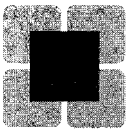

Perioperative blood transfusion and survival of breast cancer patients after modified radical mastectomy

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■ To investigate the effect of perioperative blood transfusion on the survival of patients with breast cancer, the authors reviewed the clinical records of 455 patients who underwent modified radical mastectomy between 1960 and 1979. Thirty-eight patients (8.4%) received blood transfusions. For stage I patients who received perioperative transfusions, 5- and 10-year survival rates were 53% and 47%; for the no-transfusion group, the rates were 93% and 85%. There was also a significant difference in disease-free survival for stage I patients: for the transfusion group, 5- and 10-year survival rates were 47%; for the group not receiving a transfusion, the rates were 89% and 84%. For stage II patients, there was no difference in total or disease-free survival between those who received transfusions and those who did not, and both groups had comparable distribution of nodes.

□ INDEX TERMS: BLOOD TRANSFUSION; MASTECTOMY □ CLEVE CLIN J MED 1991; 58:515–519

DURING the past 7 years, interest has grown in the effect of blood transfusion on survival and recurrence in patients with malignancies. In 1973, the beneficial effect of blood transfusion on renal graft survival was reported.[1] It is now recognized that components of transfused blood produce immunological tolerance, which improves graft survival in renal transplantation.[2] In 1982, Burrows and associates reported that perioperative blood transfusion was associated with reduced recurrence-free survival after colorectal cancer operations.[4] Our study examines the effect of perioperative blood transfusion on the prognosis of patients with potentially curable breast cancer after modified radical mastectomy.

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PATIENTS AND METHODS

We reviewed the clinical records of all patients (N = 1,413) treated for carcinoma of the breast at the Department of General Surgery, The Cleveland Clinic Foundation, between January 1, 1966 and December 31, 1979. For this study, we included 455 women: those with unilateral invasive carcinoma of the breast, those primarily treated with modified radical mastectomy and

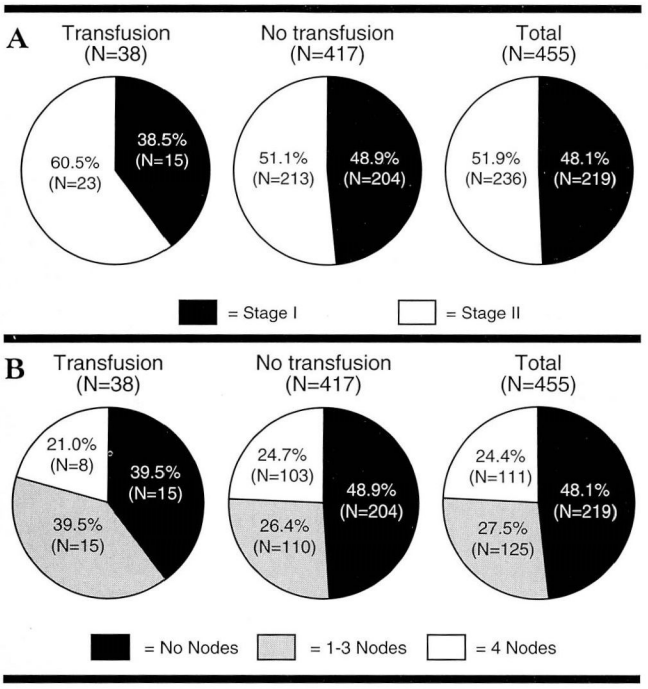

FIGURE 1. Distribution of staging (A), and distribution of axillary nodal status (B).

axillary dissection, and those with stage I or II disease with tumor diameter less than 5 cm. Patients excluded from the study were those with a second life-threatening malignancy, preoperative chemotherapy or radiation therapy, incomplete staging or survival data, treatment with simple or partial mastectomy (these patients have not required transfusion), or cause of death other than breast carcinoma. The age, stage, and axillary nodal status were recorded for each patient. Perioperative blood transfusion was defined as transfusion administered within the period 1 week before and after the day of surgery. Transfusion status, day of transfusion, volume and type of blood products used, and indications for transfusion were recorded for each patient. The admission and lowest postoperative hemoglobin and hematocrit levels were recorded when available.

Transfused blood was either whole blood or packed red blood cells obtained from volunteer donors. Most patients with axillary lymph node metastases received chemotherapy if they were premenopausal. All patients were followed for at least 10 years, and recurrences were confirmed by biopsies and histologic studies or by chest radiographs, computed tomograms, or bone scans.

