System (Amersham International Plc., UK), according to manufacturer's instructions. Preliminarly, all samples were purified according to the method reported by Kelly *et al*.[25] Briefly, aliquots of serum or culture supernatant were extracted with ethanol-water (4:1), additioned with 1% of glacial acetic acid and applied to an Amprep C18 minicolumn, primed with two column volumes of 10% ethanol and washed with water and exane. The PGE_2 fraction was eluted with ethyl acetate and evaporated until dry. Then, the extracted PGE_2 was converted into its methyl oximate derivative and stored at –30°C for up to 6 days before analysis.

Statistical analysis

Comparisons of the data were performed by SPSS package on the groups of patients: transfused vs nontransfused and infected vs noninfected.

Univariate analysis was done by Pearson's chi-square test for categorical variables; Student's t-test and Kolmogorov-Smirnov (K-S) test were used for continuous variables yielding similar results. Here we report the results obtained by the K-S test; a value of $p < 0.05$ was considered significant.

A logistic regression analysis (forced entry method) was accomplished to investigate the existence of an independent association between BT and postoperative infection, after adjustment for the effects of confounding variables. All the variables have been included except those concerning the immune functions as performed on a limited number of patients. The effects of surgery plus BT and those of surgery alone on the immunological variables were evaluated by Wilcoxon matched-pairs test. This compared pre- and postoperative data obtained from individual patients, within the appropriate group.

Results

The incidence of postoperative infections in the various groups of patients is reported in Table 1. Infection developed in 28 of the 136 patients (20.6%). Six patients (21.4%) had wound infections, fifteen (53.6%) abdominal or perineal abscess and seven (25%) urinary infections.

Table 1. Incidence of postoperative infection in transfused and non-trasfused patients.

			Infections	
			Number	*%*
All patients	(n.)	(136)	28	20.6
Non-transfused patients	(n.)	(43)	2	4.6
Transfused patients	(n.)	(93)	26	27.9
Transfused with:				
whole blood or packed RBC + plasma	(n.)	(57)	22	38.6
plasma alone	(n.)	(36)	4	11.1

©Ferrata Storti Foundation

Table 2. Clinical and laboratory features of transfused and non-transfused patients.

		Non-transfused n. (%)	Transfused n.(%)	p values
Patients (n. 136)		43 (31.6)	93 (68.4)	
*Continuous variables**				
Age (years)		64 (1.83)	66 (1.01)	0.207
Hb (g/L)		135.5 (0.27)	113.6 (0.25)	<0.001
Serum proteins (g/dL)		6.61 (0.09)	6.45 (0.06)	0.544
WBC (x10^9/L)		7.2 (0.37)	7.2 (0.30)	0.566
Time from onset of symptoms to operation (months)		3.90 (0.66)	5.34 (0.58)	0.512
Duration of surgery (min.)		138 (7.29)	171 (6.86)	0.015
Categorical variables°				
Sex				
male		22	46	
female		21	47	0.853
Tumor site				
Stomach		6	29	
Cecum, ascend., transv. colon		2	14	
Descend. colon and sigmoid		16	20	
Rectosigmoid and rectum		19	30	0.163
Dukes	A	3	11	
	B	20	37	
	C	7	26	
	D	13	19	0.278
Surgical procedures				
Gastrectomy		6	29	
Right emicolectomy		8	17	
Transv., left colectomy and sigmoid resection		10	11	
Hartmann's operation		4	6	
Ant. rectum resection and abdomino-perineal excision		14	30	0.181
Drains	No	15	3	
	Yes	28	90	< 0.001
Nutrition				
parenteral		26	47	
enteral		17	46	0.542
Infection				
No		41	67	
Yes		2	26	0.001

*means (SEM). The groups were compared by K-S test.
°groups were compared by chi-square test.

Table 3. Clinical and laboratory features of infected and non-infected patients.

