

RISK FACTORS FOR EARLY COMPLICATIONS FOLLOWING TOTAL GASTRECTOMY FOR GASTRIC CANCERS

Dr. Cengizhan YİĞİTLER (*), Dr. Bülent GÜLEÇ (*), Dr. Taner YİĞİT (*),
Dr. Ahmet YEŞİLTAŞ (*), Dr. Müjdat BALKAN (*), Dr. Orhan KOZAK (*),
Dr. İsmail ARSLAN (*), Dr. Mesut PEKCAN (*)

Gülhane Tıp Dergisi 45 (2) : 182 - 188 (2003)

ÖZET

Mide Kanseriinde Total Gastrektomiden Sonra Erken Komplikasyonlara Yol Açan Risk Faktörleri

Mide kanseri nedeniyle total gastrektomi uygulanan hastalarda erken komplikasyonlara yol açan risk faktörlerini belirlemek amacıyla, 1994-2002 yılları arasında 74 hastanın dosyası retrospektif olarak incelendi. Girişim gerektiren pulmoner komplikasyonlar, anastomoz kaçağı, intraabdominal abse, assit, kanama gibi komplikasyonlar major olarak ele alındı. Hastaların yaşı, cinsiyeti, ASA skoru, albumin ve protein değerleri gibi preoperative özellikleriyle ameliyat süresi, özefagojejunostominin tipi, beraberinde organ rezeksiyonu ve transfüzyon gerekliliği gibi ameliyat özellikleri lojistik regresyon analizi ile değerlendirildi. Toplam komplikasyon oranı %39 (29 hasta) ve bunların %41' i major komplikasyonlardı (biri bu nedenle ölen 5 hastada anastomoz kaçağı, 1 hastada kanama ve geri kalan 5' inde girişim gerektiren pulmoner komplikasyonlar). 2'den büyük ASA skoru, intraoperatif transfüzyon, beraberinde başka organ rezeksiyonu, rekonstrüksiyonun tipi, preoperatif albumin değerinin 3' mg/dL'den azlığı önemli prognostik faktörlerdendi. Regresyon analizinde kan transfüzyonu ($p=0,001$ Odds Ratio (OR):12,15), 2'den büyük ASA skoru ($p=0,01$ OR:6,60) ve ek organ rezeksiyonu ($p=0,03$ OR:4,57) önemli risk faktörleri olarak bulundu. Preoperatif anemi ve önceki tıbbi hastalıklar gibi hasta özellikleri ile perioperatif kan kaybı ve gastrektomiye eşlik eden organ rezeksiyonları gibi operatif özellikler, mide kanseri nedeniyle total gastrektomi sonrası erken komplikasyonları ön görmede önemli faktörler olarak bulunmuştur.

Anahtar Kelimeler: Total Gastrektomi, Mide Kanseri, Komplikasyon, Morbidite, Postoperatif Seyir, Transfüzyon.

(*) GATA Genel Cerrahi AD.

Reprint Request: Dr. Cengizhan YİĞİTLER, GATA Genel Cerr. AD., Etlik-ANKARA

Kabul Tarihi: 12.5.2003

SUMMARY

In order to identify the risk factors for early complications following total gastrectomy for gastric cancer, we retrospectively revised the medical records of 74 patients during last 8 years. Any pulmonary complications requiring an intervention, anastomotic leakage, intraabdominal abscess, ascites, and hemorrhage were defined as major complication. We determined the risk factors related to the early morbidity by comparing the patients' age, gender, ASA status; operative characteristics such as operating time, reconstruction type of esophagojejunostomy, concomitant organ resection, and transfusion requirement, using a logistic regression analysis.

Overall complication rate was 39% (29 patients). Of these, 41 % were major such as anastomotic leakage in 5 patients, which was fatal in one patient, hemorrhage in one and pulmonary complications necessitating an invasive procedure in remaining 6 patients. ASA score>2, intraoperative transfusion, extra organ resection, type of reconstruction, preoperative albumin level<3 mg/dL were the significant prognostic factors. In regression analysis, blood transfusion ($p=0,001$ Odds Ratio (OR): 12,15), ASA score greater than 2 ($p=0,01$ OR: 6,60), and extra organ resection ($p=0,03$ OR: 4,57) were significant risk factors. These results suggest that patients' preoperative anemia and preexisting medical condition, or operative characteristics such as perioperative blood loss, and concomitant organ resection seem to be important in predicting early complication after total gastrectomy for gastric cancer.

