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BRIEF ARTICLE

Survival trends in gastric cancer patients of Northeast China

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Abstract

AIM: To describe survival trends in patients in Northeast China diagnosed as gastric cancer.

METHODS: A review of all inpatient and outpatient records of gastric cancer patients was conducted in the First Affiliated Hospital of China Medical University. All the gastric cancer patients who satisfied the inclusion criteria from January 1, 1980 through December 31, 2003 were included in the study. The main outcomes were based on median survival and 3-year and 5-year survival rates, by decade of diagnosis.

RESULTS: From 1980 through 2003, the median survival for patients with gastric cancer (n = 1604) increased from 33 mo to 49 mo. The decade of diagnosis was not significantly associated with patient survival for gastric cancer (P = 0.084 for overall survival, and P = 0.150 for 5-year survival); however, the survival rate of the 2000s was remarkably higher than that of the 1980s (P = 0.019 for overall survival, and P = 0.027 for 5-year survival).

CONCLUSION: There was no significant difference of survival among each period; however, the survival rate of the 2000s was remarkably higher than that of the 1980s.

Key words: Survival trends; Gastric cancer; Northeast China

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INTRODUCTION

Although the prognosis of gastric cancer have improved due to early diagnosis, radical operation, and the development of adjuvant therapy, patients with gastric cancer still have a poor prognosis[1,2]. Since the 1980s, there have been substantial changes in the incidence of gastric cancer[3,4] and the causes for this change remain highly debated. Possible causes include the obesity epidemic, decreasing *Helicobacter pylori* (*H. pylori*) prevalence, and dietary changes[5,6].

Currently, various surgical approaches are being practiced, including conventional surgery, function preserving surgery, minimally invasive surgery and less extensive lymph node dissection. Previously, surgical interventions had been associated with significant perioperative risk; recently, however, this risk appears to be decreasing[7,8]. The role of chemotherapy, both preoperatively and postoperatively, has been extensively studied[9-11]. Despite these changes in treatment, it is unclear whether the survival of patients with gastric cancer has significantly improved since the 1980s.

The purpose of the current study was to use a sample population over a 24-year period to describe changes in the survival of gastric cancer patients. We compared patient survival in the 1980s with the 1990s and the 2000s, since patient survival might have improved as a result of advances in the quality of surgical techniques and other medical management.

MATERIALS AND METHODS

Patients

We enrolled 1604 histologically confirmed gastric cancer patients who underwent an operation at the First Affiliated Hospital of the China Medical University between 1980 and 2003. Of these patients, 496 were allocated to 1980s, 673 to 1990s and 435 to 2000s. The inclusion criteria were as follows: (1) gastric cancer was histologically confirmed; (2) an operation was performed; and (3) a complete medical record was available.

Follow-up for all patients was conducted by mailing letters or telephone interviews. The follow-up was completed in December 2008, with a total follow-up rate of 89%. Clinical findings, surgical findings, pathological findings and every follow-up were collected and recorded in the database. The study protocol was approved by the Ethics Committee of China Medical University.

Statistical analysis

Kaplan-Meier survival curves were used to estimate patient survival. Cox proportional hazards regression models were used to assess associations of risk factors with survival. For univariate analyses, we put the prognostic factor of interest and the diagnosis period as covariates in the Cox regression model. In multivariate analyses, the prognostic factor detected in univariate analysis and the diagnosis period were the covariates included in the Cox regression model.

Two-sided *P* values were calculated for all tests and are reported here. *P* values less than 0.05 were considered statistically significant. Analyses were performed using SPSS software, version 16.0.

