Factors That Affect Life Expectancy of Patients With Gastric Adenocarcinoma

WEI–YING CHEN,[*,‡] HSIU–CHI CHENG,[*,‡] JUNG–DER WANG,[§,‖,¶] and BOR–SHYANG SHEU[*,‡]

*Institute of Clinical Medicine, ‡Department of Internal Medicine, and §Department of Public Health, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan; and ‖Department of Internal Medicine and ¶Department of Environmental and Occupational Medicine, National Taiwan University Hospital, Taipei, Taiwan

BACKGROUND & AIMS: **We used a new, semi-parametric method to estimate life expectancy and expected years of life lost (EYLL) after diagnosis of gastric cancer and assess whether patients' sex or tumor type or location had any effects.**

METHODS: **We performed a nationwide retrospective cohort study of 35,576 patients with gastric cancer who were registered in the Taiwan Cancer Registry from 1998 through 2007; data were collected until the end of 2010. The Monte Carlo method and tables in Taiwan National Vital Statistics database were matched to the cohort reference populations on the basis of age and sex. The estimated regression line and the survival curve of reference populations were used to extrapolate the survival curve beyond 2010. We compared patients' age at diagnosis, life expectancy, and EYLL based on sex, tumor type, and location.**

RESULTS: **In Taiwan, gastric cancer is more prevalent among men, and 88.6% of tumors are adenocarcinomas. Patients with adenocarcinoma of the gastric cardia have shorter life expectancies and greater EYLL than those with noncardia tumors ($P < .05$). Women with gastric adenocarcinoma are diagnosed at a younger age and have longer life expectancies but more EYLL than men with such tumors ($P < .05$). The estimated years of life saved if gastric adenocarcinoma is diagnosed at an early stage and cured are 22,827 years (2.62 years/case) for women and 33,700 years (1.97 years/case) for men.**

CONCLUSION: **Among patients with gastric cancer, men and patients with adenocarcinomas of the cardia have shorter life expectancies and more EYLL. Early detection of gastric adenocarcinoma can increase life expectancy.**

Keywords: Population-based Study; Stomach Cancer; Asia; Database Analysis; Risk Factor.

Gastric cancer is a significant cause of mortality and morbidity throughout the world[1] and is still 1 of the 10 leading causes of cancer-related deaths in Taiwan. The prognosis of gastric cancer is usually not very good and may vary with different pathologic types, locations, staging, ages, and sexes.[2–4] In general, the outcome of gastric cancer can be reported as generally having a 5-year survival rate. It is of great interest for gastroenterologists to explore the long-term outcomes as more than 10 years from large-scale data by a nationwide approach.

On the basis of the advance of the availability of upper gastrointestinal endoscopy worldwide, the early detection of gastric cancer can be achieved. Once gastric cancer is detected earlier, the 5-year survival rate can be dramatically improved up to 90%.[5] Although there have been a number of studies showing different detection rates for early gastric cancer,[6] there are relatively few data available to address the detection rate to estimate the exact potential life-years saved by early gastric detection in nationwide long-term assessments.

The National Health Insurance was established in Taiwan in 1995 to cover more than 96% of Taiwanese residents with full reimbursement. On the basis of all of the reimbursement data for the National Health Insurance transformed and maintained by the National Health Research Institutes, we determined life lost caused by gastric cancer in Taiwan. This study applied a semi-parametric method by Hwang et al[7] on the reimbursement database of the National Health Insurance to estimate the life expectancy (LE) and expected years of life lost (EYLL) in gastric cancer patients with different pathologic types. We first strived to assess whether different pathologic types, sex, and tumor location determined such LE and EYLL. Moreover, the study illustrated the health impact of early detection on gastric cancer in Taiwan by integrating the age-specific and sex-specific incidence rates with a 13-year long-term nationwide-scale basis.

Abbreviations used in this paper: EYLL, expected years of life lost; ELYS, total life-years that would be saved if diagnosed early and cured; LE, life expectancy.