Key Words: Total Gastrectomy, Gastric Cancer, Complication, Morbidity, Postoperative Outcome, Transfusion.

INTRODUCTION

Although the overall incidence of gastric cancer has diminished during last decade, the incidence of adenocarcinoma in the proximal stomach has increased with the changing variables in cancer at the gastroesophageal junction. Tumor localization is the most prominent factor in decision-making of a surgical approach for gastric cancer. Resectable pro-

ximal gastric cancers are managed by a total gastrectomy that may include perigastric lymph nodes, splenectomy, additional organ resection such as left lobe of the liver, distal pancreas, and transverse mesocolon with the intent of cure. This may cause a high morbidity and mortality rates (1,2). Antral lesions; if they were not histologically diffuse according to Laurén (3), are best managed by a distal subtotal gastrectomy. Proximal resections are rather abandoned for midgastric and proximal lesions because of their greater morbidity rates, requirement of a drainage procedure, less therapeutic effect, and ongoing reflux problems of the patients (4,5).

However, there is no specific definition of complication after total gastrectomy. More extended operations are found to have more complications and high mortality rates in most of Western studies (1,6,7,8), however Japanese studies have revealed a survival benefits of the extended lymph node dissection in early stages of the disease and with concomitant organ resection in late stage (9,10). Thus, postoperative outcome must be presumed with use of some parameters that are helpful for the patients' prognosis, and life expectancy, following such a major operation.

In an effort to define predictive risk factors attributable to postoperative outcome, we aimed to determine the impact of patients' clinicopathological and intraoperative characteristics on early morbidity following total gastrectomy for gastric cancer.

MATERIALS and METHODS

The charts of seventy - four patients who underwent a total gastrectomy for gastric malignancy of whom 7 were gastric lymphoma, between October 1994 and January 2002 were retrospectively revised for this study. Palliative operations were strictly excluded based on both the preoperative examinations and the operation findings. All interventions were performed via a midline incision, in a standard technique with removal of entire greater omentum. The spleen was removed and lymph node dissection was carried out according to the surgeon's preference.

The patients consisted of 38 men and 36 women, with a mean age of $61,9 \pm 12$ (range: 21-85 years). Their age ($<$ or \geq 65 years-old), preexisting medical problems, if any; ASA score ($>$ or \leq 2) (11), and biochemical values were recorded. In order to elucidate the predictive clinicopathologic factors that

may affect the early postoperative course, we evaluated the followings: the operation period ($<$ or \geq 360 minutes), transfusion requirement, reconstruction type of the esophagojejunostomy (Roux-en-Y vs. other), types of anastomosis reconstruction (stapler vs. hand sutures), concomitant organ resection, extent of lymph node dissection according to the Japanese classification (12).

As splenectomy is usually a part of the total gastrectomy procedure for tumors located along the greater curvature, it was not accepted as an extra organ resection, if performed. Other organ resections for tumor involvement or benign conditions were considered extra organ resection.

Postoperative complications were stratified in two categories according to the following rules: major if pulmonary complications (pleural effusion requiring tapping or drainage, radiologically detected atelectasis that has caused moderate to severe respiratory failure, pneumonia, and pneumothorax), anastomotic leakage, intraabdominal abscess, ascites (serous fluid drainage more than 250 ml per day after day 4), wound dehiscence, and hemorrhage occurred; minor if pulmonary complications other than those cited above, and wound infection occurred.

Perioperative death was defined as death within 30 days after surgery (excluding death in the operating room which was nil), and in-hospital death was defined as death within the same hospital admission for surgery.

