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Perioperative Blood Transfusion and Prognosis of Resected Stage Ia Lung Cancer

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Abstract—*Based on the experience of blood-related immunosuppression in kidney transplants, some retrospective studies have reported an adverse relationship between blood transfusion and survival after curative resection for cancer. In order to confirm these findings, we have retrospectively evaluated our population of resected stage Ia non-small cell lung cancers* (years 1974–79). *Two hundred and eighty-three patients were included in this analysis:* 65 *underwent pneumonectomy* (23%), 205 *lobectomy* (72%) *and* 13 *sublobar resections* (5%). *Patients submitted to perioperative blood transfusions were* 157 (55%), *without major differences according to surgery or tumour extent. The cumulative survival at* 8 yr *was* 40% *for transfused patients and* 41% *for nontransfused, relapse-free survival was respectively* 36% *and* 34%; *no differences were detectable stratifying for the amount of blood transfused or the extent of operation. Our experience does not support the hypothesis of an adverse prognosis related to perioperative blood transfusion.*

INTRODUCTION

THE POSSIBILITY of a nonspecific immunosuppression determined by blood transfusions on kidney grafted patients [1, 2] has induced a series of studies aimed at evaluating this potentially negative effect on cancer patients. Two studies on lung cancer survival and blood transfusions have recently appeared in the literature. The first, from Mount Sinai Medical Center, based on 165 resections for Stage Ia non-small cell lung cancer, shows a significantly lower relapse-free survival at 5 yr for transfused vs. non-transfused patients (62% vs. 76%, $P < 0.013$) [3]. The second, from the Medical Center Hospital of Vermont, based on 105 resections for Stage I and II lung cancer, reports a 44% 5-yr survival in non-transfused patients and only 27% survival in transfused patients [4]. In order to confirm these results, we have retrospectively analysed our population of resected stage Ia non-small cell lung cancers (years 1974–79).

PATIENTS AND METHODS

Two hundred and eighty-three patients, out of 285 consecutive resections for pathologic Stage Ia non-small cell lung cancer performed at the Istituto Nazionale Tumori of Milan from January 1974 to December 1979, were considered suitable and included in this retrospective analysis. Clinical charts were reviewed and the following information recorded: age, sex, tumor size at pathology (T1–2), cell type (1978 WHO classification), preoperative cardiopulmonary risk (as defined by Kalil [5] in terms of "moderate preoperative risk"), extent of resection, quality (whole blood, packed RBC) and quantity (total number of units) of blood transfusions given preoperatively, intraoperatively, and postoperatively up to 8 days from operation. Statistical differences among survival curves were computed using the Logrank test [6].

According to TNM criteria (UICC 1978) 66 patients (23%) resulted T1 NO MO and 217 (77%) T2 NO MO. Patients submitted to perioperative blood transfusions were 157 (55%), non-transfused patients 126. Our criteria for blood transfusion included: a preoperative hemoglobin count below 9.5 g/100 ml, an intraoperative blood loss exceeding 300 ml, a postoperative drop of hemoglobin count exceeding 25% of the corresponding preoperative value.

The clinical features of the patients, according to the perioperative administration of blood transfusions, are shown in Table 1. No major differences are evident among the two groups, if we except a significant, and predictable, association between transfusion and resection volume. Sixty-five patients underwent pneumonectomy (23%), 205

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Table 1. Clinical features of patients

	Nontransfused	Transfused
Age over 60	64 (50)	75 (48)
Males	117 (93)	147 (94)
Squamous	59 (47)	79 (50)
Adeno	49 (39)	53 (34)
Large	18 (14)	25 (16)
T1	37 (24)	29 (18)
T2	89 (71)	128 (82)
Cardio-pulmonary risk	51 (40)	55 (35)
Pneumonectomy	21 (17)	44 (28)
Lobectomy	94 (75)	111 (71)
Sublobar resection	11 (8)	2 (1)
Operative mortality	3 (2.4)	6 (3.8)
	126 (100)	157 (100)

( ) Column percent

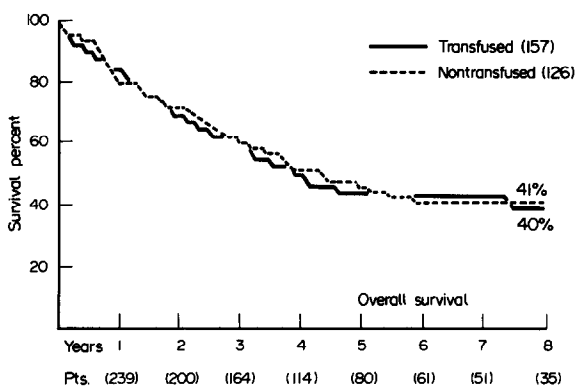

Fig. 1. Cumulative survival (%) for transfused and nontransfused patients (yr after surgery).