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2013.05.036

Materials and Methods

Gastric Cancer Cohort and the Reference Population

From 1998–2007, 35,576 gastric cancer patients with the related pathologic diagnosis were registered in the database of the Taiwan National Cancer Registry. The sex, tumor locations over cardia or noncardia of stomach, age at diagnosis, and different pathologic types of gastric cancer were obtained from the database at Taiwan National Cancer Registry. Moreover, these enrolled cases were followed up until the end of 2011 as a cohort. Because all pathologically validated gastric cancer can be registered as a catastrophic illness and this is waived from all copayment, the data are considered to be quite comprehensive. Patients with double cancers or those that metastasized from an other organ system to stomach were excluded. All data were first linked with the National Mortality Registry to determine whether a patient was still alive by the end of 2010.

Age-Specific and Sex-Specific Incidence Rates and Lifetime Risks of Gastric Cancer

From the catastrophic illness database, age-specific and sex-specific incidence rates were calculated with numbers of new cases diagnosed divided by the sum of populations at risk in the following 3 calendar periods: 1998–2002, 2003–2007, and 2008–2010. In addition, the lifetime risk was estimated on the basis of the cumulative incidence rate (20–79 years of age).

Estimation of Long-term Survival for Gastric Cancer: Extrapolation Beyond Follow-up Limit

The survival functions of different subtypes of gastric cancer were estimated the by Kaplan–Meier method up to either the limit of follow-up or December 31, 2010. We have developed a method to extrapolate the long-term or lifetime survival curve beyond the follow-up period by assuming a constant excess hazard.[7,8]

The extrapolation process was summarized as being composed of the following 3 phases. First, we created a reference population of subjects who were matched with gastric cancer cohort in age and sex from the life tables of the Taiwan National Vital Statistics according to the Monte Carlo method. Second, a simple linear regression was fitted to the logit transform of the survival ratio between the gastric cancer cohort and the reference population until the end period of follow-up. Finally, the estimated regression line and the survival curve of the reference population were used to extrapolate the long-term survival curve beyond the follow-up limit. The bootstrap method of using 100 repeated samples was performed to obtain the standard error of means. To facilitate the extrapolation process, we developed a software program, iSQoL, which can be freely downloaded from the Web site http://www.stat.sinica.edu.tw/jshwang.

Validation of the Extrapolation

The data of Taiwan National Cancer Registry were applied to validate the actual performance of the extrapolation method. Patients of the gastric cancer cohort registered between 1998 and 2003 were enrolled. We used the first 6-year database (1998–2003) to extrapolate up to the next 7 years (2004–2010) by the Monte Carlo method. The Kaplan–Meier estimates were determined for this subcohort in a 13-year period. The relative bias was analyzed between the semi-parametric extrapolation and the Kaplan–Meier estimates.

Estimation of Expected Years of Life Lost

The average EYLL for the gastric cancer cohort was defined as the mean survival difference between the specific pathologic cell type of the gastric cancer cohort and the age-matched and sex-matched reference population. Moreover, the average EYLL was the difference in the area between the mean survival curve of the gastric cancer cohort and the reference population. This parameter provided us with a measure of the burden of gastric cancers on the individual patient and the loss of the patient's life span after stratification by age and sex. The differences of LE and EYLL were compared between female and male patients, between cardiac and noncardiac sites, and also among the different pathologic types.

Estimation of the Expected Life Loss Possibly Saved by Early Detection of Gastric Adenocarcinoma

Because 90% of the patients with early detected gastric adenocarcinoma could survive more than 5 years,[9,10] they were assumed to be cured and would survive as long as the general population. Because current practice in Taiwan was able to detect 19.4% of gastric cancer[11] and 90% of them would be cured, we conservatively assumed that 18% (19.4% $\times$ 0.9) of the 31,524 patients with adenocarcinoma could be detected early and possibly cured. Then we estimated the total life-years that would be saved if diagnosed early and cured (ELYS) for different sexes and pathologic subtypes and then divided by the 82% of case numbers (who shall be advanced in stage) to achieve the ELYS per case for each subgroup.

Results

Incidence Rate and the Cumulative Incidence $Rate_{20–79}$ of Gastric Cancer

On the basis of registry of catastrophic illnesses, age-specific and sex-specific incidence rates and lifetime risks for gastric cancer in Taiwan, stratified by 3 calendar year periods, are shown in Table 1. The incidences of gastric cancers increase with age in both sexes among the 3 observation periods. The incidence of gastric cancers was higher in male than in female patients. There appears to be a decreasing trend of cumulative incidence $rate_{20–79}$ throughout the 3 observation periods during 1998–2002, 2003–2007, and 2008–2010, respectively (female: 1.42%, 1.22%, and 1.13%; male: 2.60%, 2.37%, and 2.08%).