In order to determine the predictive risk factors in the occurrence of complications, a univariate analysis using chi-square test was applied for both pre- and perioperative parameters. To further analyze independent factors that should explain the interactions between patients' and intraoperative features, and complications, statistically significant variables were submitted to a logistic regression analysis with backward selection. P values less than 0,05 were considered significant. Cumulative survival was estimated with Kaplan-Meier method using log rank test.

RESULTS

The patients' demographic and clinicopathologic features are shown in Table 1. Totally 19 patients underwent an extra organ resections, of those 12 were cholecystectomies, two distal pancreatectomies, two ooforectomies, one total esophagectomy, one small bowel resection, and one left adrenalectomy. Blood transfusion was necessary in 34 (46%) patients.

TABLE - I
Patients' Clinicopathological Features

Variables	n
Age (mean \pm SD) (range)	61.9 \pm 12 (21- 85)
ASA Score	
I	23
II	37
III	13
IV	1
Tumor localization	
Proximal 1/3	39
Mid 1/3	20
Distal 1/3	12
Anastomotic*	3
pTNM** classification	
Stage IB	3
Stage II	15
Stage III A	46
Stage III B	3
Histopathological type	
Adenocarcinoma	67
Gastric Lymphoma	7
Reconstruction type of esophagojejunostomy	
Roux en Y	43
Loop	29
J - pouch	1
Colonic transposition	1

*tumors occurred at gastrojejunostomy anastomosis in 3 patients who have had previously an antrectomy for peptic ulcer disease.

**pathologic TNM classification was used, excluding the lymphomas.

Postoperative complications occurred in 29 patients. The overall complication rate was 39,1 % and 2 (2,7%) patients among them expired during stay - in hospital. Some patients experienced more than one complication. In 15 patients (46,9% of all complications) developed pulmonary complications whereas 12 patients had wound infection and/or dehiscence, 5 had anastomotic leakage, and of these, 4 had intraabdominal abscess. 4 patients had ascites, and one patient underwent a re-laparotomy due to hemorrhage. Totally 12 patients (16,2%) had major complications.

A univariate analysis of patients' clinicopathological parameters revealed that ASA score $>$ 2 ($p=0,001$), intraoperative transfusion need ($p=0,001$), extra organ resection ($p=0,01$), type of reconstruction ($p=0,05$), and preoperative albumin below 3 mg/dL ($p=0,05$) were the significant prognostic factors (Table 2). Patients' age, sex, type of anastomosis reconstruction, splenectomy, extent of lymph node dissection, duration of operation, preoperative protein level did not show any significance.

TABLE - II
Significance of Risk Factors for Early Outcome Following Total Gastrectomy (x2 Analysis)

Variables	Complication (+)	Complication (-)	p	Odds ratio	95% Confidence interval
Age					
$<$ 64 (n=34)	16	18	0,23	1,84	0,71-4,75
$>$ 65 (n=40)	13	27			
Gender					
Men (n=38)	12	26	0,23	0,51	0,52-1,32
Women (n=36)	17	19			
ASA score					
$>$ 2 (n=14)	12	2	0,001	15,17	3,06-75,07
\leq 2 (n=60)	17	43			
Anastomosis sewing					
Manual (n=47)	18	29	1,00	0,90	0,34-2,37
By stapler (n=27)	11	16			
Splenectomy					
Present (n=55)	19	36	0,18	0,47	0,16-1,36
Absent (n=19)	10	9			
Extra organ resection					
Present (n=19)	12	7	0,01	3,83	1,28-11,43
Absent (n=55)	17	38			
Extent of lymph node dissection					
D1 (n=64)	23	4	0,17	2,67	0,68-10,46
D2 (n=10)	6	14			
Operating time (min)					
$<$ 360 (n=56)	22	34	1,00	0,98	0,33-2,92
$>$ 361 (n=18)	7	11			
Transfusion need					
Present (n=23)	17	6	0,001	9,20	2,96-28,60
Absent (n=51)	12	39			
Reconstruction type					
Roux-en-Y (n=43)	21	22	0,05	2,74	1,00-1,47
Other (n=31)	8	23			
Preoperative albumin (mg/dL)					
\leq 3 (n=18)	11	7	0,05	3,31	1,10-9,97
$>$ 3 (n=56)	18	38			
Preoperative protein (mg/dL)					
\leq 5,5 (n=14)	5	9	1,00	0,83	0,24-2,79
$>$ 5,6 (n=60)	24	36			

Risk Factors for Total Gastrectomy

These significant risk factors underwent a logistic regression analysis with backward selection. Extra organ resection (odds ratio:4,57 p=0,03), preoperative transfusion (OR:12,15 p=0,001), and ASA scoring >2 (OR: 6,60 p=0,01) were the independent unfavorable variables affecting early morbidity (Table 3).