RESULTS

In total, 1604 patients diagnosed with gastric cancer were enrolled in the 24-year study period. The median survival for gastric cancer patients increased during the 2 decades studied from 33 mo in the 1980s, and 39 mo in the 1990s to 49 mo in the 2000s. The 3-year survival for patients in the 1980s, 1990s, and 2000s was 47.6% (95% CI: 43.3%-51.9%), 51.4% (95% CI: 47.7%-55.1%), and 55% (95% CI: 49.5%-60.5%), respectively. Five-year survival estimates were 39.1% (95% CI: 34.8%-43.4%), 39.8% (95% CI: 36.1%-43.5%), and 45% (95% CI: 37.9%-52.1%) in the 1980s, 1990s, and 2000s, respectively. There was no significant difference in survival among the three periods (P = 0.084 for overall survival, and P = 0.150 for 5-year survival); however, the survival rate in the 2000s was remarkably higher than that of the 1980s

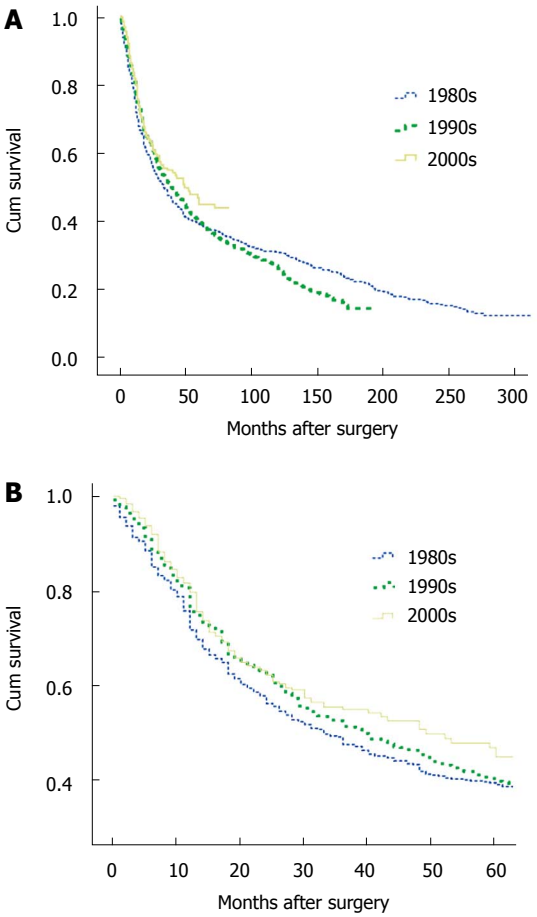

Figure 1 Kaplan-Meier survival curves for patients with gastric cancer by decade. A: Overall survival for gastric cancer patients; B: Five-year survival for gastric cancer patients.

(P = 0.019 for overall survival, and P = 0.027 for 5-year survival). Kaplan-Meier survival curves for patients with gastric cancer, by decade, are shown in Figure 1.

For those patients who had undergone resection with curative intent, the median survival of patients was 85 mo in the 1980s, 58 mo in the 1990s, and 72 mo in the 2000s, respectively The 3-year survival for patients in the 1980s, 1990s, and 2000s were 65.3% (95% CI: 60.0%-70.6%), 60.8% (95% CI: 56.5%-65.1%), and 61.0% (95% CI: 55.3%-66.7%), respectively. Five-year survival estimates were 55.6% (95% CI: 50.1%-61.1%), 48.9% (95% CI: 44.6%-53.2%), and 50.4% (95% CI: 42.8%-58.0%) in the 1980s, 1990s, and 2000s, respectively. There was no significant difference in survival among the three time periods (P = 0.169 for 5-year survival).

The distributions of patient characteristics by decade are shown in Table 1. Significant changes were detected in all areas except in the distribution of number of involved lymph nodes, hepatic metastasis and type of gastrectomy during the 24 years studied (P = 0.072, 0.244 and 0.073, respectively). The median age was 56 in the 1st period, 60 in the 2nd period, and 58 in the 3rd period. There was also a change in male to female ratio from 4:1 to 7:3. Among tumor factors, whole stomach tumors decreased from 12% to 5%, while T1 stage tumor and node negative

Table 1 Characteristics of population from the three periods (*n* = 1604)