		Non-infected n. (%)	Infected n.(%)	p values
Patients (n. 136)		108 (79.4)	28 (20.6)	
*Continuous variables**				
Age (years)		65 (1.01)	67 (2.03)	0.395
Hb (g/L)		122.6 (0.23)	112.6 (0.52)	0.179
Serum proteins (g/dL)		6.53 (0.06)	6.40 (0.14)	0.831
WBC (x10^9/L)		7.2 (0.26)	7.3 (0.55)	0.911
Time from onset of symptoms to operation (months)		4.6 (0.48)	6.0 (1.15)	0.493
Duration of surgery (min.)		154 (5.55)	187 (14.08)	0.050
Whole blood or packed RBC + plasma (units)		0.37 (0.08)	1.85 (0.59)	0.004
Plasma (units)		1.75 (0.22)	4.39 (1.20)	0.036
Categorical variables°				
Sex				
male		52	16	
female		56	12	0.396
Tumor site				
Stomach		26	9	
Cecum, ascend., transv. colon		13	3	
Descend. colon and sigmoid		32	4	
Rectosigmoid and rectum		37	12	0.418
Dukes	A	13	1	
	B	46	11	
	C	30	3	
	D	19	13	0.006
Surgical procedures				
Gastrectomy (patients)		26	9	
Right emicolectomy		21	4	
Transv., left colectomy and sigmoid resection		18	3	
Hartmann's operation		7	3	
Ant. rectum resection and abdomino-perineal excision		35	9	0.749
Drains	absent	18	0	
	present	90	28	0.020
Nutrition				
parenteral		62	11	
enteral		46	17	0.114
Transfusion				
No		41	2	
Yes		67	26	0.001

*means (SEM). The groups were compared by K-S test.
°groups were compared by chi-square test.

Significant differences in infection rate were found between patients not transfused or transfused by only plasma and those transfused by whole blood or packed RBC and plasma (p=0.002).

In Tables 2 and 3 data of the variables recorded for the 136 patients are reported.

Comparisons of categorical and continuous characteristics between transfused and untransfused patients (Table 2) evidenced that blood transfusion had a significant association with a low level of Hb, a prolonged operative time and surgical drains.

Since the assignment to transfused and untransfused groups could not be done at random, we compared the two patient groups before surgery and transfusional therapy to ascertain possible differences between them. We found that the Hb level was significantly altered at that time. No differences were identified when the patients were compared for age, sex, serum proteins, white cell count, tumor site and cancer stage.

After surgery, we found a significantly longer operation time and more frequent drains in transfused patients, while no differences in surgical procedures and enteral or parenteral nutrition were observed between the two patient groups.

Comparing the same variables between infected and non-infected patients (Table 3), we found

©Errata Storti Foundation

Table 4. Variables associated with infection.

	Unadjusted odds ratio		
	Value	*95% confidence bounds*	*p value*
Cancer stage			
I, II, III, vs IV	4.059	1.662-9.912	0.0013
Duration of surgery			
< 90' vs > 90'	1.326	0.273-6.430	0.7249
Drains			
yes/no	1.318	1.185-1.449	0.0203
Blood transfusion			
yes/no	7.955	1.793-35.291	0.0017

Table 5. Immunological variables of nontransfused and transfused patients.

	Nontransfused	*Transfused*	*p values by K-S test**
Patients (n. 76)	27 (36%)	49 (64%)	
	Mean (SEM)	Mean (SEM)	
Before surgery			
IL-2 IU/mL	18.25 (5.49)	5.82 (0.86)	0.004
IFN γ IU/mL	134.8 (16.54)	115.6 (10.20)	0.330
TNF-α pg/mL	4133 (473.87)	3741 (413.83)	0.417
NK cytotoxicity			
E:T 50:1 %	43.7 (3.44)	43.8 (3.10)	0.890
Serum PGE_2 pg/mL	25.4 (4.15)	24.25 (4.06)	0.850
Spontaneous PGE_2 release pg/mL	139.0 (46.62)	60.08 (13.30)	0.054
LPS induced PGE_2 release pg/mL	1040 (159.15)	732 (108.63)	0.102
After surgery			
IL-2 IU/mL	6.85 (1.55)	6.91 (1.53)	0.550
IFN-γ IU/mL	109.2 (13.27)	83.6 (13.91)	0.065
TNF-α pg/mL	4540 (560.99)	3614 (397.41)	0.521
NK cytotoxicity			
E:T 50:1%	34.9 (3.69)	29.3(2.65)	0.438
Serum PGE_2 pg/mL	32.2 (6.02)	38.2 (5.80)	0.499
Spontaneous PGE_2 release pg/mL	147.7 (62.23)	140.5 (39.31)	0.919
LPS induced PGE_2 release pg/mL	873 (154.14)	756 (101.74)	0.514

**T vs NT groups.*

blood transfusions, a progressive cancer stage, a longer duration of surgery and drains, significantly associated with infections.

Unadjusted odds ratio for risk of infection are reported in Table 4.

In our data set, the duration of surgery and the presence of drains were significantly associated with both blood transfusions and postoperative infections. These variables were therefore identified as true confounders.[26] Using a multiple logistic regression model, which included the confounding variables and the blood transfusion as covariates, it was observed that BT and progressive cancer stage were significantly associated with infections (respectively, p = 0.028 and p = 0.0001).