Differences between staging and axillary nodal status were tested with the chi-square test. Age and laboratory values were tested with Student's t-test and Wilcoxon tests.[5] The Kaplan-Meier[6] method was used to estimate overall and disease-free survival and the Mantel-Haenzel test[7] was used to compare survival distributions for patients receiving and not receiving transfusions.

RESULTS

Of the 455 patients who were included in this study, 38 patients (8.4%) received perioperative blood transfusions and 417 (91.6%) did not. The transfusion and no-transfusion groups were comparable in staging and axillary nodal status (*Figure 1*). The mean age of patients who received transfusions (49.0 years) was significantly younger than that of patients who did not receive transfusions (54.1 years). Both admission and postoperative hemoglobin and hematocrit values were lower in the transfusion group (*Figure 2*).

Of the 38 patients who received transfusions, 36 received them on the day of surgery and 2 within 1 week after surgery; 34 patients received packed red blood cells and 4 received whole blood. Twenty-nine patients received a single unit (0.5 L) of blood and 9 received 2 units (1.0 L) each. The indications for blood transfusion were hypotension during or after surgery (15 patients) or postoperative anemia (5 patients). For 15 patients, the record did not reflect the indication for transfusion. For the remaining 3 patients, one indication was postoperative hematemesis from a peptic ulcer; one was "prolonged operation" for breast reconstruction after mastectomy; and one was "blood lost" during breast reconstruction.

Comparison of survival rates

The differences in survival and disease-free survival showed the adverse effect of transfusion. The difference for the groups overall was not statistically significant (*Figure 3*).

For stage I patients, however, there was a statistically significant difference in both overall and disease-free survival. Both survival measures were significantly worse for those who received perioperative blood transfusions. The 5- and 10-year overall survival rates were 53% and 47% for the transfusion group and 92% and 85% for the no-transfusion group ($P = 0.0002$, *Figure 4, A*). The 5- and 10-year disease-free survival rates were both 47% for the transfusion group and 89% and 84% for the no-transfusion group ($P = 0.0005$, *Figure 4, B*).

When stage II patients from both groups were com-

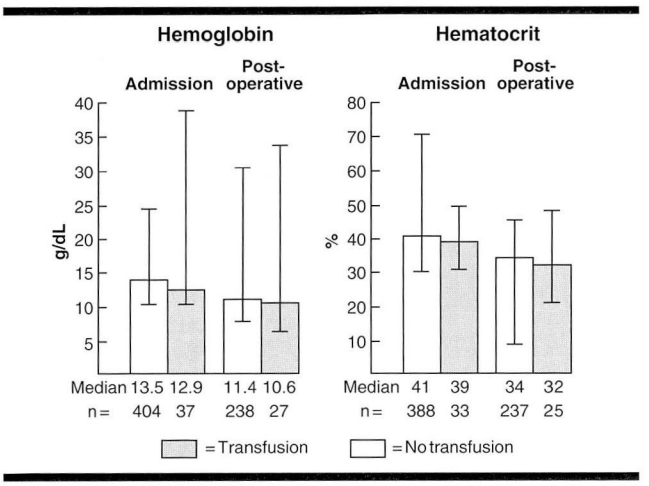

FIGURE 2. Admission and postoperative laboratory values for transfusion and no-transfusion groups (Wilcoxon test $P < 0.01$).

pared, there appeared to be no difference in either overall survival or disease-free survival (*Figure 5*).

DISCUSSION

Previous studies investigating the effect of blood transfusion on patients operated on for breast carcinoma have given conflicting results. Block and Enck[8] reported on 53 patients with node-negative T1 and T2 breast cancer, including 19 who received transfusions and 34 who did not. They noted no difference between groups in recurrence of disease after a median follow-up of 45 months (range 27 to 68 months).

Foster and associates[9] reviewed the cases of 226 surgically treated breast cancer patients, including 65 who received transfusions and 161 who did not. They found no difference in survival between the transfusion and no-transfusion groups overall or at specific stages. Median follow-up was 52 months; 11% of the patients were treated with partial mastectomy.

Nowak and Ponsky[10] reported on 81 breast cancer patients who had radical or modified radical mastectomy, including 41 who received transfusions and 40 who did not. They found no difference in disease-free survival of all patients between both groups. Only a subgroup of patients with estrogen receptors who received tamoxifen was found to have reduced disease-free survival after transfusion.