TABLE - III
Independent Risk Factors Affecting Early Morbidity After Total Gastrectomy for Gastric Cancer

Variables	Odds ratio	P value	95% Confidence Interval
Extra organ resection		0,03	1,28-11,43
Absent	1		
Present	4,57		
Perioperative transfusion		0,001	2,96-28,6
Absent	1		
Present	12,15		
ASA score		0,01	3,06-75,07
≤ 2	1		
> 2	6,60		

Two patients expired due to pulmonary insufficiency and anastomotic leakage causing multiorgan failure during hospital stay. The cumulative survival of patients is shown on Figure 1-A. Excluding two patients died during hospital stay and 7 patients lost during follow-up, the median 5-years survival was 20 months for all remaining 65 patients, and mean survival was 30 months with a mean follow-up of 22 months. Cumulative survival rates were 74, 40, and 23,5% for 1,3, and 5 years, respectively.

Among 65 patients available for survival analyses, 31 have had a perioperative transfusion and 34 did not. Perioperative blood transfusion did not affect the survival rate (log rank=0,50; p=0,47) (Figure 1-B).

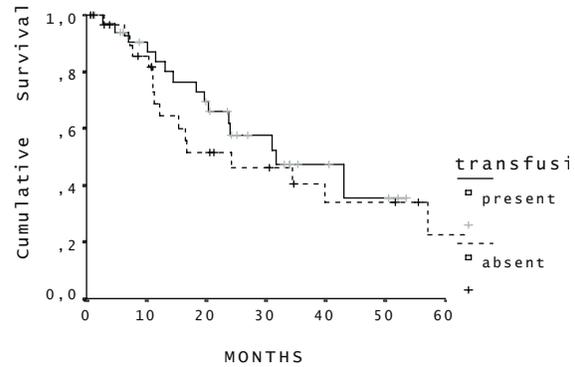
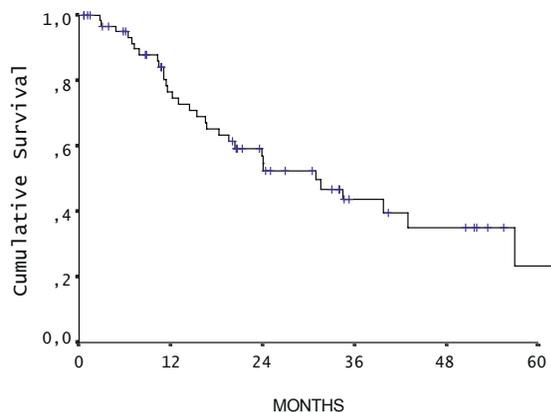


Figure 1. A. Cumulative survival for patients(1-year : 74 %, 3-years: 40 %, 5-years: 23,5%)
B. Comparison of cumulative survival in patients with or without perioperative transfusion (log rank=0,50 p=0,47)

DISCUSSION

The surgery still remains the treatment of choice for stomach cancer as well as other gastrointestinal cancers. Recent reports implicating the survival benefits of more extended resections for gastric cancers encouraged surgeons to search more convenient techniques that alleviates the postgastrectomy syndromes and improves patients' nutritional status (13-18). Total gastrectomy for stomach cancer is a major intervention, with a reasonable morbidity and mortality rates. Splenectomy, distal pancreatectomy, and even a left hepatic lobectomy may accompany the procedure. Improvements in surgical techniques and intensive care units could give the best chance; despite an extensive surgery for cure of this malady with poor prognosis.