As regarding the immunoreactivity of the patients, immunological tests were carried out in 76 patients (49 transfused and 27 untransfused), either before or after surgery, in order to verify a possible impairment of their immune responses following surgery and transfusional therapy. The results are reported in Table 5.

After surgery, no significant changes in the lymphokine synthesis and NK cytotoxic activity were observed, when the two groups of patients, transfused vs untrasfused, were compared. Similar results were found comparing infected to uninfected patients. Given the variability of immunological results, we also compared the same variables using matched-pair data obtained from individual patient before and after surgery, within the pertinent group, using the Wilcoxon test (Table 6).

Our findings demonstrated: i) significant decrease in NK cytotoxicity in all groups of patients regardless of transfusion status; ii) significant decrease in IFN-γ synthesis of the patients as a whole group and of those transfused; iii) significant decrease in IL-2 synthesis of untransfused patients.

Discussion

In our patients, allogeneic BT was associated with a postoperative infection rate of 28%, as compared with 4.6% of the untransfused patients. Similar results in transfused and non-transfused patients or those transfused with autologous blood were obtained by others;[4,5,7,8,14-18,27,28] while some investigators failed to detect an association of allogeneic BT with infection.[6,19,20,26,29,30]

The univariate analysis of the investigated variables indicates a significant association of BT, cancer stage, presence of drains and duration of surgery with infections.

After adjustment for the effects of confounding variables, that in our data set were the duration of surgery and the drains, BT and progressive cancer stage continued to be independently associated with postoperative infections.

The significant association of perioperative BT with infections strongly suggests a causal relationship between the two events, according to the hypothesis that allogeneic BT induces a non specific immunodepression which would favor postoperative infective complications. The mechanisms by which BT may cause immunodepression concern cell-mediated immunity and the function of

©Ferrata Storti Foundation

Table 6. Comparisons between pre- and post-operative immunological data.

	Non-transfused (n. 27)		*p values**	*Transfused (n. 49)*		*p values**
	Before surgery	*After surgery*		*Before surgery*	*After surgery*	
	Mean (SEM)	*Mean (SEM)*		*Mean (SEM)*	*Mean (SEM)*	
IL-2 IU/mL	18.25 (5.49)	6.85 (1.55)	0.025	5.82 (0.86)	6.91 (1.53)	0.896
IFN-γ IU/mL	134.8 (16.54)	109.2 (13.27)	0.136	115.6 (10.20)	83.6 (13.91)	0.015
TNF-α pg/mL	4133 (473.87)	4540 (560.99)	0.775	3741 (413.83)	3614 (397.41)	0.932
NK cytotoxicity E:T 50:1 %	43.7 (3.44)	34.9 (3.69)	0.039	43.8 (3.10)	29.3 (2.65)	<0.001
Serum PGE_2 pg/mL	25.4 (4.15)	32.2 (6.02)	0.322	24.25 (4.06)	38.2 (5.80)	0.187
Spontaneous PGE_2 release pg/mL	139.0 (46.62)	147.7 (62.23)	0.736	60.08 (13.30)	140.5 (39.31)	0.249
LPS induced PGE_2 release pg/mL	1040 (159.15)	873 (154.14)	0.497	732 (108.63)	756 (101.74)	0.467

**by Wilcoxon matched pairs signed-ranks test.*

macrophages, decreasing their migration toward chemotactic stimuli and/or inducing an increased production of PGE_2.[31] Accordingly, we investigated the synthesis of lymphokines, the NK cytotoxic activity and the production of PGE_2.

Limitations of our study design are that BT cannot be given in blinded crossover fashion for medico-ethical reasons. However, we analyzed separately transfused and non transfused patients, before surgery and any transfusional therapy, to assess the homogeneity of the two groups. As seen, pre-operative clinical and laboratory data and immune responses were similar in the two patient groups, with the exception of the Hb level and IL-2 synthesis by PBMC which were both lower in the transfused patients. The results regarding the Hb concentration can be reasonably explained: these patients needed perioperative transfusion; the synthesis of IL-2, significantly lower in transfused patients, suggests an impaired immunoresponsiveness prior to the operation and BT that could favor postoperative infections.

After surgery, the two groups of patients, transfused and non transfused, did not show significant differences in their immune responses. We also focused on a possible involvement of the PGE_2 in the hypothetical effect of allogeneic BT. We observed that the *in vivo* and *in vitro* synthesis of PGE_2 did not significantly rise after surgery, regardless of whether the patients were transfused or not. This indicates that if changes in the prostaglandin metabolism occur in neoplastic patients, as we also observed in respect to healthy subjects,[32] they are not due to BT, and are present in all patients.