Tartter and associates[11] reviewed the cases of 169 patients who had undergone mastectomy with axillary clearance and found a reduced disease-free survival in

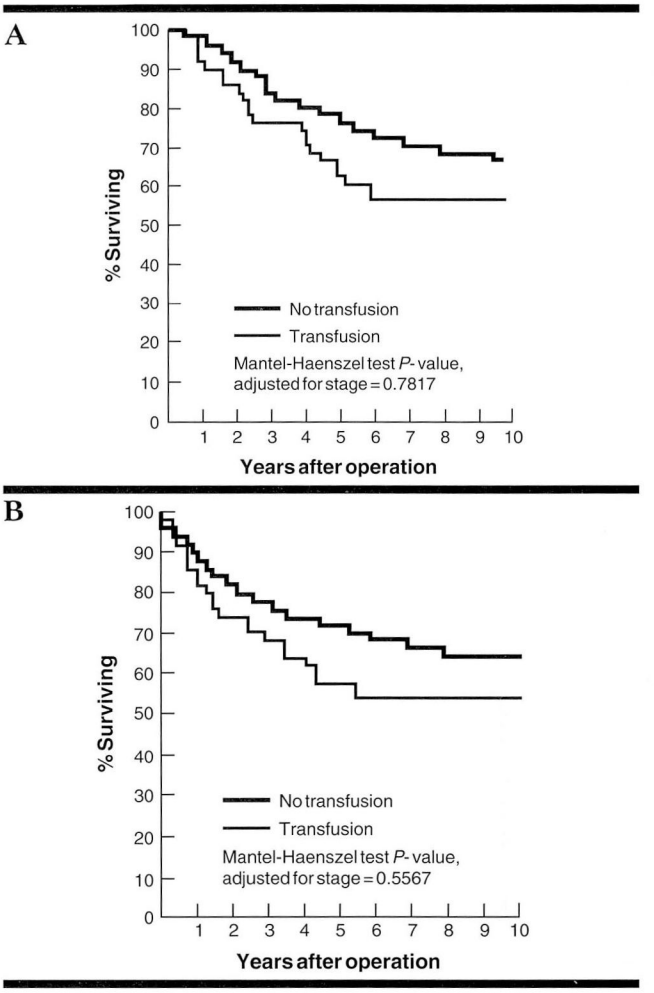

FIGURE 3. Survival (A) and disease-free survival (B) of transfusion and no-transfusion groups for patients of all stages.

transfusion patients for all three stages (TNM system). They noted no difference between groups at individual stages. Five-year disease-free survival was 51% for patients who received transfusions and 65% for those who did not. ($P = 0.0021$). Transfusion patients also had lower hemoglobin levels on admission and higher levels of operative blood loss.

Herman and Kokodziejski[12] reviewed the cases of 690 patients with stages I and II breast cancer treated with radical or modified radical mastectomy at the Maria Sklodowska-Curie Institute in Kracow, Poland. Overall and disease-free survival were reduced in transfusion patients. In addition, survival was reduced in stage I patients who received transfusions.

Our study included patients with potentially curable

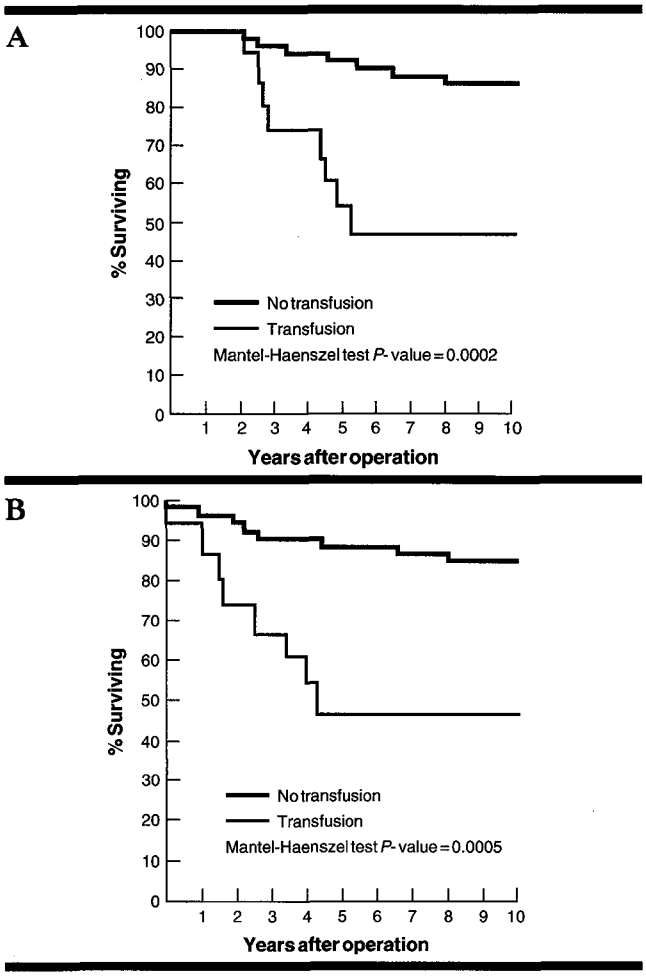

FIGURE 4. Survival (A) and disease-free survival (B) of transfusion and no transfusion groups for stage I patients.

