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ORIGINAL ARTICLE

Impact of perioperative blood transfusion on survival of patients undergoing laparoscopic gastrectomy for gastric cancer

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Summary

Purpose: *Previous studies have suggested that perioperative blood transfusion is associated with poor prognosis in patients undergoing radical gastrectomy for gastric cancer. The purpose of this study was to evaluate the impact of blood transfusion on the long-term survival of such patients.*

Methods: *Short- and long-term outcomes were retrieved from a prospectively collected database of patients who underwent laparoscopic gastrectomy with radical intent for gastric cancer.*

Results: *A total of 309 patients who underwent laparoscopic radical gastrectomy were evaluated. Sixty-one (19.7%) received blood transfusions during or within 30 days after gastrectomy. These patients were typically older, had lower preoperative hemoglobin levels, had a more advanced cancer stage, had more than two comorbidities, had a higher rate of postoperative 30-day complications, and had a higher conversion rate. The overall survival (OS) (p=0.040) and disease-free survival (DFS) (p=0.004) were significantly decreased in patients who received blood transfusions. Multivariate analysis revealed that perioperative blood transfusion was not independently associated with decreased OS and DFS but that cancer stage and having more than two comorbidities were independent risk factors.*

Conclusion: *Perioperative blood transfusion was associated with decreased OS and DFS in this patient series, but this apparently reflected the relatively poor medical condition of these patients requiring gastrectomy and was not a causative relationship.*

Key words: *blood transfusion, gastric cancer, laparoscopic gastrectomy, minimally invasive surgery*

Introduction

Perioperative blood transfusion has been associated with decreased OS and DFS of patients who undergo radical gastrectomy for gastric cancer [1-3]. Some studies have suggested a causative relationship and an impact on the immune system, resulting in increased immunosuppression [4-6]. Studies have not shown a difference in the long-term outcomes between patients undergoing laparoscopic radical gastrectomy and those undergoing open radical gastrectomy for gastric cancer [7-17]. However, compared with the open approach, laparoscopic gastrectomy for gastric cancer was found to be associated with less immunosuppression, less blood loss, and less need for blood transfusion [7-17].

The aim of this study was to evaluate the risk factors for perioperative blood transfusion and its impact on long-term outcomes in patients undergoing laparoscopic radical gastrectomy for gastric cancer.

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Methods

All patients who underwent laparoscopic radical gastrectomy for gastric cancer between December 2008 and December 2015 were included. All operations were performed by two senior surgeons. Patient age, sex, body mass index, American Society of Anesthesiologists score, medical comorbidities, tumor location, TNM stage, conversion to open gastrectomy, postoperative 30-day mortality, postoperative 30-day morbidity, and pathological data were collected directly from medical records. Long-term OS and DFS data were collected from our outpatient clinic and from personal contacts when necessary. OS was assessed from the date of surgery until the last follow-up or death from any cause. DFS was calculated from the date of surgery until the date of cancer recurrence or death from any cause.

Perioperative blood transfusions included all those given on the day of operation or during the postoperative 30-day hospitalization. Preoperative evaluation included upper gastrointestinal endoscopy, endoscopic ultrasonography, computed tomographic (CT) scans of the brain, chest, and abdomen; and ultrasonography of the abdomen. Positron emission tomography-CT (PET-CT) and bone scans were performed in selected cases when necessary. The TNM staging of gastric cancer (7th Edn), the Japanese Gastric Cancer Association, and the American Joint Committee on Cancer classification were applied [18-20]. The staging of patients with surgery before 2009 was recalculated to match the more recent TNM classification. Perioperative mortality included deaths occurring within 30 days of gastrectomy. Postoperative morbidity was graded following the Clavien–Dindo classification. Major complications included grades 3, 4, and 5; minor complications included grades 1 and 2. Details of the Clavien–Dindo classification have been reported elsewhere [21-33].