Characteristics	1980s (*n* = 496)	1990s (*n* = 673)	2000s (*n* = 435)	*P* value
Age (yr)				0.000
Median	56	60	58	
Sex (%)				0.000
Male	397 (80)	469 (70)	306 (70)	
Female	99 (20)	204 (30)	129 (30)	
Number of lymph nodes removed				0.000
Mean	12	12	18	
Number of involved lymph nodes				0.072
Mean	2	2	3	
Tumor size (cm)				0.000
Median	6	5	5	
Site of tumor (%)				0.000
Whole stomach	60 (12)	49 (7)	23 (5)	
Upper stomach	55 (11)	80 (12)	44 (10)	
Middle stomach	39 (8)	69 (10)	49 (11)	
Lower stomach	213 (43)	298 (44)	254 (58)	
> 2/3 stomach	129 (26)	177 (26)	65 (15)	
Pathological tumor stage (%)				0.003
T1	99 (20)	148 (22)	104 (24)	
T2	179 (36)	215 (32)	121 (28)	
T3	154 (31)	242 (36)	178 (41)	
T4	64 (13)	68 (10)	32 (7)	
Pathological nodal stage (%)				0.006
N0	159 (32)	195 (29)	152 (35)	
N1	193 (39)	269 (40)	161 (37)	
N2	84 (17)	155 (23)	94 (22)	
N3	60 (12)	54 (8)	28 (6)	
TNM stage (%)				0.000
Ⅰ A	47 (10)	58 (9)	36 (8)	
Ⅰ B	62 (13)	102 (15)	98 (23)	
Ⅱ	81 (16)	168 (25)	100 (23)	
Ⅲ A	108 (22)	149 (22)	86 (20)	
Ⅲ B	73 (15)	71 (11)	42 (10)	
Ⅳ	125 (25)	125 (19)	73 (17)	
Gross type (%)				0.000
Borrmann Ⅰ	15 (3)	5 (1)	2 (1)	
Borrmann Ⅱ	158 (35)	97 (16)	44 (11)	
Borrmann Ⅲ	227 (50)	439 (71)	311 (77)	
Borrmann Ⅳ	50 (11)	79 (13)	47 (12)	
Surgery (%)				0.000
Absolutely curative	277 (56)	357 (53)	172 (40)	
Relatively curative	47 (10)	163 (24)	225 (52)	
Palliative	172 (35)	153 (23)	38 (9)	
Lymph node dissection (%)				0.000
D1	51 (10)	52 (8)	46 (11)	
D2	188 (38)	399 (59)	347 (80)	
D3	90 (18)	73 (11)	16 (4)	
Palliative resection	167 (34)	149 (22)	26 (6)	
Complication (%)				0.001
Intestinal obstruction	16 (3)	7 (1)	11 (3)	
Anastomotic leakage	10 (2)	12 (2)	0 (0)	
Pneumonia	3 (1)	3 (0)	1 (0)	
Abdominal abscess	8 (2)	11 (2)	7 (2)	
Anemia	3 (1)	1 (0)	4 (1)	
Other	7 (1)	12 (2)	22 (5)	
Hepatic metastasis (%)	21 (4)	21 (3)	10 (2)	0.244
Peritoneum metastasis (%)	67 (14)	50 (7)	25 (6)	0.000
Adjunctive therapy (%)	0 (0)	41 (6)	153 (35)	0.000
Type of gastrectomy (%)				0.073
Total	94 (19)	95 (14)	76 (17)	
Subtotal	402 (81)	578 (86)	359 (83)	
Combined organ resection				0.000
Pancreas or spleen	53 (11)	56 (8)	18 (4)	
Liver or gall	11 (2)	12 (2)	19 (4)	
Transverse colon	20 (4)	51 (8)	52 (12)	
Other	15 (3)	20 (3)	12 (3)	