We aimed to determine factors that might presume poor postoperative courses related to total gastrectomy, especially in patients for whom a curative resection was intended. The definition of complication is conflicting in several studies (5,19,20). Viste et al. found an overall complication rate of 28 per cent in their study consisting of both total and subtotal gastric resection, stating that they were widely composed of general complications (i.e. pulmonary, thromboembolic, and cardiac) (5).

In addition, some papers that focused on rather specific complications of the total gastrectomy reported high esophagojejunostomy leakage rates in their study (19,21). Never seen in our patients, pancreatic necrosis was the most prominent complication in a study by Igor et al. (22). Finally, in a series including only large tumors (>10cm), Yasuda et al.

reported a morbidity rate of 39% and a mortality rate of 7% (20).

Western studies revealed that anastomotic leakage as high as 12,3% is the most important complication causing high morbidity and increase in length of hospital stay. Techniques in which anastomosis was performed by a stapler had lowered this possibly fatal outcome. Anastomosis with stapler is an easier, fast and safe procedure for intestinal anastomosis in spite of its higher cost, while in the present study, it was not a beneficial factor to reduce postoperative morbidity.

Perioperative blood transfusion is another subject of controversy (23). Some investigators thoroughly suggested that blood loss was a significant risk factor that interferes with both postoperative morbidity and prognosis (24-26). However, Moriguchi et al. claimed an indifference between blood transfusion and survival time in patients with curative gastric resection when adjusting for tumor characteristics as size, depth, and status of lymph node metastasis (27). Extension of surgery to perigastric lymph nodes or other adjacent structures needs likely more blood loss, thus more transfusion, and longer operating time. We had no D3 or more extensive lymphadenectomy. As a matter of fact, in 19 patients with concomitant organ resections, only five had D2 lymph node dissection, but almost all had preoperative transfusion because of anemia due to bleeding from their tumor. Transfusion - induced immunosuppression and subsequent tumor enhancement are another issue. A higher rate of cancer recurrence in transfused patients was found in many reports (28-31). Our data did not show that transfusion had increased the risk for recurrence. We couldn't find its impact on survival, although it was one of the most significant independent risk factor related to early morbidity. However, long operations related to advanced disease with nodal involvement, and widely infiltrating tumors, inadequate transfusions reported as high as 26% increase likely the incidence of blood transfusion (25,32)

Survival studies showed conflicting results related to the associated splenectomy (33-35). However, there is strong evidence that splenectomy itself can also cause severe postoperative complications (35,36). Analyzing the postoperative complications, we excluded the patients with splenectomy from the concomitant surgery group as removal of spleen is still recommended for complete lymph node dissection of splenic hilum and should be considered a part of the surgical procedure for tumors situated along the greater curvature and upper third of the stomach. Our results emphasize that, besides removal of

spleen, additional surgery should be avoided especially in patients for whom a longer operating period is needed.

Preoperative nutritional status and also type of esophagojejunostomy reconstruction (stated that Roux-en-Y anastomosis was prone to produce more complication) are predictive risk factors, but they were not found to be independent factors for poor outcomes. Our results including all specific and non-specific unfavorable outcomes in total gastrectomy revealed that pulmonary complications are the mostly confronted complications after surgery for gastric carcinoma. Both patients' and operative characteristics may be explained by the fact that postoperative atelectasis and pleural effusion are usually related to pain from upper abdominal incision, and large peritoneal dissection that induce poor lung function and translocation of peritoneal lymphoid fluid (20,37).

This study revealed that extra organ resection, blood loss and accompanying medical conditions were the significant factors of poor postoperative courses after total gastrectomy in patients with gastric cancer. Thus, patients with poor general condition, and/or associated surgical problems should be managed more meticulously and special attention should be paid to minimize the blood loss and transfusion for these cases.