Following discharge, patients were followed up as outpatients every 3 months for the first 2 years, every 6 months for the next 3 years, and at either 6 months or annually thereafter. At each visit, they underwent physical examination and general blood and serum tests. The 6-month follow-up alternated between thoracic and abdominal CT or abdominal ultrasonography and chest radiography. Disease recurrence was defined as radiologically or pathologically confirmed locoregional or distant metastasis, and the time of diagnosis was determined by the interval between surgery and the last follow-up. The last scheduled study follow-up was August 2016. The study was approved by the institutional review board of our institution. The need for informed consent from patients was waived because this was a retrospective study.

Statistics

Statistical analysis was performed using SPSS 14.0 (SPSS Inc., Chicago, IL, USA). Normally distributed data were presented as mean and standard deviation (SD), and differences were analyzed by Student's t-test. Data that were not normally distributed were expressed as median and range, and differences were compared by the Mann-Whitney U test. Differences of semiquantitative results were analyzed by the Mann-Whitney U test. Differences of qualitative results were analyzed by the chi-square or Fisher exact test where appropriate. The survival rates were estimated by the Kaplan-Meier method, and the significance of differences was deter-

Table 1. Clinical and pathological characteristics of the two groups

	No transfusion (n=248)	*Transfusion (n=61)*	*p value*
Age, years (range)	59 (41-75)	67 (57-81)	0.010
Gender (male:female)	149:99	35:26	0.700
Preoperative hemoglobin level (g/L) (range)	117 (81-158)	93 (74-148)	0.026
Number of comorbidities			
0	190	44	0.465
1	39	9	1.000
2	18	5	1.000
≥3	1	3	0.031
ASA score			
I	193	46	0.687
II	48	13	0.731
III	7	2	1.000
Retrieved lymph nodes	17 (15-29)	14 (16-27)	0.189
Residual tumor (R0/R1/R2)	248/0/0	61/0/0	1.000
Histological differentiation			0.625
Differentiated	146	38	
Undifferentiated	102	23	
Pathological TNM stage			
I	97	2	0.000
II	77	26	0.086
III	74	33	0.000

mined by the log-rank test. Univariate analyses were performed to identify prognostic variables related to OS and DFS and those that were found to be significant ($p<0.10$) were selected for inclusion in a multivariate Cox proportional hazard regression model. Adjusted hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) were calculated. A p value < 0.05 was considered statistically significant.

Results

During the study period, 309 patients underwent laparoscopic radical gastrectomy procedures for gastric cancer and were included in this study. Sixty-one patients (19.7%) received blood transfusions on the day of gastrectomy or during the 30 days of hospitalization following surgery. Compared with patients who did not receive perioperative blood transfusions, patients who received blood transfusions were typically older, had a lower preoperative hemoglobin level, had more than two comorbidities, had a more advanced cancer stage, had a higher rate of conversion to open surgery, and had a higher rate of postoperative 30-day complications (Table 1 and Table 2).

The median follow-up time was 38 months, and 5 patients (3 in the transfusion group and 2 in the no transfusion group) were lost to follow-up at various time points. Both OS and DFS were significantly decreased in patients who received transfusions (Figures 1 and 2). Cancer stage and more than two comorbidities were found to be independently associated with both OS (Tables 3 and 4) and DFS (Tables 5 and 6). Receiving perioperative blood transfusions was not found to be independently associated with the risk of decreased OS or DFS.

Table 2. Surgical outcomes of the two groups

Outcomes	*No transfusion (n=248)*	*Transfusion (n=61)*	*p value*
Type of gastrectomy			0.661
Total gastrectomy	97	22	
Distal gastrectomy	151	39	
Conversion to open surgery	12	10	0.004
Operative time, min (range)	180 (140-290)	200 (160-280)	0.102
Estimated blood loss, ml (range)	210 (160-490)	220 (180-440)	0.098
Length of postoperative stay, days (range)	10 (7-29)	13 (7-25)	0.078
Postoperative 30-day complications	19	13	0.002
Major complications	4	2	0.879
Minor complications	15	11	