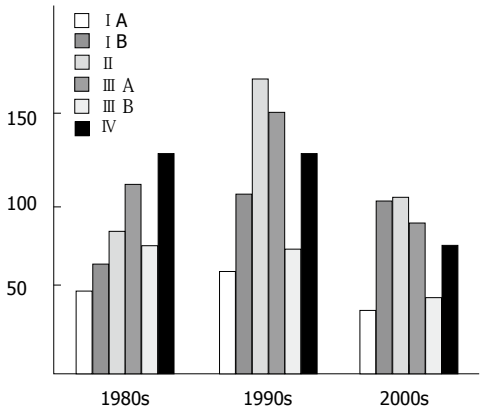

Figure 2 The shift in the distribution of TNM stage of disease at diagnosis.

cancers were found more frequently in the later periods, though this may not be significant, as early gastric cancers increased only from 20% to 24%. Curative resection rates were markedly increased during the 24-year period. Most recently, the curative resection rate was 92% (Table 1). Most cases were diagnosed at advanced stages (T2-T4, N1-N3) throughout the 2-decade period. Figure 2 shows the shift in the distribution of TNM stage of disease at diagnosis.

The operative mortality rate in the 1st period was 2% and 1.3% in the 2nd period, whereas it was less than 1% in the 3rd period. The multivariate Cox proportional hazards models for gastric cancer are shown in Table 2. In the Cox model for gastric cancer, adjusting for sixteen variables, there was no significant association between the decade of diagnosis and patient survival ($P = 0.385$). For the decade of the 1990s relative to the 1980s, the hazard ratio for gastric cancer cases was 1.025 (95% CI: 0.807-1.301), and for the decade of the 2000s relative to the 1980s, the hazard ratio was 0.914 (95% CI: 0.674-1.241). Patient survival was significantly associated with surgical extent ($P = 0.000$). Cases involving curative surgery were associated with prolonged survival. Figure 3 illustrate the Kaplan-Meier survival curves of patients with gastric cancer, by surgical intervention (absolutely curative, relatively curative, and palliative). Stage-by-stage comparison was performed among the 3 periods; for the Ⅱ stage patients the survival rate of 1990s was significantly worse than that of the 1980s.

DISCUSSION

In this study of gastric cancer diagnosed in Northeast China, we found that the median survival of patients with gastric cancer actually appeared to increase between 1980 and 2000. There was a significant change in patient survival in the 2000s compared to that in the 1980s, and decade of diagnosis was not significantly associated with

Table 2 HR for death in population (n = 1604) - univariable and multivariable analyses

