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ABOUT COVER

Editorial board member of *World Journal of Gastrointestinal Oncology*, Adriana Ciocalteu, MD, PhD, is a Researcher at the Research Center of Gastroenterology and Hepatology and a Teaching Assistant in the Department of Gastroenterology of the University of Medicine and Pharmacy, Craiova (Romania). Having received her Bachelor's degree from University of Medicine and Pharmacy of Craiova in 2011, she undertook her postgraduate training at the Clinical Emergency County Hospital Craiova in the Gastroenterology Unit, Copenhagen University Hospital, Herlev and at Aarhus University Hospital (Denmark), receiving her PhD in 2016. Upon return to Craiova, she began her practice as Specialist in Gastroenterology and Teaching Assistant in the Department of Gastroenterology at the University of Medicine and Pharmacy. Her ongoing research interests involve studying malignant pathology of the digestive system using state-of-the-art techniques. (L-Editor: Filipodia)

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (*WJGO*, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

  WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

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Retrospective Cohort Study

Changing trends of clinicopathologic features and survival duration after surgery for gastric cancer in Northeast China

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Abstract

BACKGROUND

Through analyzing the data from a single institution in Northeast China, this study revealed the possible clinicopathologic characteristics that influence the prognosis of patients with gastric cancer (GC).

AIM

To evaluate the changing trends of clinicopathologic features and survival duration after surgery in patients with GC in Northeast China, which is a high-prevalence area of GC.

METHODS

The study analyzed the difference in clinicopathologic features and survival duration after surgery of 5887 patients who were histologically diagnosed with GC at the Harbin Medical University Cancer Hospital. The study mainly analyzed the data in three periods, 2000 to 2004 (Phase 1), 2005 to 2009 (Phase 2), and 2010 to 2014 (Phase 3).

RESULTS

Over time, the postoperative survival rate significantly increased from 2000 to 2014. In the past 15 years, compared with Phases 1 and 2, the tumor size was smaller in Phase 3 ($P < 0.001$), but the proportion of high-medium differentiated tumors increased ($P < 0.001$). The proportion of early GC gradually increased from 3.9% to 14.4% ($P < 0.001$). A surprising improvement was observed in the mean number of retrieved lymph nodes, ranging from 11.4 to 27.5 ($P < 0.001$). The overall 5-year survival rate increased from 24% in Phase 1 to 43.8% in Phase 3. Through multivariate analysis, it was found that age, tumor size, histologic type,

tumor-node-metastasis stage, depth of invasion, lymph node metastasis, surgical approach, local infiltration, radical extent, number of retrieved lymph nodes, and age group were independent risk factors that influenced the prognosis of patients with GC.

CONCLUSION
The clinical features of GC in Northeast China changed during the observation period. The increasing detection of early GC and more standardized surgical treatment effectively prolonged lifetimes.

Key Words: Gastric cancer; Clinicopathologic features; Survival; Time trends; Epidemiology; Gastrectomy

Core Tip: In recent decades, due to the increasing heterogeneity of gastric cancer (GC), GC has attracted wide attention from epidemiologists, especially in terms of risk factors. More advanced technologies and concepts have been involved in the diagnosis and surgery of GC. The improvements include the dissection method, resection range, surgical techniques and instruments, as well as the emphasis on perioperative nursing and the strengthening of the concept of rapid recovery, which have effects that can help patients with GC directly or indirectly. Therefore, this study performed a comparative analysis of the clinicopathological characteristics and postoperative survival of patients with GC from the Harbin Medical University Cancer Hospital over 15 years starting in 2000. The factors affecting the prognosis of GC were clarified based on the time trend.

INTRODUCTION

Currently, the morbidity and mortality of gastric cancer (GC) have decreased sharply; however, it is still an important global public health burden[1,2]. Nearly 450000 cases of GC were recorded in 2018, accounting for 10.6% of all cancers. Among them, nearly 390000 patients died from GC, which account for 13.6% of all the people who died because of cancer[3]. Therefore, GC is the third most common cancer after lung and colorectal cancers and is the second leading cause of cancer death after lung cancer[4,5].

In the past few decades, although the prognosis of patients with GC has improved in China, the survival rate is still lagging[6]. However, the prognosis also varies significantly by geographic area[7]. It was reported that due to the launch of a massive national cancer screening program, the 5-year survival rate in South Korea and Japan is significantly better than that in Western countries[8,9]. The difference is attributed to early detection, prolonged lymphadenectomy, and tumor characteristics. The survival rate of patients with GC in China is higher than those in the United States and some European countries but far lower than those in Japan and South Korea[10-13].