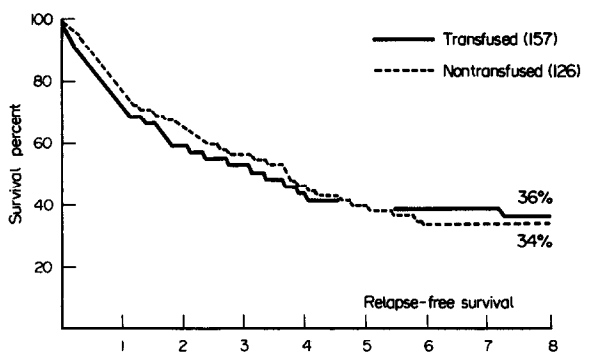

Fig. 2. Relapse-free survival for transfused and nontransfused patients.

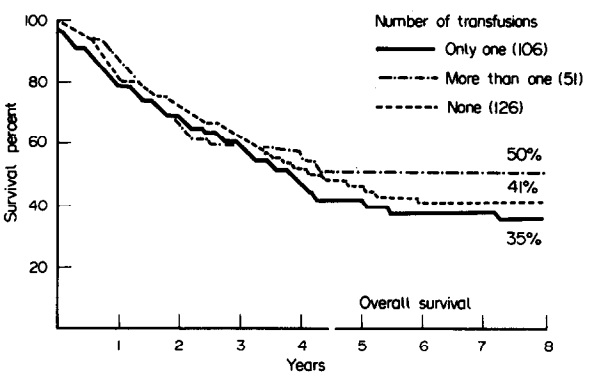

Fig. 3. Cumulative survival according to the units of blood transfused.

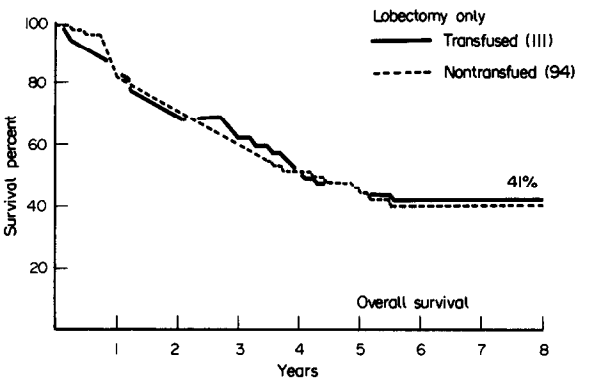

Fig. 4. Cumulative survival after lobectomy: transfused vs nontransfused patients.

lobectomy (73%) and 13 sublobar resection (4%), a larger proportion of pneumonectomies being related to perioperative transfusion.

RESULTS

The cumulative survival at 8 yr is 40% for transfused patients and 41% for non-transfused patients (Fig. 1), the relapse-free survival being 36% and 34%, respectively (Fig. 2). No differences were detectable stratifying for the amount of transfused blood or the extent of operation. Figure 3 shows the long term survival rates according to the number of transfused blood units: 106 patients who were given a single blood unit present a lower survival rate (35%) than 51 patients receiving more than one unit (50%), but the difference is

not significative. Considering only the subjects who underwent the same operation, namely lobectomy, the 8-yr survival rates are absolutely superposable: 41% for both transfused and non-transfused patients (Fig. 4).

DISCUSSION

The rationale for a detrimental effect of blood transfusion in cancer patients is strongly suggested by kidney graft experience [2, 7, 8], and various effects of immunomodulation have been related to blood transfusions, from aspecific immunosuppression to selective stimulation of T-suppressor cells [2, 9–12]. Unfortunately, experimental studies on rats, using different models, ended up with conflicting results, showing both enhancement [13] and inhibition [14] of tumour growth in blood transfused animals compared with the nontransfused. Besides the above mentioned studies on human lung cancer [3, 4], a negative effect on survival associated with blood transfusion has been described in colonic cancer [15] and most recently in breast cancer [16]. Nevertheless, a previous study conducted by Foster *et al.* on mastectomized patients at Vermont Cancer Center failed to demonstrate any difference in survival [17], and a new study on colorectal carcinoma could not confirm the adverse effect of blood transfusions [18].

Our data, based on a large series of stage Ia lung cancer, do not support the hypothesis of an adverse prognosis related to perioperative blood transfusion. Both overall and relapse-free survival rates of the subset of transfused patients were superimposable to those of non-transfused patients. Even though this is a retrospective and non-randomized study, the results are compatible with a total lack of effect of perioperative blood transfusion on long-term survival in resected lung cancer. Previous reports could have been affected by selection biases: in fact in the study of Vermont Medical Center [4] there was a higher proportion of stage II disease in the transfused group (18% vs. 7%), while in the study from Mount Sinai [3] only data from relapse free survival are reported and most of the difference is due to the small subset of pneumonectomies (15 pts.). In this respect, the resection volume can be a major confounder, being related to the need of blood transfusion and at the same time to the tumour extent. Moreover, bad prognosis and need of blood supply may well depend on the presence of occult micrometastatic disease, which again is stage-related. As a matter of fact, strong determinants of prognosis like tumor and nodal extent of disease are difficult to assess in a retrospective analysis, even comparing subjects with a well defined and uniform pathologic stage.

Since the practical impact of this concept of "harmful transfusion" could be relevant enough to modify the present policies of cancer surgery, a prospective study to find out if transfusions may really shorten survival of potentially cured cancer patients could be of value. A possible way to answer the question might be to randomize patients to allogeneic blood transfusion or autologous blood transfusion through preoperative hemodilution.

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