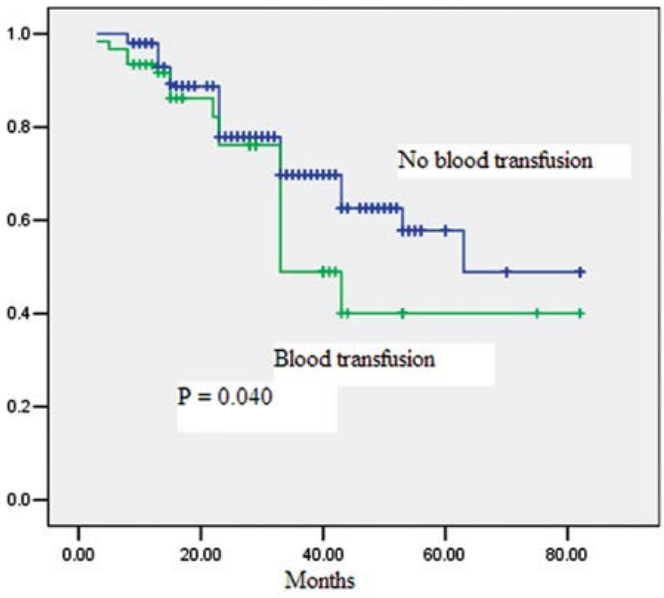

Figure 1. Overall survival curve in the two groups of patients with gastric carcinoma (p=0.040).

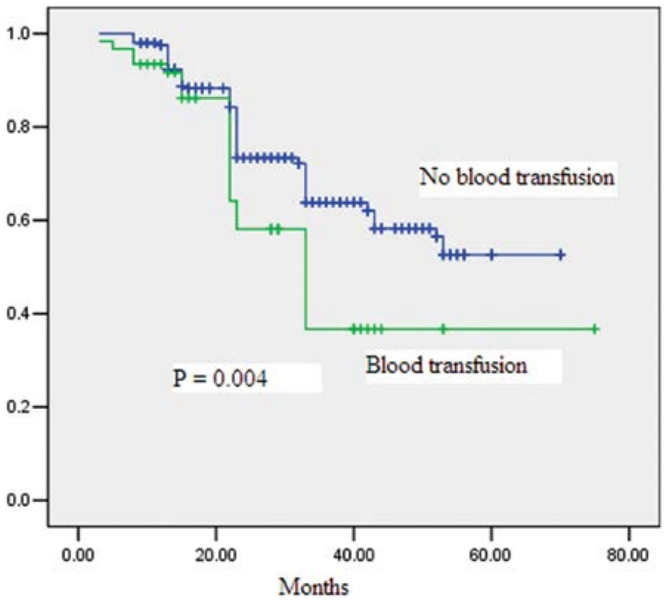

Figure 2. Disease-free survival curve in the two groups of patients with gastric carcinoma (p=0.004).

Table 3. Univariate analysis of 5-year overall survival of the 309 patients

Variables	*5-year overall survival %*	*p value*
Age, years		0.127
<65	55	
≥65	41	
Gender		0.122
Male	50	
Female	39	
ASA score		0.128
I-II	51	
III	37	
More than two comorbidities		0.035
No	59	
Yes	32	
Type of gastrectomy		0.128
Total gastrectomy	52	
Distal gastrectomy	40	
Pathological TNM stage		0.000
I-II	69	
III	32	
Histological differentiation		0.205
Differentiated	46	
Undifferentiated	37	
Major complication		0.059
No	54	
Yes	41	
Blood transfusion		0.040
No	48	
Yes	40	

Discussion

In our study, blood transfusion was associated with significantly poorer OS and DFS following laparoscopic radical gastrectomy for gastric cancer. Patients who received blood were typically older, had lower preoperative hemoglobin levels, had a more advanced cancer stage, had more than two comorbidities, had a higher rate of complications, and had a higher conversion rate. However, multivariate analysis did not find that blood transfusion was independently related to the risk of decreased OS or DFS. Differences in the demographic and clinical characteristics of the two patient groups might explain the differences in survival.

This study differs from other investigations on the effect of perioperative blood transfusion on OS and DFS in gastric cancer patients by its inclusion of only laparoscopic gastrectomy patients [1-6]. Furthermore, in our series, all surgical procedures were performed by the same two surgeons. To the best of our knowledge, this is the first English language report to investigate the effects of perioperative blood transfusion on long-term OS and DFS outcomes in patients with laparoscopic gastrectomy for gastric cancer.