	Univariable analyses		Multivariable analyses	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age (yr)		0		0.005
≤ 55	1 (Ref)		1 (Ref)	
> 55	1.383 (1.222-1.565)	0	1.240 (1.036-1.484)	0.019
Sex		0.734		0.582
Male	1 (Ref)		1 (Ref)	
Female	0.977 (0.855-1.117)	0.734	1.030 (0.854-1.241)	0.760
Tumor size		0		0.024
≤ 5 cm	1 (Ref)		1 (Ref)	
5-7 cm	1.782 (1.534-2.071)	0	1.250 (1.006-1.553)	0.044
> 7 cm	2.587 (2.244-2.982)	0	1.211 (0.956-1.533)	0.113
Tumor site		0		0.071
Whole stomach	1 (Ref)		1 (Ref)	
Upper stomach	0.625 (0.489-0.798)	0	1.247 (0.825-1.886)	0.295
Middle stomach	0.358 (0.273-0.471)	0	0.844 (0.541-1.315)	0.453
Lower stomach	0.401 (0.327-0.490)	0	0.846 (0.574-1.247)	0.399
> 2/3 stomach	0.588 (0.475-0.727)	0	0.845 (0.590-1.210)	0.358
Gross appearance		0		0.002
Borrmann types Ⅰ	1 (Ref)		1 (Ref)	
Borrmann types Ⅱ	0.541 (0.338-0.867)	0.011	0.405 (0.179-0.915)	0.030
Borrmann types Ⅲ	0.807 (0.510-1.278)	0.361	0.626 (0.284-1.381)	0.246
Borrmann types Ⅳ	1.357 (0.841-2.191)	0.211	1.328 (0.317-1.672)	0.454
Tumor stage		0		0.408
T1	1 (Ref)		1 (Ref)	
T2	3.336 (2.542-4.377)	0	1.458 (0.797-2.667)	0.221
T3	4.275 (3.218-5.678)	0	1.780 (0.510-2.287)	0.841
T4	7.873 (5.689-10.894)	0	1.991 (0.459-2.590)	0.844
Lymph-node stage		0		0.874
N0	1 (Ref)		1 (Ref)	
N1	2.980 (2.411-3.682)	0	1.176 (0.913-2.073)	0.127
N2	3.430 (2.754-4.271)	0	1.443 (0.595-1.826)	0.883
N3	5.174 (3.934-6.804)	0	1.756 (0.324-2.766)	0.518
TNM stage		0		0.019
ⅠA	1 (Ref)		1 (Ref)	
ⅠB	1.920 (1.381-2.671)	0	0.642 (0.288-1.431)	0.279
Ⅱ	2.645 (1.938-3.608)	0	0.779 (0.293-2.068)	0.616
ⅢA	4.306 (3.171-5.847)	0	1.303 (0.429-3.961)	0.641
ⅢB	4.847 (3.510-6.693)	0	1.459 (0.409-5.204)	0.561
Ⅳ	8.982 (6.613-12.199)	0	3.286 (0.779-13.857)	0.105
Surgery		0		0
Absolutely curative	1 (Ref)		1 (Ref)	
Relatively curative	1.907 (1.631-2.230)	0	1.372 (1.114-1.690)	0.003
Palliative	4.368 (3.782-5.044)	0	3.361 (1.752-6.448)	0
Lymph node dissection		0		0.867
D1	1 (Ref)		1 (Ref)	
D2	0.931 (0.750-1.155)	0.515	1.169 (0.821-1.664)	0.387
D3	0.807 (0.616-1.058)	0.121	1.146 (0.738-1.780)	0.543
Palliative resection	3.236 (2.573-4.070)	0	1.359 (0.457-1.612)	0.636
Joint organ removal		0		0.007
None	1 (Ref)		1 (Ref)	
Pancreas or spleen	1.997 (1.640-2.433)	0	1.086 (0.709-1.372)	0.933
Liver or gall	1.514 (1.029-2.227)	0.035	1.108 (0.649-1.891)	0.707
Transverse colon	2.093 (1.699-2.579)	0	1.466 (1.107-1.942)	0.008
Other	2.453 (1.797-3.350)	0	1.008 (0.586-1.731)	0.978
Gastrectomy		0		0.512
Total	1 (Ref)		1 (Ref)	
Subtotal	0.573 (0.494-0.664)	0	0.912 (0.693-1.200)	0.511
Hepatic metastasis		0		0.796
No	1 (Ref)		1 (Ref)	
Yes	4.002 (2.991-5.354)	0	1.285 (0.403-1.529)	0.476
Peritoneum metastasis		0		0.947
No	1 (Ref)		1 (Ref)	
Yes	2.835 (2.359-3.406)	0	1.127 (0.382-1.381)	0.329
Complication		0.41		0.157
None	1 (Ref)		1 (Ref)	
Intestinal obstruction	0.796 (0.522-1.216)	0.292	1.311 (0.670-2.565)	0.428
Anastomotic leakage	1.474 (0.946-2.294)	0.086	1.893 (0.904-3.965)	0.091
Pneumonia	1.069 (0.400-2.856)	0.894	1.207 (0.323-4.525)	0.929
Abdominal abscess	1.212 (0.795-1.850)	0.372	1.295 (0.700-2.397)	0.410
Anaemia	0.487 (0.157-1.514)	0.214	0.479 (0.116-1.980)	0.309
Other	0.702 (0.421-1.172)	0.176	0.488 (0.240-0.992)	0.047
Adjunctive therapy		0.022		0.364
No	1 (Ref)		1 (Ref)	
Yes	0.744 (0.577-0.959)	0.022	0.850 (0.643-1.124)	0.254
Diagnosis period		0.395		0.385
1980s	1 (Ref)		1 (Ref)	
1990s	1.072 (0.937-1.226)	0.311	1.025 (0.807-1.301)	0.840
2000s	0.884 (0.735-1.063)	0.191	0.914 (0.674-1.241)	0.565