Sex, Tumor Locations, and Age at Diagnosis of Gastric Cancer Related to the Life Expectancy and Expected Years of Life Lost

From 1998–2007, there were 12,403 women and 23,173 men diagnosed as having gastric cancer with pathologic proof in the database of the Taiwan National Cancer Registry. In Table 2, the mean age of women was significantly younger than that of men at diagnosis of gastric cancer (64.1 vs 67.6 years, $P < .05$). The mean LE after gastric cancer diagnosis was higher in women than in men (9.0 vs 6.4 years, $P < .05$), but the EYLL remained

Table 1. Incidence Rate (per 100,000 Person-years), Cumulative Incidence Rate$_{20-79}$ (CIR$_{20-79}$) of Stomach Cancer Stratified by Age, Sex, and Calendar Years Based on Registry of Catastrophic Illnesses

Calendar years, age (*y*)	IR (1998–2002)		IR (2003–2007)		IR (2008–2010)	
	Female	Male	Female	Male	Female	Male
0–9	0.00	0.02	0.00	0.06	0.03	0.03
10–19	0.04	0.07	0.03	0.06	0.04	0.0
20–29	0.92	0.56	0.52	0.46	0.46	0.39
30–39	3.82	3.45	3.33	2.59	2.94	2.21
40–49	9.35	10.57	8.66	9.56	8.45	8.94
50–59	18.08	27.72	15.52	23.40	15.60	24.45
60–69	37.48	77.66	31.38	61.93	28.36	51.85
70–79	73.64	143.38	62.96	141.46	57.49	121.88
80+	99.07	201.91	100.45	185.29	108.32	189.07
CIR$_{20-79}$ (%)	1.42	2.60	1.22	2.37	1.13	2.08
Total no. of cancer	N = 16,506		N = 17,038		N = 10,789	

IR, incident rate.

higher in women than in men (11.5 vs 9.2 years, $P < .05$). Patients with cardiac gastric cancer have a shorter LE than those in noncardiac locations for both sexes (female: 6.2 vs 9.2 years, $P < .05$; male: 4.3 vs 6.7 years, $P < .05$). However, in Table 2, for both men and women, EYLL was not different between cardia and noncardia gastric cancers ($P > .05$). For patients with gastric cancer pathologically proven as adenocarcinoma, the younger the age of diagnosis as gastric cancer should have a longer LE and a larger EYLL for both sexes (Table 2). Within each age interval defined from 30–39, 40–49, 50–59, 60–69, and 70–79 years for the diagnosis as gastric cancer, the women uniformly had longer LE and larger EYLL than men ($P < .05$).

Life Expectancy and Expected Years of Life Lost Among the Different Gastric Cancer Types

Among the 12,403 women and 23,173 men diagnosed as having gastric cancer with pathologic proof in this study, nearly 88.6% of them had adenocarcinoma. In Table 3, the case number of men was usually nearly 2-fold more than that of women with adenocarcinoma with most pathologic types except for the diffuse type and signet ring cell type. There were similar case numbers between men and women with gastric lymphoma and mesenchymal tumor. The mean age at diagnosis was older in men than in women among the different histologic types of gastric cancer ($P < .05$) except for mesenchymal tumors (62.5 vs 62.3 years, $P > .05$). The mean age at diagnosis of gastric adenocarcinoma was older than that of gastric lymphoma. Within the cases defined as adenocarcinoma of the same sex, the mean age at diagnosis was younger in diffuse type and signet ring cell types than others ($P < .05$). In Table 3, patients with gastric adenocarcinoma in both sexes have not only older mean diagnostic age but also a shorter LE and a greater EYLL than those with gastric lymphoma and mesenchymal tumor ($P < .05$). Irrespective of the pathologic type of gastric cancer, women had a longer LE but a greater EYLL than men ($P < .05$). Gastrointestinal stromal sarcoma, mucosa-associated lymphoid tissue lymphoma, and other gastric cancers showed irregularities on the logit transform values to assume the violation of constant hazard and thus without extrapolation. Also in Table 3, the ELYS for gastric adenocarcinoma in this study series were as high as 22,827 for women (2.62 years per case) and 33,700 (1.97 years per case) for men, respectively. The ELYS per case was higher in women than in men for diffuse type (3.37 vs 2.72 years), signet ring cell type (3.31 vs 2.63 years), tubular adenocarcinoma (1.63 vs 1.38 years), and mucinous