A possible cause of tumor recurrence in patients receiving perioperative blood transfusions during gastrectomy for gastric cancer is immunosuppression, resulting from both blood transfusion and the surgery itself. Previous reports have associated the decrease in tissue injury during laparoscopic gastrectomy compared with open gastrectomy with better preservation of the immune function [7-10]. Theoretically, producing less tissue injury could reduce the impact of perioperative blood transfusion on the immune system, with its consequent decrease in OS and DFS.

Intraoperative blood loss is often lower in laparoscopic than in open gastrectomy. A reduction in the blood transfusion rate is not a necessary consequence of lesser blood loss, but laparoscopic gastrectomy has been reported to reduce the number of units of perioperatively transfused blood as well as the number of patients receiving blood transfusions. In the present study, the rate of perioperative blood transfusions was relatively high and was probably related to both patient characteristics and the lack of standard guidelines for perioperative blood transfusion. However, comparative studies have shown less blood transfusion in laparoscopically-treated patients [7-12]. Perioperative blood transfusion has been shown to increase the risk of postoperative morbidity following open but not laparoscopic surgery.

Our study findings are in line with those that did not find a causal relationship between perioperative blood transfusion and worse prognosis following open gastrectomy. Previous reports suggested that the poor prognosis observed in gastric cancer patients who received perioperative blood transfusion was related to the circumstances that necessitated the transfusion and not to the transfusion *per se* [34-36].

Regarding conversion to open gastrectomy, laparoscopic gastrectomy procedures for gastric cancer have been associated with lower postop-

Table 4. Cox proportional hazards model for overall survival

Variables	*Hazard ratio (95% CI)*	*p value*
Stage: I-II vs stage III	2.158 (1.269-4.870)	0.018
Comorbidities: Up to 2 vs >2	2.510 (1.257-4.020)	0.021

Table 5. Univariate analysis of 5-year disease-free survival

Variables	*5-year disease-free survival %*	*p value*
Age, years		0.189
<65	59	
≥65	43	
Gender		0.303
Male	56	
Female	47	
ASA score		0.139
I-II	62	
III	46	
More than two comorbidities		0.026
No	68	
Yes	42	
Type of gastrectomy		0.242
Total gastrectomy	56	
Distal gastrectomy	41	
Pathological TNM stage		0.000
I-II	71	
III	36	
Histological differentiation		0.158
Differentiated	54	
Undifferentiated	39	
Major complication		0.070
No	59	
Yes	44	
Blood transfusion		0.004
No	55	
Yes	38	

Table 6. Cox proportional hazards model for disease-free survival

Variables	*Hazard ratio (95% CI)*	*p value*
Stage I-II vs stage III	1.805 (1.520-2.310)	0.006
N0-N1 vs N2-N3	2.059 (1.269-3.350)	0.010

erative morbidity, mortality, and similar survival outcomes compared with open gastrectomy procedures [7-9]. Nevertheless, recent evidence suggests a negative impact of conversion on long-term outcome in gastric cancer patients. Interestingly, in this series, a greater proportion of patients who received transfusions experienced conversion to open surgery.

The patients in this series who received transfusions had less favorable baseline characteristics compared with those who did not receive transfusions. Previous reports explained the lower survival rates among gastric cancer patients who received perioperative blood transfusions by the presence of a lower transfusion threshold in patients with underlying cardiovascular or pulmonary diseases. Moreover, an increase in the number of blood units given during surgery was associated with an increase in postoperative mortality. These studies suggest that avoiding the need for perioperative blood transfusion improves poor prognosis, irrespective of the existence of a causal relationship.

We showed a non-causal relationship between blood transfusion and prognosis in patients who underwent laparoscopic gastrectomy. Similar to reports of outcomes of open surgery, we found that the poor health of patients who received blood transfusions could explain their poor prognosis [4-6]. It has been suggested that improving surgical procedures might improve prognosis by reducing the need for blood transfusion. The advantages of laparoscopic gastrectomy that may be related to the need for blood transfusion are better preservation of immune function and reduced blood loss during surgery.