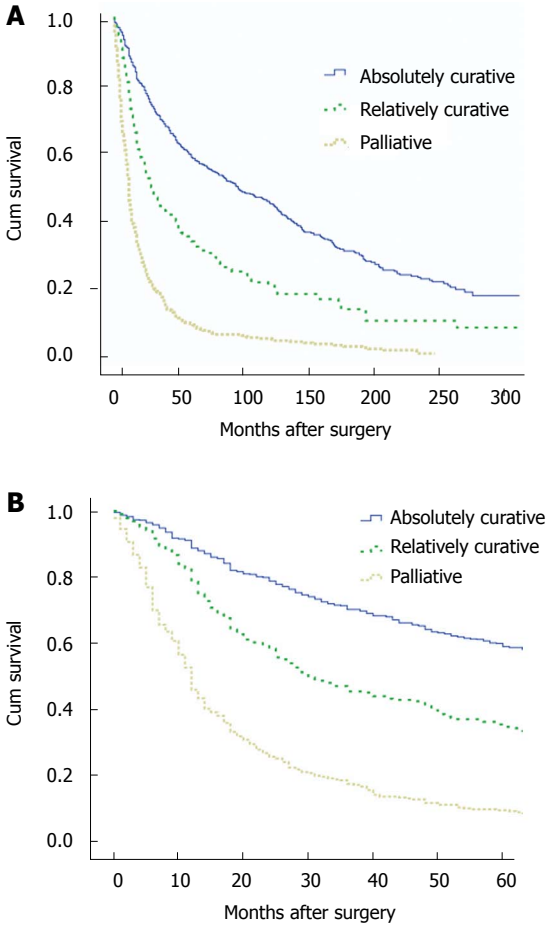

Figure 3 Kaplan-Meier survival curves of patients with gastric cancer, by surgical intervention (absolutely curative, relatively curative, palliative). A: Overall survival for gastric cancer patients; B: Five-year survival for gastric cancer patients.

patient survival for gastric cancer during the 24 years. The improving prognosis of gastric cancer in recent years has been reported[12-18]. For example, the 5-year relative survival rate for gastric cancer increased from 13% to 18% in Sweden from 1960-1964 to 1985-1986[13]. However, for those patients who had a curative intent resection, there was no significant difference in survival between 1980 and 2000. As the patients operated on for palliative purpose decreased with percentages over time, it is possible that the inclusion of these patients could explain

some of the trend of increasing survival between 1980 and 2000.

In this study, we found that the proportion of patients with early gastric cancer increased to 24% in the 3rd period. With the increasing incidence of early gastric cancer, node negative cancers were also increased; however, as the increasing proportions were too little and may not be significant, there were still too many patients diagnosed at an advanced stage. We also found that the incidence among women increased in the later period from 20% to 30%. We speculate that this may be due to the changes in lifestyle of Chinese women, such as more smoking and greater alcohol intake, suggesting that we should strengthen the primary prevention of gastric cancer. Currently, a surgical cure remains the only intervention that may significantly improve a patient's chance of survival; moreover, surgery is the only treatment modality offering hope for a cure. Nevertheless, most patients die from locoregional recurrence or distant metastasis even after curative surgery for advanced stage cancers[19]. As metastasis to lymph nodes is linked to the outcome, extensive lymph node dissection is a statistically favorable prognostic factor[20]. Without surgical intervention, 2-year survival for patients with gastric cancer remained essentially zero[21]. Baba *et al*[22] reported that the rate of recurrence was higher in patients treated with dissection of group 1 lymph nodes than for those with dissection of group 2 or 3 nodes. In our study, 84% of the patients were treated with D2 or D3 lymph node dissection in the later period, which was much more than in the previous two periods. Besides the increase of early gastric cancer patients, advances in treatment factors mostly contributed to the improved survival.