Table 2. Demographic Characteristics, LEs, and EYLL of Patients With Stomach Cancer and Adenocarcinoma Only, Stratified by Sex, Age, and Location

Stomach cancer		No. of cases	Mean age at diagnosis (*y*)	Mean LE (*y*)	EYLL (*y*)
Total cases	F:M	12,403:23,173	64.1:67.6[a]	9.0:6.4[a]	11.5:9.2[a]
Location					
Cardia	F:M	755:2862	66.7:69.8[a]	6.2:4.3[a]	12.2:9.9[a]
Noncardia	F:M	11,648:20,311	63.9:67.3[a]	9.2:6.7[a]	11.5:9.0[a]
Adenocarcinoma only					
30–39 y	F:M	581:528	35.5:35.5	17.1:14.3[a]	29.2:26.2[a]
40–49 y	F:M	1422:1669	44.9:45.3	12.7:12.1[a]	24.3:19.9[a]
50–59 y	F:M	1612:2631	54.5:54.7	11.4:9.8[a]	16.6:14.4[a]
60–69 y	F:M	2165:4595	64.8:65.1	8.0:6.7[a]	11.1:9.6[a]
70–79 y	F:M	2824:7573	74.4:74.5	4.6:4.0[a]	7.4:6.6[a]
80+ y	F:M	1812:3653	84.3:83.8	NA	NA
Location					
Cardia	F:M	640:2527	67.0:70.5[a]	5.4:3.9[a]	12.8:9.8[a]
Noncardia	F:M	9899:18,218	64.2:67.6[a]	8.3:6.4[a]	12.2:9.2[a]

F, female; M, male; NA, not available because mean survival age is less than 80 years in Taiwan for both sexes.
[a]Significant difference between both sexes.

Table 3. Demographic Characteristics, LE, EYLL, and ELYS for the Different Pathologic Types of Gastric Cancers

Pathologic type		Number	Mean age at diagnosis (*y*)	Mean LE (*y*)	EYLL (*y*)	ELYS (year-case)
Adenocarcinoma	F:M	10,623:20,901	64.4:68.0[a,b]	8.0:6.0[a]	12.3:9.3[a,b,c]	22,827:33,700
Adenocarcinoma, NOS	F:M	7619:16,393	66.1:68.7[a,d,e]	7.1:5.7[a]	11.9:9.2[a,d,e]	15,830:23,625
Diffuse type	F:M	294:322	57.4:61.8[a,d]	9.2:6.8[a]	16.8:12.8[a,d]	812:720
Signet ring cell carcinoma	F:M	1815:1856	57.1:61.6[a,e]	10.1:7.4[a]	15.9:12.4[a,e]	5010:4001
Intestinal type	F:M	250:645	69.1:68.2[a]	10.2:7.1[a]	6.6:8.2[a]	288:925
Tubular adenocarcinoma	F:M	332:1034	66.8:68.3[a]	10.9:8.5[a]	7.4:6.5[a]	430:1171
Mucinous adenocarcinoma	F:M	119:308	64.4:68.4[a]	9.2:6.7[a]	10.9:8.2[a]	221:451
Gastric lymphoma	F:M	864:849	61.5:63.6[a,b]	16.2:11.8[a]	6.1:6.5[b]	
Large B-cell lymphomas	F:M	425:455	64.4:62.9[a]	13.2:10.1[a]	8.0:7.7	
MALToma	F:M	216:161	59.0:63.2[a]			
Mesenchymal tumor	F:M	652:735	62.5:62.3[c]	18.0:13.4[a]	3.7:5.8[c]	
GIST	F:M	458:496	63.0:63.4			
Myomatous neoplasms	F:M	178:204	61.3:59.3			
Other histology	F:M	264:688	66.0:67.6			

F, female; GIST, gastrointestinal stromal tumor; M, male; MALToma, mucosal-associated lymphoid tissue lymphoma; NOS, not otherwise specified; Number, number of histologic subtypes in the Cancer Registry Database.
[a]Difference between both sexes ($P < .05$, Student *t* test).
[b]Difference between adenocarcinoma and gastric lymphoma for either male or female ($P < .05$, Student *t* test).
[c]Difference between adenocarcinoma group and mesenchymal tumor for either male or female ($P < .05$, Student *t* test).
[d]Difference between diffuse cell type and adenocarcinoma of NOS subtype ($P < .05$, Student *t* test).
[e]Difference between signet ring cell and adenocarcinoma of NOS subtype ($P < .05$, Student *t* test).

adenocarcinoma (2.26 vs 1.38 years), except for the intestinal type (1.44 vs 1.66 years).