The morbidity of GC is different geographically even within a country[14-16]. There are significant geographical distribution clusters of GC in China, and high morbidity is mainly seen in the northern part of China[7]. Because of geographical conditions, dietary habits, economic development, *etc.*, high morbidity and mortality of GC have been seen in Northeast China. Thus, it is necessary to conduct systematic research on the clinical characteristics and survival rate of GC in this densely populated area. However, there are few studies on the tumor characteristics and treatment outcomes of GC based on a large amount of data from GC[17]. Therefore, a high-capacity data center that collected data from more than 1000 GC surgeries in Northeast China was used in this study. Through analyzing the data from the data center in the past 15 years from 2000 to 2014, this study revealed changes in postoperative clinical characteristics and

survival. The results of this study will help people better understand the characteristics and development trends of GC. It may also provide a reference for the diagnosis and prevention of regional GC.

MATERIALS AND METHODS

This study reviewed and analyzed 5887 patients who were treated for GC at the Harbin Medical University Cancer Hospital from January 2000 to December 2014. The data in this study were from the Gastric Cancer Information Management System V1.0 of gastrointestinal surgery in the Harbin Medical University Cancer Hospital, including demographics, clinicopathological features, diagnosis, surgical records, postoperative results, and follow-up visits. All data were stored in the database in advance. The patients' survival period was updated every 6 mo. The case inclusion criteria included the following: (1) Patients who were pathologically diagnosed with GC and whose complete cases and follow-up could be accessed; (2) Patients without neoadjuvant chemotherapy or perioperative chemoradiotherapy; (3) Patients without other gastric tumors (lymphoma, stromal tumor, residual GC, *etc*.) or malignant tumors (breast cancer, colorectal cancer, *etc*.) at the same time; and (4) Cases without surgery or resection, such as laparotomy, gastrojejunostomy, and endoscopic mucosal dissection. Eventually, 4744 patients met the requirements. To demonstrate changes over time, time trends were certified by comparing the following three periods: 2000-2004 (Phase 1), 2005-2009 (Phase 2), and 2010-2014 (Phase 3).

Pathologists followed the standard procedures for pathological diagnosis of preoperative endoscopic biopsy, intraoperative marginal biopsy, and major postoperative pathology. The location of the tumor was divided into four types, including the upper, middle, and lower thirds and the entire stomach. Tissue types were divided into highly, moderately, and lowly differentiated and undifferentiated. Tumor staging was based on the Seventh Edition of the American Joint Committee on Cancer/International Union for Cancer Control[18,19]. Early GC was defined as a tumor limited to the mucosa or submucosa according to the Japanese Society of Gastric Cancer Research[20]. All potentially curable patients were treated by gastrectomy and D1+ or D2 (or D2+ lymphadenectomy). Patients with stage IV GC and incurable lesions in preoperative assessments underwent palliative surgery to control symptoms to gain better quality of life. According to the standards of the Union for International Cancer Control, R0 was defined as radical resection, and R1 and R2 were identified as patients with residual tumors visible under the microscope (R1) or to the naked eye (R2). For tumors located in the middle and lower thirds of the stomach, subtotal gastrectomy was usually the first choice. The criteria for completing the gastrectomy were leaving enough resection margins and removing all of the omentum majus and lymph nodes around the stomach. Extended lymph node excision was based on the standards of the Japanese Gastric Cancer Association. Multiple organ resections due to suspected invasion by the tumor were defined as the combined excision of adjacent organs (spleen, liver, pancreas, colon, *etc*.). After the operation, the surgeon carefully examined and counted all resected specimens and determined their distribution immediately. After radical resection, patients with stage II or later stages of GC usually received adjuvant chemotherapy based on their physical condition, acceptance level, and economic status. However, as previously reported[21], adjuvant chemotherapy regimens have changed significantly in the past decades, which has led to heterogeneity in chemotherapy, the number of cycles, and treatment regimens. Therefore, the details of adjuvant chemotherapy were not considered for statistical analysis in this study.

Statistical analysis

The commercially available software SPSS was used for statistical analyses. All patient data were entered into the SPSS database, and the analysis was run. The mean value was used to represent continuous data. Student's *t* test was used to evaluate the significant differences among the mean values. Categorized variables were evaluated by the Pearson χ^2 test. The cumulative survival rate was calculated by the Kaplan-Meier method, and the difference among different groups was evaluated by the long-rank test. A Cox regression model was used for multivariate prognostic analysis. $P < 0.05$ was used as the standard for considering if the data were statistically significant.

RESULTS

From January 2000 to December 2014, a total of 5887 patients were pathologically confirmed to have gastric adenocarcinoma. Among these patients, 268 were unsuitable for laparotomy; 370 only received palliative resection; 505 did not receive surgery; and the remaining 4744 underwent gastrectomy successfully. The overall resection rate was 80.6%. This study analyzed the data from 4744 patients who underwent gastrectomy successfully. Table 1 shows the different types of treatment for all patients.