Early diagnosis has markedly improved the survival of patients with gastric cancer, and mass screening has a definite role in diagnosing gastric cancer in its early stages[23]. In Japan, where the incidence of gastric cancer is high, survival of patients with gastric cancer does seem to be improving. This improvement appears to be the result, at least in part, of the frequent diagnosis of early-stage gastric cancer in a mass population screening program in Japan[24]. The high curative resectability rate in the screened group is related to a smaller tumor size and to a lower incidence of lymph node metastasis, liver metastasis and peritoneal dissemination than in the non-screened group. Depth of tumor invasion, lymph node involvement and distant metastasis are important prognostic factors according to the UICC/AJCC staging system of gastric cancer[25]; therefore, every attempt should be made to increase early diagnosis. Currently, gastric cancer is one of the most prevalent cancers in China, making endoscopic or radiologic examinations more common. Awareness among Chinese has also increased, similar to colorectal or prostate cancer in Western countries[26,27]. However, because of the huge rural population whose diseases are often diagnosed at a more advanced stage, current efforts at cancer prevention and early screening of high-risk populations for premalignant lesions have not resulted in a significant change in the stage of presentation of disease. Following the mass population screening being carried out widely in China, especially these past ten years, the proportion of early gastric cancer has increased very slowly.

Another important change observed in this study was the decreased prevalence of operative mortality. Although the surgical extent of recent years was more extensive than before, postoperative mortality in the 3rd period was decreased to less than 1%. The large decrease in operative mortality is due to improved surgical techniques and also to improvements in anesthesia, metabolic care and intravenous nutrition[28]. Besides these factors, the accumulation of treatment experience with gastric cancer and becoming a large volume hospital also have an impact on the improved treatment outcome of gastric cancer patients[29-34]. The specialization in gastric cancer treatment might also influence the lower mortality rate, especially in addition to technical advances.

Therefore, currently in China, we need increased efforts at refining prevention and early diagnosis of gastric cancer as only resection offers the best hope for a cure[21]. We should put emphasis on rural gastric cancer screening, improve the rural level of diagnosis and treatment, and progress the health education of gastric cancer-related knowledge.

COMMENTS

Background

Although the results of gastric cancer have improved due to early diagnosis, radical operation, and the development of adjuvant therapy, patients with gastric cancer still have poor prognosis. To describe survival trends in patients in Northeast China diagnosed as gastric cancer, the authors conducted a review of records of gastric cancer patients from 1980 to 2003 in the First Affiliated Hospital of China Medical University.

Research frontiers

Currently, gastric cancer in China is one of the most prevalent cancers, making endoscopic or radiologic examinations more common. However, because of the huge rural population whose diseases are often diagnosed at a later stage, current efforts at cancer prevention and early screening of high-risk populations for premalignant lesions have not resulted in a significant change in the stage of presentation of disease, and following the mass population screening being carried out widely in China, especially these ten years, the proportion of early gastric cancer has increased very slowly.

Innovations and breakthroughs

In this article, the authors found that there was no significant difference of survival among the three periods. Besides that, they also found that the proportion of patients with early gastric cancer increased in the later period, as well as the proportion of node negative cancers, and the incidence among women increased from 20% to 30%.

Applications

All the findings indicate that, nowadays in China, the authors need increased efforts at refining primary prevention and early diagnosis of gastric cancer as only resection offers the best hope for cure, and they should put emphasis on rural gastric cancer screening, improve the rural level of diagnosis and treatment, and improve health education with regard to gastric cancer-related knowledge.

Peer review

Dr. Zhang *et al*. described survival trends of gastric cancer among Chinese between 1980 and 2003. Although there is no significant change in survival between these periods, the authors observed a significantly increased survival rate in 2000s as compared to that of 1980s. Results of this study were supported by many previous studies. Strengths of this study are (1) a large sample size; and (2) long follow-up data.

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