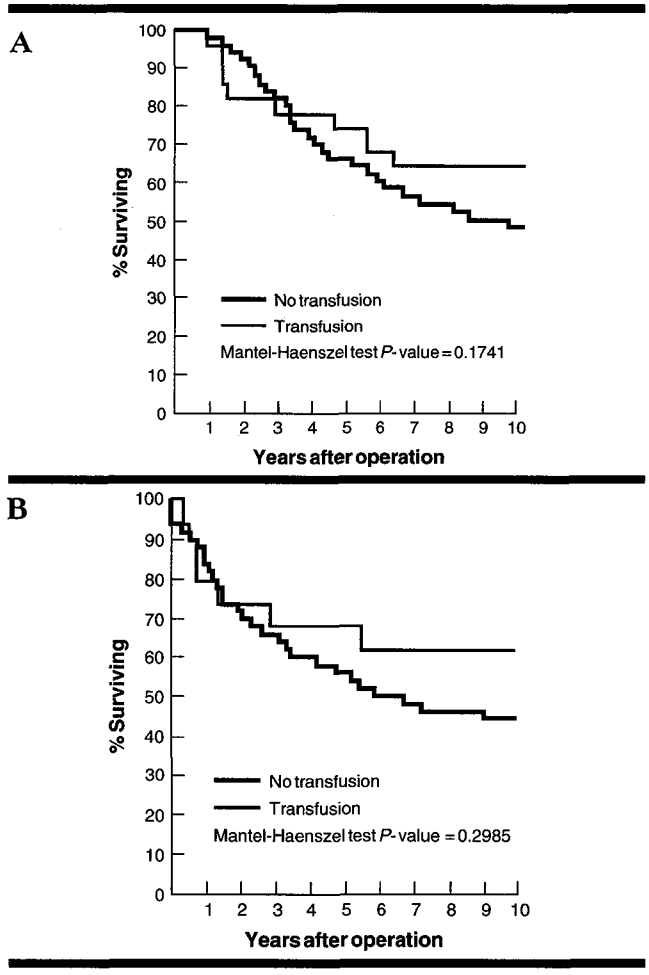

FIGURE 5. Survival (A) and disease-free survival (B) of transfusion and no transfusion groups for stage II patients.

breast cancer, all treated with the same operation and followed for at least 10 years. Our results indicate that perioperative blood transfusion does have an adverse effect on the survival and recurrence rate of node-negative stage I breast cancer after modified radical mastectomy. However, transfusion patients were also found to have lower admission and postoperative hemoglobin and hematocrit values. It may be that anemia, diminished nutrition, depressed hematopoiesis, or other factors separate from the effect of blood transfusion could be involved in reducing survival.

Several reports on the effect of blood transfusion on survival for other types of malignancy have also found reduced survival among transfusion patients, for example in less advanced lung cancer,[13] colorectal cancer,[14] and in well-differentiated gastric cancer.[15] The effects of blood transfusion on the immune system have been well reviewed.[16,17] As little as 2 units of packed red blood cells can induce temporary, nonspecific suppressor cell activity in chronic renal failure patients who received no previous transfusions.[18] The trauma of surgery itself enhances reversible depression of cellular immunity.[19–21]

It is likely that in cancer patients all of these factors interplay to alter the immune defense system to the extent that circulating cancer cells are tolerated, allowed to escape immune surveillance, and implant at distant sites. This event is more evident in node-negative breast cancer in our study, since node-positive patients are more likely to have distant metastases, making the effect of transfusion less evident.

Both surgeons and anesthesiologists are coming to

realize that blood transfusion is not innocuous. In addition to the possibility of transfusion reaction, coagulopathy, metabolic complications, and transmission of viral hepatitis and AIDS, we now have begun to identify possible harm to cancer patients. Although the concept that cancer patients' long-term survival may be compromised by allogenic blood transfusion is still not firmly established, it is advisable to exercise caution in using allogenic blood or blood products. One cannot withhold allogenic blood from all patients undergoing surgery who lose blood or need transfusions, but its use should be limited whenever possible. Using autologous blood, blood substitutes, and delaying reconstruction in patients undergoing breast cancer operations could circumvent this problem for some patients. Prospective, randomized studies comparing autologous and allogenic blood transfusions should be planned to study this issue further.

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