For clinicopathological features, Table 2 lists all the details of the clinicopathological characteristics of all patients. As we predicted, certain characteristics changed during the three treatment phases. The number of patients with gastric adenocarcinoma in northeastern China increased sharply from 647 in the first phase to 2645 in the third phase. The average age was 58.6 years (range, 21-91 years), and the number of patients aged 45 to 65 years increased significantly, from 56% in the first period to 64.1% in the last period (P = 0.000). The male to female ratio was 2.82:1, with no significant change. For the composition of the tumor location, in Phase 3, the most common (58.9%) location was the lower third, followed by the entire stomach (15%). Smaller tumors (< 50 mm) gradually increased over time, from 192 cases (29.7%) in the first stage to 1105 cases (41.8%) in the last stage (P = 0.000). The proportion of highly/moderately differentiated tumors increased from 28.4% to 41.6% (P = 0.000). Over time, more early GCs were diagnosed, from 3.9% in Phase 1 to 14.4% in Phase 3 (P = 0.000). In terms of lymph node metastasis, the number of patients with N1 and N2 decreased significantly (P = 0.000), but the number of patients with N3 increased significantly (P = 0.000). This immediately changed the tumor-node-metastasis (TNM) stage.

In terms of surgery, Table 3 records the changes in the surgical characteristics of patients with GC at different periods. Among the three phases, distal GC resection was the most common, representing more than half. Overall, 80.3% of patients underwent radical GC surgery, which was not significantly different between the three periods. The combined resection rate was significantly reduced, but early complications increased. It is worth noting that the number of lymph nodes retrieved during surgery improved significantly (Figure 1). The average number of searched lymph nodes increased from 11.4 in Phase 1 to 27.5 in Phase 3 (P = 0.000). These data were derived from pathological reports.

In terms of survival, at the last follow-up visit (September 1, 2019), a total of 1845 patients survived, and 2899 patients had died. The average 5-year survival rate was 38.9%. Over time, the 5-year survival rate improved significantly in the three periods: Phase I: 24%, Phase II: 36.6%, and Phase III: 43.8% (Figure 2). According to the subgroup analysis by TNM staging, the 5-year survival rate of patients with stages I + II and III disease was significantly improved compared with the earlier stage (P = 0.000) (Figure 3A and B). In contrast, the 5-year survival rate of patients with stage IV disease did not change significantly (P = 0.210) (Figure 3C). Through univariate survival analysis, we found that some clinicopathological variables were significantly related to survival (Table 4), including age, tumor location, tumor size, histological type, TNM stage, depth of invasion, lymph node metastasis, distant metastasis, surgical method, local infiltration, extent of radical resection, joint resection, number of retrieved lymph nodes, and age group. In addition, when multivariate analysis was performed, age, tumor size, histological type, TNM stage, depth of invasion, lymph node metastasis, surgical approach, local invasion, radical extent, number of retrieved lymph nodes, and age group were all independent prognostic factors.

DISCUSSION

In recent decades, due to the increasing heterogeneity of GC, it has successfully attracted wide attention from epidemiologists, especially in terms of risk factors[22-24]. More advanced technologies and concepts have been involved in the diagnosis and surgery of GC. The improvements include the dissection method, resection range, surgical techniques and instruments, as well as the emphasis on perioperative nursing and the strengthening of the concept of rapid recovery[25-28], which have effects that can help patients with GC directly or indirectly. Therefore, this study performed a comparative analysis of the clinicopathological characteristics and postoperative survival of patients with GC from the Harbin Medical University Cancer Hospital over 15 years starting in 2000. The factors affecting the prognosis of GC were identified based on the time trend.

Table 1 Treatments for all patients, *n* (%)

Surgical procedure	2000-2004 (*n* = 853)	2005-2009 (*n* = 1707)	2010-2014 (*n* = 3327)	2000-2014 (*n* = 5887)
Proximal gastrectomy	60 (7)	152 (8.9)	228 (6.9)	440 (7.5)
Subtotal distal gastrectomy	398 (46.7)	946 (55.4)	1646 (49.5)	2990 (50.8)
Total gastrectomy	189 (22.2)	354 (20.7)	771 (23.2)	1314 (22.3)
Palliative surgery	80 (9.4)	97 (5.7)	193 (5.8)	370 (6.3)
Exploratory laparotomy	23 (2.7)	45 (2.6)	200 (6)	268 (4.6)
No surgery	103 (12.1)	113 (6.6)	289 (8.7)	505 (8.6)

