ORIGINAL ARTICLE

Surgeon Subspecialty as a Factor in Improving Long-term Outcomes for Gastric Cancer

Twenty Years of Experience in Korea

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Background: The results of gastric cancer treatment have improved during the past 2 decades. In addition to early diagnosis, surgeon experience and subspecialty may influence long-term outcomes. This study analyzed data accumulated during the past 20 years regarding the impact of surgical subspecialty on gastric cancer prognosis.

Design: A 20-year, retrospective study.

Setting: Korea University Guro Hospital, Seoul.

Patients: A total of 2797 patients admitted between 1984 and 2003 with surgically treated, pathologically confirmed, primary gastric adenocarcinoma.

Main Outcome Measure: Long-term survival.

Results: The incidence of total gastrectomy and the number of retrieved lymph nodes increased during the study period. In curative cases, 5-year survival improved from 66.1% to 76.6%, and this survival gain was restricted to stages I, III, and IV. A Cox proportional hazards regression model showed that age, sex, tumor location, type of resection, stage, and the interaction between period of study and surgical subspecialty were independent prognostic factors.

Conclusions: This large, long-term cohort study demonstrates that the management of gastric cancer has been largely successful, with favorable trends in prognostic factors. Successful outcomes are realized more often by gastric surgical specialists. Efforts must be made to improve the treatment of patients with stage II gastric cancer because the improvements in long-term results have plateaued.

Arch Surg. 2010;145(11):1091-1096

Although gastric cancer has declined in incidence from being the second most frequent cancer in 1990 to the fourth, behind lung, breast, and colorectal cancers, gastric cancer still remains the second most common cause of cancer-related deaths worldwide.[1,2] Surgery is the only curative treatment for gastric cancer. Fortunately, results have improved over the years, not only in the high-risk area of East Asia but also in Europe. Efforts to increase rates of early diagnosis, nationwide surveillance programs that detect higher proportions of less advanced tumors, advances in surgical and adjuvant treatments, and changes in tumor biology may all contribute to improved outcomes.[3-10]

See Invited Critique at end of article

Although the optimal management strategy for gastric cancer remains controversial, curative resection with D2 lymphadenectomy is the standard treatment option in Asia and some European countries, regardless of survival benefit.[11-13] However, the quality of surgical treatment for gastric cancer cannot be strictly controlled, and surgical skill or experience is at least partly responsible for improved outcomes, although other factors also play a role.[4,14,15] For this reason, a surgeon's experience and subspecialty may affect the long-term prognosis for his or her patients with gastric cancer.[16-20] To better understand the factors that contribute to the improvements in long-term surgical outcome for patients with gastric cancer, we reviewed surgical outcomes during 2 decades at a single institution and evaluated whether surgical subspecialty affected prognosis.

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METHODS

PATIENTS

During the period between 1984 and 2003, 2797 patients with primary gastric adenocarcinoma were surgically treated in the Depart-

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Table 1. Patient Demographics and Resection Status

	Period of Study, No. (%)		
	Early (1984-1993) (n=1115)	Late (1994-2003) (n=1682)	*P* Value
Age, y, mean (SD)	54.17 (11.44)	56.32 (12.08)	<.001[a]
Sex			
Male	748 (67.1)	1107 (65.8)	.48[b]
Female	367 (32.9)	575 (34.2)	
Type of surgery			
Palliative without resection	85 (7.6)	73 (4.3)	.001[b]
Open and closure	45 (4.0)	61 (3.6)	
Resection	985 (88.3)	1548 (92.0)	
Cure status for resection			
Noncurative	166 (16.9)	189 (12.2)	<.001[b]
Curative	819 (83.1)	1359 (87.8)	

[a] Calculated with an independent 2-sample *t* test.
[b] Calculated with the Pearson χ^2 test.

ment of Surgery of Korea University Guro Hospital in Seoul. Cases resulting in postoperative in-hospital mortality were excluded from this analysis. The 20-year period covered by this study was divided into 2 consecutive 10-year periods: an early group (1984 to 1993, 1115 patients) and a late group (1994 to 2003, 1682 patients). The institutional review board of Korea University Guro Hospital approved this study. The data we analyzed included prospectively collected demographic data, clinical findings, surgical procedure details, histopathological findings, and follow-up data.