Our immunological results are in line with those of some reports[29,33,34] and in contrast to the findings of others.[16-18,35,36] Also in animal models, different changes in the immunoresponsiveness of transfused hosts have been described.[37-40]

Given the diversity of methodology used to assess the patient immune responses, it is very difficult to make comparisons with the reported data and to explain the discrepancies with our results.

In summary, this study showed a significant association of BT and advanced cancer stage with postoperative infections, also after adjustment for the effects of the variables we analysed, while clear alterations of immune responses in transfused patients, as compared to untransfused, were absent. For this reason, we agree with Vamvakas *et al.*[41] who believe that this relationship could be due to other not analyzed or unknown confounders. The results we obtained by comparing pre- and postoperative data from anyone patient, seem to support such interpretation, as we observed decreased NK cytotoxicity and IFN-γ production in all patients, irrespective of their transfusional status and decreased IL-2 synthesis only in non transfused patients. This suggests that anesthesia, operative trauma or blood loss play a role in inducing immunosuppressive effects.

On the whole, these results, while not excluding, do not support the notion that BTs are the only factor responsible for an immunosuppressive condition that might lead to infection or to a worse outcome in these patients.

©Fondazione Clinica Editoriale

References

1. Blumberg N, Chuang-Stein C, Heal JM. The relationship of blood transfusion, tumor staging, and cancer recurrence. Transfusion 1990; 30:291-4.
2. Busch ORC, Hop WCJ, Hoynck van Papendrecht MAW, Marquet RL, Jeekel J. Blood transfusions and prognosis in colorectal cancer. N Engl J Med 1993; 328:1372-6.
3. Tartter PI. Blood transfusion and postoperative infections. Transfusion 1989; 29:456-9.
4. Tartter PI. Blood transfusion and infectious complications following colorectal cancer surgery. Br J Surg 1988; 75:789-92.
5. Pinto V, Baldonedo R, Nicolas C, Barez A, Perez A, Aza J. Relationship of transfusion and infectious complications after gastric carcinoma operations. Transfusion 1991; 31:114-8.
6. Jahnson S, Andersson M. Adverse effects of perioperative blood transfusion in patients with colorectal cancer. Eur J Surg 1992; 158:

419-25.
7. Braga M, Vignali A, Radaelli G, Gianotti L, Di Carlo V. Association between perioperative blood transfusion and postoperative infection in patients having elective operations for gastrointestinal cancer. Eur J Surg 1992; 158:531-6.
8. Ford CD, Van Moorleghem G, Menlove RL. Blood transfusions and postoperative wound infection. Surgery 1993; 113:603-7.
9. Andreu G. Transfusion et infections post-opératoires: revue et synthèse des recherches et de l'expérience clinique. Transf Clin Biol 1994; 3:231-6.
10. Kaplan J, Sarnaik S, Gitlin J, Lusher J. Diminished helper/suppressor lymphocyte ratios and natural killer activity in recipients of repeated blood transfusions. Blood1984; 64:308-10.
11. Waymack JP, Balakrishnan K, McNeal N, et al. Effect of blood transfusions on macrophage-lymphocyte interaction in an animal model. Ann Surg 1986; 204:681-6.
12. Galandiuk S, George CD, Pietsch JD, Byck DC, DeWeese RC, Polk HC. An experimental assessment of the effect of blood transfusion on susceptibility to bacterial infection. Surgery 1990; 108:567-71.
13. Jensen LS. The influence of blood transfusion on natural killer cell activity and postoperative infections. In: Houbiers JGA, ed. Blood transfusion in cancer surgery, 1994. p. 29-34.
14. Murphy P, Heal JM, Blumberg N. Infection or suspected infection after hip replacement surgery with autologous or homologous blood transfusions. Transfusion 1991; 31:212-7.
15. Mezrow CK, Bergstein I, Tartter PI. Postoperative infections following autologous and homologous blood transfusions. Transfusion 1992; 32:27-30.
16. Triulzi DJ, Vanek K, Ryan DH, Blumberg N. A clinical and immunologic study of blood transfusion and postoperative bacterial infection in spinal surgery. Transfusion 1992; 32:517-24.
17. Heiss MM, Mempel W, Jauch KW, et al. Beneficial effect of autologous blood transfusion on infectious complications after colorectal cancer surgery. Lancet 1993; 342:1328-33.
18. Jensen LS, Andersen AJ, Christiansen PM, et al. Postoperative infection and natural killer cell function following blood transfusion in patients undergoing elective colorectal surgery. Br J Surg 1992; 79:513-6.
19. Fernandez MC, Gottlieb M, Menitove JE. Blood transfusion and postoperative infection in orthopedic patients. Transfusion 1992; 32:318-22.
20. Busch ORC, Hop WCJ, Marquet RL, Jeekel J. Autologous blood and infections after colorectal surgery [letter]. Lancet 1994; 343:668.
21. Vamvakas EC, Moore SB, Cabanela M. Blood transfusion and septic complications after hip replacement surgery. Transfusion 1995; 35:150-6.
22. George CD, Morello PJ. Immunologic effects of blood transfusion upon renal transplantation, tumor operations, and bacterial infections. Am J Surg 1986; 152:329-37.
23. Quintiliani L, Buzzonetti A, Di Girolamo M, et al. Effects of blood transfusion on the immune responsiveness and survival of cancer patients: a prospective study. Transfusion 1991; 31:713-8.
24. Mincheff MS, Meryman HT, Kapoor V, Alsop P, Wotzel M. Blood transfusion and immunomodulation: a possible mechanism. Vox Sang 1993; 65:18-24.
25. Kelly RW, Graham BJM, O'Sullivan MJ. Measurement of PGE2 as the methyl oximate by radioimmunoassay using a novel iodinated label. Prostaglandins Leukot Essent Fatty Acids 1989; 37:187-91.
26. Vamvakas EC, Moore SB. Blood transfusion and postoperative septic complications. Transfusion 1994; 34:714-27.
27. Vignali A, Braga M, Gianotti L, et al. A single unit of transfused allogeneic blood increases postoperative infections. Vox Sang 1996; 71:170-5.
28. Jensen LS, Kissmeyer-Nielsen P, Wolff B, Qvist N. Randomised comparison of leucocyte-depleted versus buffy-coat poor blood transfusion and complications after colorectal surgery. Lancet 1996; 348:841-5.
29. Tietze M, Kluter H, Troch M, Kirchner H. Immune responsiveness in orthopedic surgery patients after transfusion of autologous or allogeneic blood. Transfusion 1995; 5:378-3.
30. Houbiers JGA, Brand A, van de Watering LMG, et al. Randomised controlled trial comparing transfusion of leucocyte-depleted or buffy-coat-depleted blood in surgery for colorectal cancer. Lancet 1994; 344:573-8.
31. Alexander JW. Transfusion-induced immunomodulation and infection. Transfusion 1991; 31:195-6.
32. Quintiliani L, Iudicone P, Di Girolamo M, et al. Immunoresponsiveness of cancer patients: effect of blood transfusion and immune reactivity of tumor infiltrating lymphocytes. Cancer Detect Prev 1995; 19:518-26.
33. Vandekerckhove BAE, van Bree S, Zhang L, Datema G, Zantvoort F, Claas FHJ. Increase of donor-specific cytotoxic T lymphocyte precursors after transfusion. Transplantation 1989; 48:672-5.
34. Vandekerckhove BAE, Datema G, Zantvoort F, Claas FHJ. An increase of donor-specific T helper precursors resulting from blood transfusions. Transplantation 1990; 49:987-91.
35. Jensen LS, Hokland M, Nielsen HJ. A randomized controlled study of the effect of bedside leucocyte depletion on the immunosuppressive effect of whole blood transfusion in patients undergoing elective colorectal surgery. Br J Surg 1996; 83:973-7.
36. Gafter U, Kalechman Y, Sredni B. Blood transfusion enhances production of T-helper-2 cytokines and transforming growth factor β in humans. Clin Sci 1996; 91:519-23.
37. Waymack JP, Warden GD, Miskell P, et al. Effect of varying number and volume of transfusions on mortality rate following septic challenge in an animal model. World J Surg 1987; 11:387-92.
38. Waymack JP, Yurt RW. The effect of blood transfusions on immune function. V. The effect on the inflammatory response to bacterial infections. J Surg Res 1990; 48:147-53.
39. Babcock GF, Alexander JW. The effects of blood transfusion on cytokine production by TH1 and TH2 lymphocytes in the mouse. Transplantation 1996; 61:465-8.
40. Martini F, Iudicone P, Guglielmetti M, Giuliani E, Quintiliani L. Allogenic blood transfusion effects in mice. La Trasfusione del Sangue 1987; 4:196-204.
41. Vamvakas EC, Carven JH, Hibberd PL. Blood transfusion and infection after colorectal cancer surgery. Transfusion 1996; 36:1000-8.

©Ferrata Storti Foundation