Some of the clinicopathological indicators, which are related to the prognosis as proven by the multivariate analysis, are beyond medical control. There is still no unified conclusion. For example, there is a debate regarding the influence of age on the prognosis of GC. Nelen *et al*[29] believe that age is not an independent factor for the prognosis of patients with GC . However, some other scholars believe that the reason why young patients have a worse prognosis than old patients is due to the more aggressive behavior of tumors and delayed diagnosis[30,31]. In contrast, Solaini *et al*[32] believe that the prognosis of old patients is worse because elderly patients have higher risks of postoperative complications and are less tolerant of chemotherapy, which is consistent with the findings in this study that patients older than 65 years had a worse prognosis than patients younger than 45 years, and multivariate analysis showed that age can be an independent prognostic factor. On the issue of sex, based on the results of this study, there was no significant difference in the long-term survival of GC between the sexes. This result is also similar to that in other studies[33]. According to the studies performed by authors from Western countries[34,35], the number of tumors in the upper third is increasing each year, which is also similar to the result obtained by some researchers from Asia[36]. It is estimated that the change in location may be caused by risk factors, as it is speculated that changes in the location may be caused by related risk factors, such as gastroesophageal reflux disease, smoking, drinking alcohol, and obesity. However, this is in stark contrast to the findings in this study. Tumors in the lower third were the most common type of GC in Northeast China. This is mostly likely due to the lack of transesophageal and esophagogastric junction cancers. Additionally, some studies have reported that although cardiac cancer is often combined with GC in epidemiological statistics, they are obviously different diseases. The prognosis of cardiac cancer is significantly worse than that of distal GC[37]. This conclusion is also supported by the results of this study. Liang *et al*[38] reported that the prognosis of GC is significantly related to the size of the tumor. Patients with gastric tumors smaller than 4 cm have a better prognosis than those with tumors larger than 8 cm. Additionally, involving the tumor size in the PT staging system can improve the accuracy of prognosis prediction of patients with lymph node-negative GC. In this study, by comparing different cutoff values, it was finally found that when the cutoff value was set at 5 cm, tumor size could be used as an independent prognostic factor for GC, and the prognosis of patients with tumors smaller than 5 cm was far better than that of patients with tumors larger than 5 cm. In terms of the histological types of GC, Miyamae *et al*[39] believe that histologically mixed GC composed of differentiated and undifferentiated GC is associated with aggressive clinical features and poor prognosis. However, most of the scholars' research results are similar to this study[33]. Patients with well-differentiated and moderate histology have a better prognosis than patients with poor differentiation, especially signet ring cell carcinoma or mucinous adenocarcinoma. Our data showed that over time, the proportion of highly differentiated and moderately differentiated patients increased annually, from 28.4% to 41.6% (*P* = 0.000). This also provides evidence for a steady improvement in survival performance.

The prognosis of GC is closely related to the stage of the cancer at the time of diagnosis. According to the results of this study, the detection rate of early GC (T1) has increased each year among the three phases, from 3.9% in Phase 1 to 14.4% in Phase 3 (*P* = 0.000), which is partly attributed to accurate diagnostic methods, equipment support, and people's strengthening of the concept of early diagnosis and early treatment. This is similar to the results of studies in Western countries[13] but still far from the respective 61% and 58% diagnostic rates reported by South Korea and Japan, which have already conducted early GC screening programs[40,41]. In this study, open

Table 2 Clinicopathological characteristics of gastric cancer patients at different time periods, *n* (%)