SURGERY AND PATHOLOGICAL EXAMINATION

The surgical procedures were performed by several attending faculty surgeons or surgical fellows under faculty supervision. Thirteen surgeons operated on patients in the early group, and 4 surgeons operated on patients in the late group. Surgery was considered curative when the resection margins were clear, there was no evidence of macroscopic disease at the end of surgery, and the intention at the procedural outset was to cure.[21] Total or partial (proximal or distal subtotal) gastrectomy was performed according to the location and clinical stage of the tumor. Clinicopathological variables were classified according to the criteria of the Japanese Gastric Cancer Association.[22] Lymph node dissection was classified as follows: D1, complete removal of group 1 lymph nodes alone, and D2, complete removal of group 1 and 2 lymph nodes. Histological findings were grossly divided into differentiated (papillary and tubular adenocarcinoma) and undifferentiated (poorly differentiated adenocarcinoma, signet ring cell carcinoma, mucinous carcinoma, and miscellaneous) types. Final pathological staging was assessed according to TNM/International Union Against Cancer classification criteria.[21]

SURGICAL SUBSPECIALTY

Surgeons with a surgical subspecialty or major surgical interest in gastric cancer included surgeons who were members of the Korean Gastric Cancer Association (formerly the Korean Gastric Cancer Study Group) and the International Gastric Cancer Association, and who identified themselves as primarily gastric surgeons during the study period, specializing in gastric cancer and performing at least 50 gastrectomies a year. There were 13 surgeons in total involved in this study, and 3 of these surgeons identified themselves as having a surgical subspecialty for gastric cancer.

STATISTICAL ANALYSIS

All statistical analyses were performed with SAS statistical software, version 9.1 for Windows (SAS Institute Inc, Cary, North Carolina). Comparisons between the groups were based on the patients' clinicopathological characteristics and were performed with either a χ^2 test or Fisher exact test for discrete data and with independent 2-sample *t* tests or Wilcoxon rank sum tests for continuous variables. Survival analysis was performed by the Kaplan-Meier method. The log-rank test was used for comparison of survival functions. The Cox proportional hazards model was used to calculate hazard ratios and 95% confidence intervals for the independent factors of long-term survival. Two-sided *P* values were reported in this study and were considered significant if less than .05.

RESULTS

PATIENT DEMOGRAPHICS AND RESECTABILITY

Table 1 gives an overview of the surgical treatments for gastric cancer during the past 20 years. The patients in the late group (1994-2003) were older on average than the patients in the early group (1984-1993; $P<.001$). There were no significant differences in sex distribution between the 2 groups ($P=.48$). The overall resectability rate improved from 88.3% during the early years to 92.0% during the late years ($P=.001$). In addition, the incidence of curative gastrectomy increased from 83.1% to 87.8% during the study period ($P<.001$).

CLINICOPATHOLOGICAL CHARACTERISTICS OF CURATIVELY RESECTED TUMORS

As seen in **Table 2**, there was a significant increase over time in the proportion of proximal tumors ($P=.02$). During the late period, tumors were predominantly differentiated (53.3%), whereas undifferentiated tumors constituted more than half (54.5%) of the tumors in the early period ($P<.001$). The average tumor size was smaller during the late period ($P<.001$), and the proportion of T1 tumors (early gastric cancers) in the late period (42.8%) was higher than that in the early period (27.6%). In contrast, the incidence of advanced cancers belonging to other T stages (advanced gastric cancers) decreased ($P<.001$) during the late period. Similar to the T stage, the proportion of N0 stage lesions increased over time ($P=.004$), and accordingly, the overall stages improved and stage I lesions constituted more than half (51.1%) the lesions during the late period.

SURGICAL TREATMENT FACTORS FOR PATIENTS UNDERGOING CURATIVE RESECTION

For all patients who underwent subtotal or total gastrectomy, the incidence of total gastrectomy increased rapidly up to 29.4% during the late period ($P<.001$) (**Table 3**). Although the number of retrieved lymph nodes in the late period (mean [SD], 38.02 [14.55]) was

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Table 2. Clinicopathological Characteristics of Resected Tumors Resulting in Cures