A limitation of our study was the decision to administer blood transfusions based on clinical and laboratory factors, without definitive guidelines regarding indications for transfusion. Accepted guidelines for blood transfusion should be followed to standardize the indications for blood transfusion and to avoid unnecessary transfusions. A controlled comparative study of open and laparoscopic surgery, with a larger number of patients, may show the impact of blood transfusion on long-term outcomes more clearly.

In summary, perioperative blood transfusion was associated with decreased OS and DFS in patients who underwent laparoscopic radical gastrectomy for gastric cancer. The association reflected the clinical condition of patients requiring surgery and was not a causal relationship.

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Conflict of interests

The authors declare no confict of interests.

References

1. Elmi M, Mahar A, Kagedan D et al. The impact of blood transfusion on perioperative outcomes following gastric cancer resection: an analysis of the American College of Surgeons National Surgical Quality Improvement Program database. Can J Surg 2016;59:322-329.
2. Reim D, Strobl AN, Buchner C et al. Perioperative transfusion of leukocyte depleted blood products in gastric cancer patients negatively influences oncologic outcome: A retrospective propensity score weighted analysis on 610 curatively resected gastric cancer patients. Medicine (Baltimore) 2016;95:e4322.
3. Sun C, Wang Y, Yao HS, Hu ZQ. Allogeneic blood transfusion and the prognosis of gastric cancer patients: systematic review and meta-analysis. Int J Surg 2015;13:102-110.
4. Kosumi K, Baba Y, Harada K, Yoshida N, Watanabe M, Baba H. Perioperative Blood Transfusion, Age at Surgery, and Prognosis in a Database of 526 Upper Gastrointestinal Cancers. Dig Surg 2015;32:445-453.
5. Xu YQ, Jiang TW, Cui YH, Zhao YL, Qiu LQ. Prognostic value of ABO blood group in patients with gastric cancer. J Surg Res 2016;201:188-195.
6. Li B, Liu HY, Guo SH et al. The postoperative clinical outcomes and safety of early enteral nutrition in operated gastric cancer patients. J BUON 2015;20:468-472.
7. Wen J, Linghu EQ, Yang YS et al. Associated risk factor analysis for positive resection margins after endoscopic submucosal dissection in early-stage gastric cancer. J BUON 2015;20:421-427.
8. Shu B, Lei S, Li F, Hua S, Chen Y, Huo Z. Short and long-term outcomes after gastrectomy for gastric carcinoma in elderly patients. Int J Clin Exp Med 2015;8:13578-13584.
9. Zhang Y, Qi F, Jiang Y, Zhai H, Ji Y. Long-term follow-up after laparoscopic versus open distal gastrectomy for advanced gastric cancer. Int J Clin Exp Med 2015;8:13564-13570.
10. Gu J, Zhao E. Laparoscopic gastrectomy for locally advanced gastric carcinoma: long-term survival outcomes and prognostic factors. Int J Clin Exp Med 2016;9: 11485-11493.
11. Caruso S, Patriti A, Roviello F et al. Laparoscopic and robot-assisted gastrectomy for gastric cancer: Current considerations. World J Gastroenterol 2016;22:5694-5717.
12. Aurello P, Sagnotta A, Terrenato I et al. Oncologic value of laparoscopy-assisted distal gastrectomy for advanced gastric cancer: A systematic review and meta-analysis. J Minim Access Surg 2016;12:199-208.
13. Suda K, Nakauchi M, Inaba K, Ishida Y, Uyama I. Minimally invasive surgery for upper gastrointestinal cancer: Our experience and review of the literature. World J Gastroenterol 2016;22:4626-4637.
14. Nunobe S, Kumagai K, Ida S, Ohashi M, Hiki N. Minimally invasive surgery for stomach cancer. Jpn J Clin Oncol 2016;46:395-398.