REFERENCES

1. Deguili, M., Sasako, M., Ponzetto, A., Allone, T., Soldati, T., Calgaro, M., Balcet, F.: *Extended lymph node dissection for gastric cancer; results of a prospective, multicentre analysis of morbidity and mortality in 118 consecutive cases. Eur J Surg Onc* 23: 310-314, 1997.
2. Eigo, O., Toshiharu, Y., Kiyoshi, S., Miyakatsu, O., Toshio, T.: *End results of simultaneous splenectomy in patients undergoing total gastrectomy for gastric carcinoma. Surgery* 120: 40-44, 1996.
3. Laurén, P.: *The two histological main types of gastric carcinoma: diffuse and so-called intestinal-type carcinoma. Acta Pathol Microbiol Scand* 64: 31-49, 1965.
4. Siewart, J.R., Feith, M., Werner, M., Stein, H.J.: *Adenocarcinoma of the esophagogastric junction: results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. Ann Surg* 232: 353-361, 2000.
5. Viste, A., Haugstvedt, T., Eide, G.E., Soreide, O.: *Postoperative complications and mortality after surgery for gastric cancer. Ann Surg* 207: 7-13, 1988.

6. Wanebo, H.J., Kennedy, B.J., Chmiel, J., Steele, G. Jr., Winchester, D., Osteen, R.: *Cancer of the stomach. A patient care study by the American College of Surgeon.* *Ann Surg* 218: 579-582, 1993.
7. Cuschieri, A., Fayers, P., Fielding, J., Craven, J., Bancewicz, J., Joypaul, V., Cook, P.: *Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomized controlled surgical trial.* *Lancet* 347 : 995-999, 1996.
8. Deguili, M., Sasako, M., Ponzetto, A., Allone, T., Soldati, T., Calgaro, M., Balcet, F.: *Recent advances in surgical treatment have improved the survival of patients with gastric carcinoma.* *Cancer* 82: 1233-1237, 1998.
9. Wu, C., Hsieh, M., Lo, S., Wang, L.: *Morbidity and mortality after radical gastrectomy for patients with carcinoma of the stomach.* *J Am Coll Surg* 181: 26-32, 1997.
10. Tomoda, M., Kakeji, Y., Mehara, Y., Sugimachi, K.: *Total gastrectomy.* *Hepato-gastroenterology* 46 : 859-862, 1999.
11. Owens, W.D., Felts, J.A., Spitznagel, E.L. Jr.: *ASA physical status classifications: A study of consistency of ratings.* *Anesthesiology* 49: 239-243, 1978.
12. Maruyama, K., Okabayashi, K., Kinoshita, T.: *Progress in gastric cancer surgery in Japan and its limits of radicality.* *World J Surg* 11, 418-425, 1987.
13. Kodama, Y., Sugimachi, K., Soejima, K., et al.: *Evaluation of extensive lymph node dissection for carcinoma of the stomach.* *World J Surg* 5: 241-248, 1981.
14. Nozoe, T., Anai, H., Sugimachi, K.: *Usefulness of reconstruction with jejunal pouch in total gastrectomy for gastric cancer in early improvement of nutritional condition.* *Am J Surg* 181: 274-278, 2001.
15. Buhl, K., Lehnert, T., Scлаг, P., Herfath, C., Roder, J.D., Eckel, F.: *Reconstruction after gastrectomy and quality of life.* *World J Surg* 19: 558-564, 1995.
16. Bae, J.M., Park, J.W., Yang, H.K., Kim, J.P.: *Nutritional status of gastric cancer patients after total gastrectomy.* *World J Surg* 22: 254-261, 1998.
17. Svedlund, J., Sullivan, M., Liedman, B., Lundell, L., Sjödin, I.: *Quality of life after gastrectomy for gastric carcinoma: controlled study of reconstructive procedures.* *World J Surg*; 21: 422-433, 1997.
18. Davies, J., Johnston, D., Sue-Ling, H., Young, S., May, J., Griffith, J., Miller, G., Martin, I.: *Total or subtotal gastrectomy for gastric carcinoma? A study of quality of life.* *World J Surg* 22: 1048-1055, 1998.