	2000-2004 (*n* = 647)	2005-2009 (*n* = 1452)	2010-2014 (*n* = 2645)	2000-2014 (*n* = 4744)	*P* value
Gender					0.321
Male	462 (71.4)	1079 (74.3)	1961 (74.1)	3502 (73.8)	
Female	185 (28.6)	373 (25.7)	684 (25.9)	1242 (26.2)	
Age (yr)					0.000
≤ 45	110 (17)	177 (12.2)	286 (10.8)	573 (12.1)	
45-65	362 (56)	822 (56.6)	1695 (64.1)	2879 (60.7)	
> 65	175 (27)	453 (31.2)	664 (25.1)	1292 (27.2)	
Tumor location					0.017
Upper third	74 (11.4)	158 (10.9)	336 (12.7)	568 (12)	
Middle third	89 (13.8)	237 (16.3)	343 (13)	669 (14.1)	
Lower third	373 (57.7)	836 (57.6)	1586 (60)	2795 (58.9)	
Whole stomach	115 (17.8)	221 (15.2)	380 (14.3)	712 (15)	
Tumor size (mm)					0.000
< 50	192 (29.7)	593 (40.8)	1105 (41.8)	1890 (39.8)	
≥ 50	455 (70.3)	859 (59.2)	1540 (58.2)	2854 (60.2)	
Histologic type					0.000
Well/moderately differentiated	184 (28.4)	492 (33.9)	1101 (41.6)	1777 (37.5)	
Lowly/undifferentiated	463 (71.6)	960 (66.1)	1544 (58.4)	2967 (62.5)	
T stage					0.000
T1	25 (3.9)	121 (8.3)	380 (14.4)	526 (11.1)	
T2	112 (17.3)	197 (13.6)	258 (9.8)	567 (12)	
T3	110 (17)	155 (10.7)	820 (31)	1085 (22.9)	
T4	400 (61.8)	979 (67.4)	1187 (44.9)	2566 (54.1)	
N stage					0.000
N0	226 (34.9)	493 (34)	999 (37.8)	1717 (36.2)	
N1	195 (30.1)	285 (19.6)	407 (15.4)	888 (18.7)	
N2	126 (19.5)	217 (14.9)	422 (16)	765 (16.1)	
N3	100 (15.5)	457 (31.5)	817 (30.9)	1374 (29)	
M stage					0.000
M0	572 (88.4)	1352 (93.1)	2484 (93.9)	4408 (92.9)	
M1	75 (11.6)	100 (6.9)	161 (6.1)	336 (7.1)	
TNM stage					0.000
I	65 (10)	184 (12.7)	468 (17.7)	717 (15.1)	
II	167 (25.8)	360 (24.8)	587 (22.2)	1114 (23.5)	
III	340 (52.6)	808 (55.6)	1429 (54)	2577 (54.3)	
IV	75 (11.6)	100 (6.9)	161 (6.1)	336 (7.1)	

TNM: Tumor-node-metastasis.

surgery was one of the criteria, and the study did not include patients who underwent endoscopic resection (such as endoscopic mucosal resection and endoscopic submucosal dissection). Therefore, the diagnosis rate of early GC may be lower than it actually is. However, the M stage, which had significant prognostic significance in the univariate analysis, did not show independent prognostic significance in the multivariate analysis of these data, which is similar to the results of Wang *et al*[17]. It was believed that the possible reason is that the study included the indicator of radical cure. The radical treatment of GC has a significant correlation with M stage, which may affect the prognostic significance of M stage in the Cox regression model. Therefore, improving the early detection rate of patients with GC and increasing the survival advantage of patients are still an important task for surgical treatment.

The study also analyzed the impact of changes in GC surgical treatment standards on patient prognosis across the three periods in 15 years. As shown in Figure 1, over time, the number of retrieved lymph nodes improved significantly. In the first phase, only 13.6% of patients had a lymph node detection rate greater than 15/case. However, by the third phase, the number had increased to 86.8%. The average number of resected nodes also increased from 11.4 to 27.5 per case. This is also an independent prognostic factor in multivariate analysis, which is similar to the results of other studies verifying that extending prolonged lymphadenectomy could effectively improve the survival advantage[17,42]. These results strongly illustrate that the improvement in surgical standards could effectively improve the prognosis of GC.

According to the results, the 5-year survival rate of patients with GC has significantly improved over time, which is similar to the results of studies performed in other regions[17,28,33,43]. The results of this study showed that the 5-year survival rate of patients with GC increased from 24% in the first stage to 43.8% in the third stage. In addition, as shown in Figure 3, from the subgroup analysis, the 5-year survival rate of patients with stages I and II disease was significantly improved (46.6%-73.4%, P = 0.000). The improvement in the survival rate in stage III disease was not significant (13.8%-26.9%, P = 0.000). The overall 5-year survival rate of patients with stage IV did not change significantly over time (P = 0.210). The reason why the survival rate of patients with stages I-III disease has risen significantly is undoubtedly because the GC treatment system has improved significantly in the past 10 years, including more accurate early detection and diagnosis, more reasonable surgical strategies, and more complete perioperative care (improvement in anesthesia, timely support in the intensive care unit, *etc*.)[44-46]. Moreover, in our data, more than half of the patients had stage III GC. Therefore, more efforts should be made to explore more standardized surgical treatments, which will help improve overall patient survival. The survival of patients with stage IV disease did not improve significantly. We believe that this may be because emergency surgery, for example, to treat bleeding, perforation, or obstruction, is needed to relieve symptoms in patients with stage IV disease, and surgical treatment alone is limited for improving survival. Recent studies[47,48] have shown that DCS (docetaxel, cisplatin, and TS-1) regimen, R0 resection, and trastuzumab-assisted chemotherapy may be effective strategies for patients with stage IV HER2-positive GC. This also shows that for these patients, we should seek more comprehensive treatment. Of course, in recent years, a large number of prospective randomized studies have confirmed that adjuvant chemotherapy and neoadjuvant chemotherapy have significantly improved the prognosis of advanced GC[49,50]. This is also strong evidence for the improvement in the survival of patients with GC in recent decades.