15. Zhao EH, Ling TL, Cao H. Current status of surgical treatment of gastric cancer in the era of minimally invasive surgery in China: Opportunity and challenge. Int J Surg 2016;28:45-50.
16. Son T, Hyung WJ. Laparoscopic gastric cancer surgery: Current evidence and future perspectives. World J Gastroenterol 2016;22:727-735.
17. Marano L, Polom K, Patriti A et al. Surgical management of advanced gastric cancer: An evolving issue. Eur J Surg Oncol 2016;42:18-27.
18. Yamashita K, Hosoda K, Ema A, Watanabe M. Lymph node ratio as a novel and simple prognostic factor in advanced gastric cancer. Eur J Surg Oncol 2016;42:1253-1260.
19. Hase K, Naomoto Y, Ninomiya M, Watanabe M, Omoto T, Wang H. Staging of gastric cancer. Asian Pac J Surg Oncol 2016;2:75-86.
20. Spiliotis J, Efstathiou E, Matsubara A, Osman MM, Choo SP. Molecular biology of gastric cancer. Asian Pac J Surg Oncol 2016;2:86-100.
21. Clavien PA, Barkun J, de Oliveira ML et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187-196.
22. Xiao H, Xie P, Zhou K et al. Clavien-Dindo classification and risk factors of gastrectomy-related complications: an analysis of 1049 patients. Int J Clin Exp Med 2015;8:8262-8268.
23. Dong J, Wang W, Yu K et al. Outcomes of laparoscopic surgery for rectal cancer in elderly patients. J BUON 2016;21:80-86.
24. Guo C, Zhang Z, Ren B, Men X. Comparison of the long-term outcomes of patients who underwent laparoscopic versus open surgery for rectal cancer. J BUON 2015;20:1440-1446.
25. Sheng W, Zhang B, Chen W, Gu D, Gao W. Laparoscopic colectomy for transverse colon cancer: comparative analysis of short- and long-term outcomes. Int J Clin Exp Med 2015;8:16029-16035.
26. Jiang X, Liu L, Zhang Q et al. Laparoscopic versus open hepatectomy for hepatocellular carcinoma: long-term outcomes. J BUON 2016;21:135-141.
27. Luo L, Zou H, Yao Y, Huang X. Laparoscopic versus open hepatectomy for hepatocellular carcinoma: short- and long-term outcomes comparison. Int J Clin Exp Med 2015;8:18772-18778.
28. Wu D, Li Y, Yang Z, Feng X, Lv Z, Cai G. Laparoscopic versus open gastrectomy for gastric carcinoma in elderly patients: a pair-matched study. Int J Clin Exp Med 2016;9:3465-3472.
29. Wu H, Li W, Chen G et al. Outcome of laparoscopic total gastrectomy for gastric carcinoma. J BUON 2016;21:603-608.
30. Shu B, Lei S, Li F, Hua S, Chen Y, Huo Z. Laparoscopic total gastrectomy compared with open resection for gastric carcinoma: a case-matched study with long-term follow-up. J BUON 2016;21:101-107.
31. Zhang X, Sun F, Li S, Gao W, Wang Y, Hu SY. A propensity score-matched case-control comparative study of laparoscopic and open gastrectomy for locally ad-

vanced gastric carcinoma. J BUON 2016;21:118-124.

32. Wang Y, Chen C. Survival following video-assisted thoracoscopic versus open esophagectomy for esophageal carcinoma. J BUON 2016;21:427-433.
33. Zhu Y, Chen W. Very long-term outcomes of minimally invasive esophagectomy for esophageal squamous cell carcinoma. J BUON 2015;20:1585-1591.
34. Cui J, Deng J, Ding X et al. Blood transfusion does not affect survival of gastric cancer patients. J Surg Res 2016;200:98-104.
35. Tarantino I, Ukegjini K, Warschkow R et al. Blood transfusion does not adversely affect survival after elective colon cancer resection: a propensity score analysis. Langenbecks Arch Surg 2013;398:841-849.
36. Müller SA, Mehrabi A, Rahbari NN et al. Allogeneic blood transfusion does not affect outcome after curative resection for advanced cholangiocarcinoma. Ann Surg Oncol 2014;21:155-164.