	Period of Study, No. (%)		
	Early (1984-1993) (n=819)	Late (1994-2003) (n=1359)	*P* Value
Location			
Upper third	65 (7.9)	143 (10.5)	.02[a]
Middle third	325 (39.7)	497 (36.6)	
Lower third	426 (52.0)	719 (52.9)	
Entire area	3 (0.4)	0	
Differentiation			
Differentiated	373 (45.5)	724 (53.3)	<.001[b]
Undifferentiated	446 (54.5)	635 (46.7)	
Tumor size, cm, mean (SD)	4.41 (2.58)	3.98 (2.54)	<.001[c]
T stage			<.001[b]
T1	226 (27.6)	581 (42.8)	
Mucosa	120 (14.7)	302 (22.2)	.775[b]
Submucosa	106 (12.9)	279 (20.6)	
T2	240 (29.3)	266 (19.6)	
Muscularis propria	118 (14.4)	215 (15.8)	<.001[b]
Subserosa	122 (14.9)	51 (3.8)	
T3	327 (39.9)	486 (35.7)	
T4	26 (3.2)	26 (1.9)	
N stage			
N0	379 (46.3)	732 (53.9)	.004[b]
N1	271 (33.1)	371 (27.3)	
N2	125 (15.2)	178 (13.1)	
N3	44 (5.4)	78 (5.7)	
Stage			<.001[b]
I	348 (42.5)	695 (51.1)	
Ia	200 (24.4)	516 (38.0)	<.001[b]
Ib	148 (18.1)	179 (13.2)	
II	145 (17.7)	215 (15.8)	
III	265 (32.4)	350 (25.8)	
IIIa	175 (21.4)	212 (15.6)	.165[b]
IIIb	90 (11.0)	138 (10.2)	
IV	61 (7.4)	99 (7.3)	

[a] Calculated with Fisher exact test.
[b] Calculated with Pearson χ^2 test.
[c] Calculated with an independent, 2-sample *t* test.

significantly greater than in the early period (26.19 [12.31], $P<.001$), there was no difference in the extent of lymph node dissection recorded between the 2 consecutive periods ($P=.53$). However, subspecialist surgeons retrieved more lymph nodes than nonspecialists did (36.01 [14.73] vs 25.00 [12.07], $P<.001$), and, within the group of subspecialist surgeons, the number of harvested nodes increased over time (27.84 [12.58] in the early period vs 38.15 [14.50] in the late period, $P<.001$). Although only 42.9% of surgical procedures were performed by gastric subspecialist surgeons during the early period of this study, subspecialist surgeons performed 98.9% of the surgical procedures during the late period.

KAPLAN-MEIER METHOD FOR COMPARING SURVIVAL DISTRIBUTIONS IN PATIENTS WITH CURATIVE RESECTION

The Kaplan-Meier survival analysis showed the mean survival time for the early and late groups to be 8.2 and 7.8 years, respectively.

Table 3. Surgical Treatment Factors for Patients Undergoing Curative Resection

	Period of Study, No. (%)		
	Early (1984-1993) (n=819)	Late (1994-2003) (n=1359)	*P* Value
Resection type			
Total	147 (17.9)	400 (29.4)	<.001[a]
Partial	672 (82.1)	959 (70.6)	
Extent of lymphadenectomy			
<D2	199 (24.3)	314 (23.1)	.53[a]
≥D2	620 (75.7)	1045 (76.9)	
No. of retrieved LNs, mean (SD)	26.19 (12.31)	38.02 (14.55)	<.001[b]
Surgical subspecialty			
Yes	351 (42.9)	1344 (98.9)	<.001[a]
No	468 (57.1)	15 (1.1)	

Abbreviation: LNs, lymph nodes.
[a] Calculated with Pearson χ^2 test.
[b] Calculated with Wilcoxon rank sum test.

Table 4. Kaplan-Meier Comparison of Survival Distributions of Patients Undergoing Curative Resection

	5-y Survival by Period of Study, %		
TNM Stage	Early (1984-1993)	Late (1994-2003)	*P* Value[a]
Total	66.1	76.6	<.001
Stage I	87.9	96.1	<.001
Stage II	76.6	78.3	.99
Stage III	40.5	59.4	.001
Stage IV	11.5	20.7	.003

[a] Calculated with the log-rank test.

Table 4 shows the 5-year survival rates for the 2 groups after curative resection and the results of the log-rank test for comparison of the survival distributions. Regardless of the tumor stage, the 5-year overall survival rate was 66.1% for patients in the early period and 76.6% in the late period ($P<.001$). When subgroup analysis was performed for each tumor stage, significant improvement with respect to survival distribution occurred in stages I ($P<.001$), III ($P=.001$), and IV ($P=.003$), whereas the survival distributions between the groups were not significantly different for stage II ($P=.99$).