Accurate Validity of Extrapolation to Life Expectancy

The validity of extrapolation was summarized in Table 4. Although the censoring rates of different pathologic types of gastric cancer at the end of the first 6-year period ranged between 43.6% and 82.7%, the relative bias between the 2 estimated methods of 13-year survival based on Kaplan–Meier estimate and extrapolation based on the first 6-year follow-up ranges from 2.4%–3.7%, indicating acceptable accuracy by extrapolation method.

Discussion

On the basis of large-scale data by a nationwide approach, this study illustrates more than 10-year long-term outcomes of gastric cancers with different histologic types. It illustrates a decline of age-specific and sex-specific incidence rates and lifetime risks of gastric cancer in Taiwan during the past decade. This study confirmed the sex, tumor location, and the different pathologic types, sex shall have determined to the LE and EYLL. So, this study supports the quantitative health impact of early detection on gastric cancer in Taiwan by integrating the age-specific and sex-specific incidence rates on a 13-year long-term nationwide-scale basis.

Because gastric cancer treatment has been fully reimbursed by the National Health Insurance system and waived from copayment, our registry has been quite comprehensive. The total numbers of gastric cancer validated by pathologic diagnosis and registered in the catastrophic illnesses during 1998–2007 were 35,576 and 33,544, respectively. Thus for a large-scale nationwide approach, the equivocal diagnosis as gastric cancer was just 5.7%. This indicated that histologic data should be reliable in such large-scale databases.

Although adenocarcinoma is usually diagnosed at an older age, it has longer EYLL and a shorter LE than those with either lymphoma or mesenchymal tumor in both sexes (Table 3). Thus a worse prognosis should in general be related to the pathologic type itself instead of an older diagnostic age.[11]

The early detection rate for gastric cancer was reported as more than 40% in Japan and just around 20% in Western countries.[12] On the basis of the current practice in Taiwan,[9] this study conservatively applied 19.4% as the early detection rate for gastric adenocarcinoma. Because nearly 90% of the patients

Table 4. Estmates of Mean Survival Months in 13-year Follow-up by Using the Semi-parametric Method of Extrapolation and Kaplan–Meier Estimates Between Different Pathologic Types of Gastric Cancer

Stomach cancer	Sex	Cohort size	Age at diagnosis (standard deviation) (*y*)	Censored rate (%)	13-y survival based on Kaplan–Meier estimate (standard error) (*mo*)	Extrapolation based on first 6-year follow-up (standard error) (*mo*)	Relative bias (%)
Adenocarcinoma	Male	12,449	67.5 (12.9)	43.6	50.1 (0.6)	48.8 (1.2)	−2.6
	Female	6060	63.8 (15.2)	46.4	55.8 (0.9)	55.3 (1.5)	−0.9
Gastric lymphoma	Male	475	62.8 (15.7)	63.8	83.6 (3.0)	83.5 (7.7)	−0.1
	Female	482	60.9 (14.9)	69.1	97.7 (3.1)	94.1 (6.0)	−3.7
Mesenchymal tumor	Male	360	61.2 (14.1)	72.8	89.8 (3.4)	92.0 (9.4)	2.4
	Female	324	61.8 (13.9)	82.7	111.7 (3.6)	110.2 (6.3)	−1.3

NOTE. Relative bias = (Estimate from extrapolation − Kaplan–Meier estimate)/Kaplan–Meier estimate.