Limitations of the study

The limitations of this study include the following: (1) The results were from a single hospital; (2) The follow-up visit was just for a small number of patients in the last 5 years, which would make the result incomplete; (3) There may be differences in the analysis of patients treated in consecutive time periods with different follow-up times; and (4) There is insufficient evidence on adjuvant chemotherapy and neoadjuvant chemotherapy.

CONCLUSION

Overall, based on our 15 years of experience in treating patients with GC, we have observed that by attaching great importance to the perioperative period, including the improvement in surgical techniques and other techniques, a significant improvement in patient survival was noted. Despite this, even when patients with GC are diagnosed

Table 3 Surgical characteristics of patients with gastric cancer at different time periods, *n* (%)

	2000-2004 (*n* = 647)	2005-2009 (*n* = 1452)	2010-2014 (*n* = 2645)	2000-2014 (*n* = 4744)	*P* value
Type of gastrectomy					0.010
Proximal gastrectomy	60 (9.3)	152 (10.5)	228 (8.6)	440 (9.3)	
Subtotal distal gastrectomy	398 (61.5)	946 (65.2)	1646 (62.2)	2990 (63)	
Total gastrectomy	189 (29.2)	354 (24.4)	771 (29.1)	1314 (27.7)	
Local infiltration					0.014
Yes	100 (15.5)	268 (18.5)	538 (20.3)	906 (19.1)	
No	547 (85.5)	1184 (81.5)	2107 (79.7)	3838 (80.9)	
Margin status					0.050
R0	536 (82.8)	1139 (78.4)	2133 (80.6)	3808 (80.3)	
R1/R2	111 (17.2)	313 (21.6)	512 (19.4)	936 (19.7)	
Joint resection					0.000
Yes	59 (9.1)	36 (2.5)	106 (4)	201 (4.2)	
no	588 (90.9)	1416 (97.5)	2539 (96)	4543 (95.8)	
Early postoperative complications					0.000
Yes	24 (3.7)	20 (1.4)	141 (5.3)	185 (3.9)	
No	623 (96.3)	1432 (98.6)	2504 (94.7)	4558 (96.1)	
No. of retrieved lymph nodes					0.000
< 15	559 (86.4)	633 (43.6)	349 (13.2)	1541 (32.5)	
15-30	81 (12.5)	678 (46.7)	1294 (48.9)	2053 (42.3)	
≥ 30	7 (1.1)	141 (9.7)	1002 (37.9)	1150 (24.2)	

with a local disease, their prognosis is not optimistic. Obviously, surgery alone is not enough to achieve the ideal survival. We urgently need to develop a multimodal, multidisciplinary, and individualized comprehensive treatment system to achieve better results.

Table 4 Univariate and multivariate analyses of prognostic factors in patients with gastric cancer

Factor	Univariate analysis			Multivariate analysis		
	HR	95%CI	*P* value	HR	95%CI	*P* value
Gender	1.026	0.944-1.114	0.547	-	-	-
Age (yr)	1.091	1.026-1.160	0.005	1.105	1.039-1.176	0.002
Tumor location	1.150	1.096-1.206	0.000	0.979	0.936-1.024	0.353
Tumor size (mm)	2.578	2.375-2.797	0.000	1.206	1.100-1.322	0.000
Histologic type	1.484	1.373-1.604	0.000	1.172	1.082-1.270	0.000
TNM stage	2.640	2.498-2.791	0.000	1.267	1.136-1.412	0.000
T stage	1.756	1.679-1.836	0.000	1.189	1.120-1.262	0.000
N stage	1.657	1.607-1.708	0.000	1.344	1.287-1.403	0.000
M stage	4.140	3.686-4.651	0.000	1.150	0.968-1.365	0.112
Type of gastrectomy	1.677	1.569-1.792	0.000	1.201	1.122-1.286	0.000
Local infiltration	0.320	0.295-0.347	0.000	0.662	0.602-0.727	0.000
Margin status	4.029	3.713-4.372	0.000	1.843	1.666-2.040	0.000
Joint resection	0.539	0.461-0.629	0.000	0.919	0.783-1.079	0.304
Early postoperative complications	0.975	0.808-1.177	0.794	-	-	-
No. of retrieved lymph nodes	0.872	0.830-0.916	0.000	0.847	0.796-0.901	0.000
Year group	0.774	0.737-0.813	0.000	0.859	0.808-0.913	0.000