COX PROPORTIONAL HAZARDS REGRESSION MODEL FOR SURVIVAL OF PATIENTS UNDERGOING CURATIVE RESECTION

A univariate Cox proportional hazards regression model with a single variable identified the following significant factors influencing the survival of patients who underwent curative resection, except in the cases in which the tumors involved the entire stomach: the period of study ($P<.001$; **Figure 1**), age ($P<.001$), sex ($P=.008$), tumor location ($P=.01$), differentiation ($P<.001$), tumor size ($P<.001$), type of resection ($P<.001$), extent

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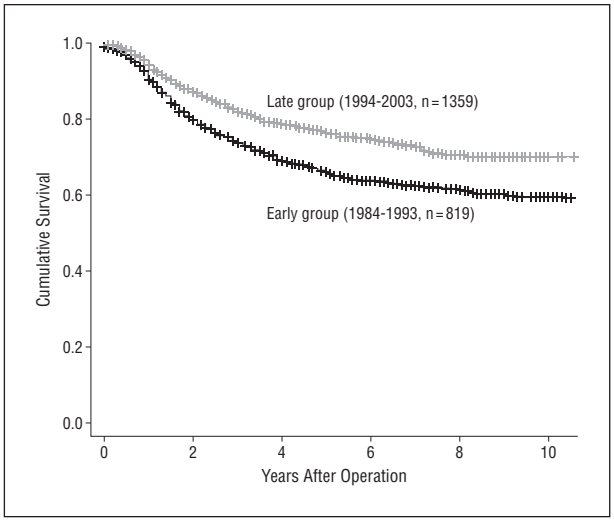

Figure 1. Five-year survival rate by year of surgery in patients who underwent curative gastrectomy. A significant difference ($P<.001$ by log-rank test) was observed in postoperative survival between the early and late groups.

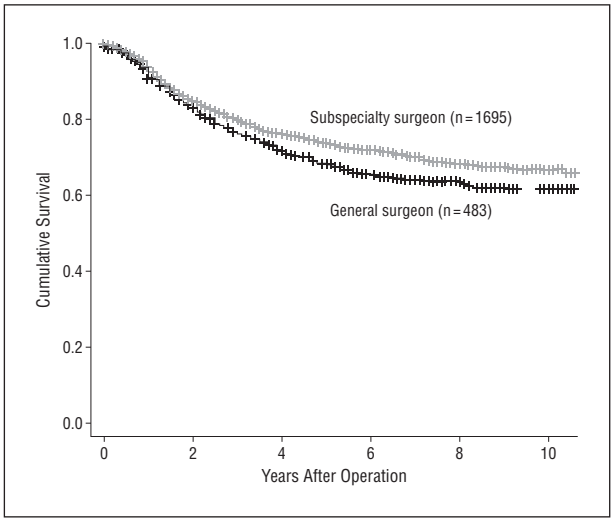

Figure 2. Five-year survival rate by surgeon type in patients who underwent curative gastrectomy. Survival of patients operated on by subspecialty surgeons was superior to that of patients operated on by general surgeons ($P=.05$).

of lymphadenectomy ($P=.004$), surgical subspecialty ($P=.05$; **Figure 2**), and TNM stage ($P<.001$).

With these variables as independent prognostic factors, the Cox proportional hazards regression model was used. Age ($P<.001$), sex ($P=.002$), tumor location (lower third vs upper third; $P=.03$), type of resection ($P<.001$), and stage ($P<.001$) were all independent prognostic factors (**Table 5**). It is of interest that the interaction effect ($P=.009$) between the period of study ($P=.26$) and the surgical subspecialty ($P=.39$) was significant even though the individual variables did not contribute significantly to the model. This significant interaction effect indicates that improvement in survival was related to the subspecialty of the operating surgeon during the late period of the study much more than the other combinations (period of study and surgical subspecialty).