19. Bozzetti, F., Marubini, E., Bonfanti, G., Miceli, R., Piano, C., Gennari, L.: *Total versus subtotal gastrectomy.* *Ann Surg* 226: 613-620, 1997.
20. Yasuda, K., Shiraishi, N., Adachi, Y., Inomata, M., Sato, K., Kitano, S.: *Risk factors for complications following resection of large gastric cancer.* *Br J Surg* 88: 873-877, 2001.
21. Budisin, N., Budisin, E., Golubovic, A.: *Early complications following total gastrectomy for gastric cancer.* *J Surg Oncol* 77: 35-41, 2001.
22. Igor, B., Stephen, R.T., Vyacheslav, A.: *Postoperative complications requiring relaparotomies after 700 gastrectomies performed for gastric cancer.* *Am J Surg* 171: 270-273, 1996.
23. Grossman, E.M., Longo, W.E., Virgo, K.S., Oprian, C.A., Henderson, W., Daley, J., Khuri, S.F.: *Morbidity and mortality of gastrectomy for cancer in Department of Veterans Affairs Medical Centers.* *Surgery* 131: 484-490, 2002.
24. Wobbles, T., Bemelmans, B.L., Kuypers, J.H., Beerthuizen, C.I., Thecuwes, A.G.: *Risk of postoperative septic complications after abdominal surgical treatment in relation to perioperative blood transfusion.* *Surg Gynecol Obstet* 171: 59-62, 1990.
25. Hyung, W.J., Noh, S.H., Shin, D.W., Huh, B.J., Choi, S.H., Min, S.J.: *Adverse effects of perioperative transfusion on patients with stage III and IV gastric cancer.* *Ann Surg Oncol* 9: 5-12, 2002.
26. Fong, Y., Karpeh, M., Mayer, K., Brennan, M.F.: *Association of perioperative transfusions with poor outcome in resection of gastric adenocarcinoma.* *Am J Surg* 167: 256-260, 1994.
27. Moriguchi, S., Machara, Y., Akazawa, K., Sugimachi, K., Nese, Y.: *Lack of relationship between perioperative blood transfusion and survival time after curative resection for gastric cancer.* *Cancer* 66: 2331-2335, 1990.
28. Blumberg, N., Chuang-Stein, C., Heal, J.M.: *The relationship of blood transfusion, tumor staging, and cancer recurrence.* *Transfusion* 30: 291-294, 1990.
29. Knults, A.C., Bazuin, C., Benner, R.: *Blood transfusion-induced suppression of delayed-type hypersensitivity to allogeneic histocompatibility antigens.* *Transplantation* 48: 829-833, 1989.
30. Francis, D.M., Shenton, B.K.: *Blood transfusion and tumor-growth: evidence from laboratory animals.* *Lancet* 2 : 871, 1981.
31. Edna, T.H., Bjerkeset, T.: *Perioperative blood transfusions reduce long-term survival following surgery for colorectal cancer.* *Dis Colon Rectum* 41:451-459, 1998.
32. Stehling, L.C., Esposito, B.: *An analysis of the appropriateness of intraoperative transfusion.* *Anesth Analg* 68: 5278, 1989.
33. Noguchi, Y., Imada, T., Matsumoto, A., Coit, D.G., Brennan, M.F.: *Radical surgery for gastric cancer: a review of the Japanese experience.* *Cancer* 64: 2053-2062, 1989.

34. Suehiro, S., Nagasue, N., Ogawa, Y., Sasaki, Y., Hirose, S., Yukawa, H.: *Negative effect of splenectomy on the prognosis of gastric cancer* *Am J Surg* 148: 645-648, 1984.
35. Bonenkamp, J.J., Hermans, J., Sasako, M., Van De Velde, C.J.H.: *Extended lymph-node dissection for gastric cancer*. *N Eng J Med* 340: 908-914, 1999.
36. Otsuji, E., Yamagushi, T., Sawai, K., Ohara, M., Takahashi, T.: *End results of simultaneous splenectomy in patients undergoing total gastrectomy for gastric carcinoma*. *Surgery* 120: 40-44, 1996.
37. Shea, R.A., Brooks, J.A., Dayhoff, N.E., Keck, J.: *Pain intensity and postoperative complications among the elderly after abdominal surgery*. *Heart Lung* 31: 440-449, 2002.