TNM: Tumor-node-metastasis.
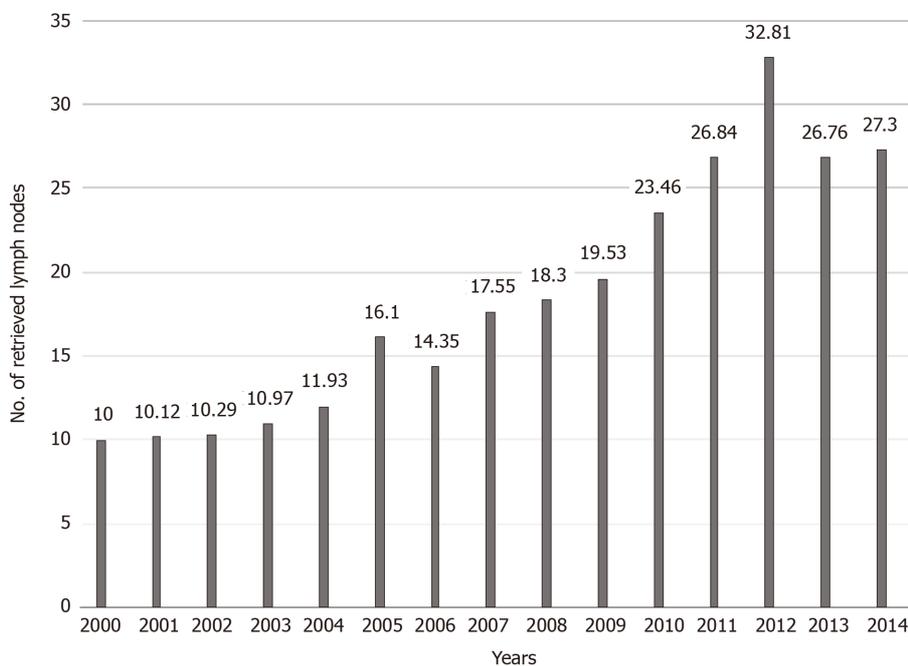
Figure 1 Number of lymph nodes retrieved from 2000 to 2014.
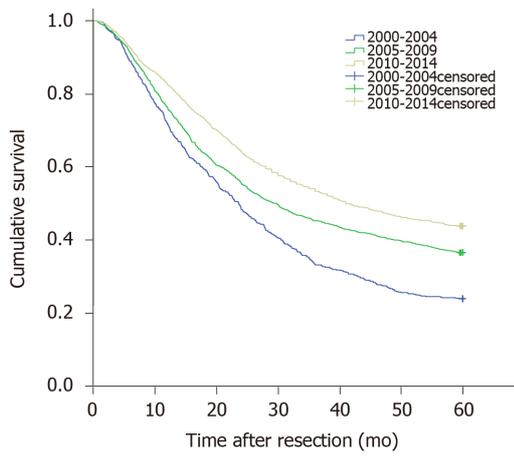
Figure 2 Overall survival curves for the three periods calculated by the Kaplan-Meier method (*P* = 0.000).
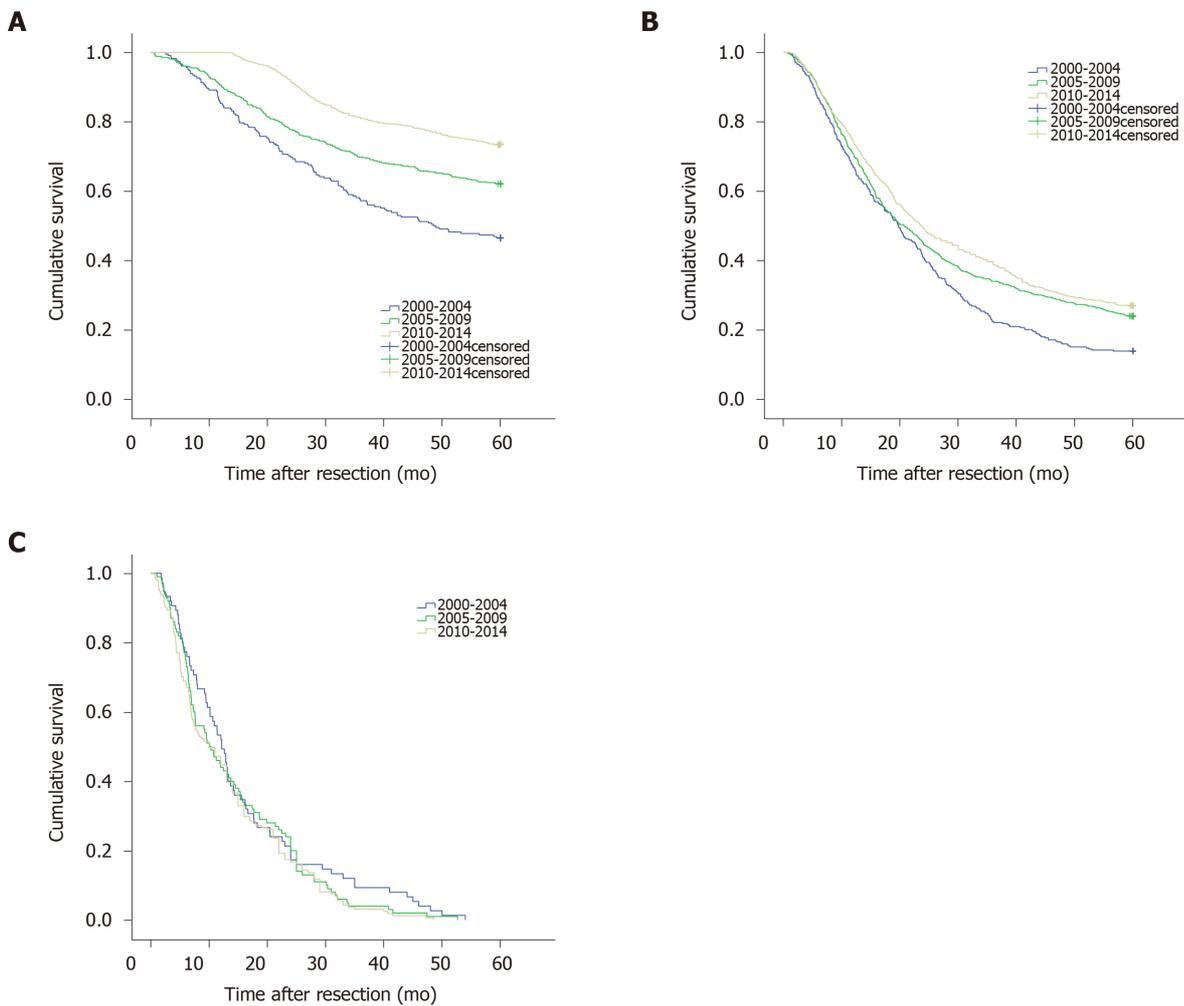