Table 5. Cox Proportional Hazards Model for Survival of Patients Undergoing Curative Resection[a]

Variable	HR (95% CI)	*P* Value
Period of study (late vs **early**)	1.46 (0.71-2.98)	.31
Age	1.02 (1.01-1.02)	<.001
Sex (male vs **female**)	1.32 (1.11-1.58)	.002
Tumor size, cm	1.02 (0.99-1.06)	.25
Differentiation (differentiated vs **undifferentiated**)	0.95 (0.80-1.13)	.58
Extent of lymphadenectomy (≥D2 vs <**D2**)	0.86 (0.70-1.06)	.15
Tumor location		
Middle third vs **upper third**	1.08 (0.82-1.43)	.58
Lower third vs **upper third**	1.42 (1.04-1.95)	.03
Resection type (total vs **partial**)	1.52 (1.20-1.92)	<.001
Surgical subspecialty (yes vs **no**)	1.15 (0.91-1.45)	.25
Period of study × surgical subspecialty (late × yes vs **others**)	0.38 (0.18-0.80)	.01
TNM stage		
II vs **I**	3.18 (2.38-4.26)	<.001
III vs **I**	7.13 (5.52-9.21)	<.001
IV vs **I**	18.66 (13.57-25.67)	<.001

Abbreviations: CI, confidence interval; D2, complete removal of group 1 and group 2 lymph nodes; HR, hazard ratio.
[a] Reference conditions are indicated in boldface type.

COMMENT

During the past 20 years, the nature of gastric cancer has changed. Some of these changes are beneficial to patients, while others are not. Nevertheless, many surgical approaches to the treatment of gastric cancer have been improved through vigorous research and education.

Most studies on the surgical outcomes for gastric cancer indicate time-related improvements. Improvements in short-term surgical results, mainly of postoperative morbidity and mortality, have been attributed to improvements in surgical quality resulting from specialized interest and training.[4-6,19] With regard to long-term outcomes, early diagnosis followed by changes in the proportion of gastric cancer stages has clearly contributed to improvement in patient survival rates.[3,5,7,9] Despite the increasing incidence of gastric cancer in Korea, mortality due to gastric cancer is decreasing.[23] This is a result of advanced surgical techniques, multidisciplinary approaches including chemotherapy, and molecularly targeted therapy for advanced gastric cancer.[24] In addition, the Korean government initiated a national cancer screening program in 1999 that provides free screening for gastric cancers to those older than 40 years on a biannual basis. This program may be leading to earlier detection of gastric cancers.[25] However, it is difficult to delineate exactly which treatment factors are most clearly related to survival gains. Almost no data are available with regard to the surgical point of view, and analyzing all treatment factors is extremely important for patient treatment and the development of the best surgical strategies.

Compared with treatments for other solid abdominal tumors, surgery for gastric cancer consists of 2 distinctive parts: curative gastrectomy and thorough lymphadenectomy. The outcomes of these elements are largely

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dependent on surgical skill and academic knowledge and are based on a surgeon's interest in the specific disease as well as treatment experience over a certain period of time through subspecialization.

Surgical resection of the stomach is the only known curative therapy for gastric cancer. Our results demonstrate gradual increases in resectability and curability over time, while also showing that procedures not related to promoting survival or managing symptoms, such as open and closed and noncurative resections, decreased over time. Because resectability does not always lead to cure, outcomes may be affected by factors related to clinician competence, such as clinical judgment and performance of the optimal surgical procedure. These are prerequisites for high-quality care in surgical oncology.

There is some controversy regarding the importance of extended lymphadenectomy for the treatment of gastric cancer. Some view lymphadenectomy as a staging tool, while others view it as a therapeutic modality. Chew et al[26] reported that extended lymphadenectomy offered a survival benefit for patients with gastric cancer when performed by well-trained, experienced surgeons. The thoroughness of lymphadenectomy, regarded as the main factor related to surgical quality control for gastric cancer, has also been debated.[4,5,11,12,18,27,28] The extent of lymphadenectomy, the number of retrieved lymph nodes, surgical subspecialty, and surgical experience all affect the thoroughness of lymphadenectomy. Although there was no increase in the proportion of D2 dissections between the 2 consecutive periods in this study, the time-related increase in the number of retrieved lymph nodes suggests that surgeons have improved during the past 2 decades and are now equipped with sufficient techniques and knowledge to perform integral lymphadenectomies. We believe that there was no increase in the extent of lymphadenectomy in the recorded D2 dissections during the early period because the operating surgeons themselves could not achieve a sufficient quality of D2 dissection as designated by the recent guidelines for modern gastric cancer surgery.[13]

Together with the changing epidemiology of proximally located tumors,[3,5,6] more total gastrectomies now achieve an R0 resection. As reported earlier,[29] data for most clinicopathological variables, such as differentiation, size, and stage of the tumor, but not location of the tumor, have changed over time, resulting in improved prognoses for patients with gastric cancer.

These results support our hypothesis that a greater number of total gastrectomies were performed in the late period because predominantly subspecialist surgeons were performing the procedures. Furthermore, more lymph nodes were harvested, even within the subspecialist group, between the early and late periods, and overall curability also increased over time. Therefore, the quality of medical service delivered to patients by subspecialist surgeons in the late period was better than that for the patients treated during the early period. This is most likely because of improved clinician competence leading to more appropriate treatment decisions.

Considering long-term prognosis, most studies report a worldwide increase in 5-year survival rates for gastric cancer, most likely owing to increases in the proportion of patients whose gastric cancer is detected early and who then undergo curative resection.[3,5,7,9,10] In the present study, to eliminate the stage and curability effects, which are confounding factors when attempting to uncover surgical variables affecting survival, we performed stage-stratified survival analysis only for curative cases. The results of the current study demonstrate periodic survival gains in all stages except stage II; we could not determine why only stage II demonstrated no survival benefit after subgroup analysis. One possible explanation is that the management of stage II gastric cancer has always been a late treatment consideration because this stage has an acceptable oncologic prognosis after surgery alone. As a result, physicians have been ambiguous in their attitude toward the development of preoperative and postoperative therapeutic modalities for cancers of this stage. Therefore, we suggest that this is the time to concentrate effort on this stage to attain improvement in long-term outcomes.

We observed a significant interaction between the period of study and surgical subspecialty on long-term prognosis. These results indicate that there were intangible factors influencing surgical outcomes. Douek and Taylor[30] reported that the most important components of high-quality care in surgical oncology are sound clinical judgment, surgical skill, and multidisciplinary care; we believe that these prerequisites are best achieved by specialization. In addition to Douek and Taylor's criteria, we would stress the importance of surgeon experience, not only operative experience but also observational management through long-term patient follow-up, as well as an interest or at least willingness to learn and research the latest knowledge in the field of oncology. We did not analyze the use of adjuvant chemotherapy because, during our study periods, we used various methods with heterogeneous groups and with various chemotherapeutic regimens. Therefore, evaluation of survival including analysis of adjuvant chemotherapy may complicate the interpretation of our study. We believe that the most important point with regard to adjuvant chemotherapy is that some patients with gastric cancer will respond more favorably to adjuvant chemotherapy than others. It is our assertion that experienced subspecialty surgeons can make better decisions about patient selection for adjuvant chemotherapy. Because a controlled trial comparing the outcomes of specialist- vs nonspecialist-performed operations is not practically feasible, the confounding factor of chemotherapy still implies a connection to the surgeon as a prognostic factor, as has been suggested by other researchers.[4,16]

During the past 2 decades, management of gastric cancer has achieved noticeable success; the primary reason for these improvements rests with specialized gastric surgeons, together with favorable trends in prognostic factors. Therefore, increased recruitment and training of gastric subspecialists may be one way to improve long-term results for gastric cancer.

Accepted for Publication: September 14, 2009.
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Financial Disclosure: None reported.

Additional Contributions: Sae-Min Kim, MD, PhD, professor emeritus of Korea University, contributed to the treatment and research of gastric cancer and provided leadership. The following 10 attending surgeons are not mentioned elsewhere in this article but treated the patients enrolled in this study: Bum-Hwan Koo, MD, PhD, Seon-Hahn Kim, MD, PhD, Young-Chul Kim, MD, PhD, Pyung-Chul Min, MD, PhD, Hong-Young Moon, MD, PhD, Jeoung-Won Bae, MD, PhD, Sung-Gyu Lee, MD, PhD, Sung-Ock Suh, MD, PhD, Sang-Yong Choi, MD, PhD, and Cheung-Wung Whang, MD, PhD.

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INVITED CRITIQUE

Does Surgeon Volume Matter for Gastric Cancer Surgery?

Jang et al present a well-done study concluding that surgeon subspecialty is an important factor in improving survival for patients with gastric cancer. The authors conclude that high-volume gastric surgeons (those performing ≥50 gastric cancer operations per year) provide better outcomes for patients.

The topic of surgical subspecialization has been widely debated in the field of surgical oncology. Studies have established that operations such as pancreaticoduodenectomy, when performed at high-volume centers, improve patient outcomes.[1] For gastric cancer, this is more difficult to study given the relatively lower incidence of

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