Figure 3 The five-year survival for the three periods, stratified by pathological tumor-node-metastasis stage. A total of 4744 patients undergoing gastric cancer resection were analyzed. A: Stage I-II (*P* = 0.000); B: Stage III (*P* = 0.000); C: Stage IV (*P* = 0.210).

ARTICLE HIGHLIGHTS

Research background

Currently, the morbidity and mortality of gastric cancer (GC) have decreased sharply; however, it is still an important global public health burden. The survival rate of patients with GC in China is higher than those in the United States and some European countries but far lower than those in Japan and South Korea. The morbidity of GC is different geographically even within a country. There are significant geographical distribution clusters of GC in China, and high morbidity is mainly seen in the northern part of China. Because of geographical conditions, dietary habits, economic development, *etc.*, high morbidity and mortality of GC have been seen in Northeast China. Thus, it is necessary to conduct systematic research on the clinical characteristics and survival rate of GC in this densely populated area of China.

Research motivation

A high-capacity data center that collected data from more than 1000 GC surgeries in Northeast China was used in this study. Through analyzing the data from the data center in the past 15 years from 2000 to 2014, this study revealed changes in postoperative clinical characteristics and survival. The results of this study will help people better understand the characteristics and development trends of GC. It may also provide a reference for the diagnosis and prevention of regional GC.

Research objectives

This study performed a comparative analysis of the clinicopathological characteristics and postoperative survival of patients with GC from the Harbin Medical University Cancer Hospital over 15 years starting in 2000. The factors affecting the prognosis of GC are identified based on the time trend.

Research methods

Student's *t* test was used to evaluate the significant differences among the mean values. Categorized variables were evaluated by the Pearson χ^2 test. The cumulative survival rate was calculated by the Kaplan-Meier method, and the difference among different groups was evaluated by the long-rank test. A Cox regression model was used for multivariate prognostic analysis.

Research results

At the last follow-up visit, a total of 1845 patients survived, and 2899 patients had died. The average 5-year survival rate was 38.9%. Over time, the 5-year survival rate improved significantly in the three periods: Phase I: 24%, Phase II: 36.6%, and Phase III: 43.8%. According to the subgroup analysis by tumor-node-metastasis staging, the 5-year survival rate of patients with stages I + II and III disease was significantly improved compared with the earlier stage. In contrast, the 5-year survival rate of patients with stage IV disease did not change significantly.

Research conclusions

Overall, based on our 15 years of experience in treating patients with GC, we have observed that by attaching great importance to the perioperative period, including the improvement in surgical techniques and other techniques, a significant improvement in patient survival was noted.

Research perspectives

When patients with GC are diagnosed with a local disease, their prognosis is still not optimistic. Obviously, surgery alone is not enough to achieve the ideal value for survival. We urgently need to develop a multimodal, multidisciplinary, and individualized comprehensive treatment system to achieve better results.

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