with early detected gastric adenocarcinoma can achieve 5-year survival rate,[9,10] then these cases were assumed to be cured to attain the average survival of the general population. Accordingly, it would be possible to save 56,527 life-years for gastric cancer with histologic type as adenocarcinoma (Table 3). Because of the EYLL possibly saved by the early diagnosis of gastric adenocarcinoma in Taiwan, it is rational to screen for *Helicobacter pylori* infection in Taiwan, which is a high *H pylori*–infected endemic area with highly virulent *cagA-vacA-babA2* triple-positive strains.[13–16] To support the success of early detection of gastric adenocarcinoma, it should also be rational to eradicate the *H pylori* infection for those at risk to prevent or to stop gastric carcinogenesis at earlier stages. Possibly because of the policy support for *H pylori* eradication by the National Health Insurance in Taiwan, there is a decreasing trend of age-specific and sex-specific incidence rates and cumulative incidence rates_{20-79} for both sexes during the past decade (Table 1). However, because of the lack of linkage to anti–*H pylori* treatment history, it still needs further validation of the impact of a national *H pylori* eradication program on gastric cancer incidence in Taiwan.

The age-specific incidence rates of men are similar to those of women before 50 years of age, but men are about 1.5–2 times more likely to develop such cancer after 50 years of age (Table 2). It is clearly shown that there is a younger diagnostic age for women as compared with men. When stratified by age groups in gastric adenocarcinoma, although there was a higher LE in women than in men, there remains a higher EYLL in women than in men ($P < .05$) (Table 1). Moreover, the ELYS per case of women was significantly higher than that of men with different pathologic types of adenocarcinoma except for the intestinal type. Accordingly, there should be better advantage to conduct earlier screening and treatment of *H pylori* infection in women who carry a higher ELYS per case after diagnosis as gastric cancer.

Previous studies reported that cardiac gastric cancer was more advanced in severity with higher incidences of metastasis and recurrence after operation than gastric cancers at the noncardia sites.[17–19] In this study with a larger sample size and long period of follow-up, patients with cardiac gastric cancer had an older age at diagnosis and had a shorter LE. However, the EYLL were quite similar to the noncardia cancers in stomach after stratified by sexes (Table 1).

There are still conflicting results about the prognosis of signet ring cell carcinoma and diffuse type adenocarcinoma.[10,20–24] In this 13-year follow-up study with a nationwide collection of cases for both sexes, we discovered both signet ring cell type and diffuse type adenocarcinoma should have a younger age at diagnosis, thus a longer mean LE, but still have a poor ELYS per case than the other types of adenocarcinoma (Table 3). Such evidence supports that the histologic types of adenocarcinoma should determine LE and EYLL. Accordingly, specific improvement in treatment strategy should be tailored for each specific histologic type.

It is rather interesting to show that the intestinal type of gastric cancer in both sexes had an older diagnostic age than other subtypes of adenocarcinoma; this resulted in a shorter EYLL. Because such gastric cancers are strongly related to *H pylori*, the strategy to eradicate *H pylori* should be started as early as possible to prevent cancer formation to improve ELYS in both sexes.

The reason why women have a bigger ELYS per case for gastric cancer than men remains uncertain. The higher mean LE for women in Taiwan's general population as compared with men may be the possible answer. Nevertheless, even though the mean age of the gastric cancer diagnosis is younger in women than in men, we still found a bigger loss of LE in women than in men diagnosed as having gastric adenocarcinoma. These data strongly indicated an earlier screening policy of gastric cancer, such as endoscopy checkup or *H. pylori* infection test-and-treat strategy, should be used to help women improve their LE.

This study has a number of limitations. First, because we do not have staging and treatment information in these databases, we cannot classify the patients and their life-year loss according to different staging and/or treatment. Even though we have estimated the possible efficacy of early detection and treatment to save more LE loss in this study, it would be more promising in future studies to determine the exact impact of different gastric cancer stages for loss of LEs. Second, because the pathologic diagnoses in our data for adenocarcinoma had some cases as not specified, it leaves the sample sizes of more specific diagnoses to be smaller.

In summary, with a comprehensive collection of cases and 13 years of follow-up, this study showed that sex, location, and pathologic types of adenocarcinoma result in different LEs and EYLL after accounting for lead-time bias and age. Because early detection of gastric cancer may be helpful to save the patient's life, it would be worthwhile to set up a policy for early screening to prevent thousands of life-year loss, especially for women.

References

1. Ferlay JSH, Bray F, Forman D, et al. Cancer incidence and mortality worldwide: IARC Cancer Base No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer, 2010. Available at: http://globocan.iarc.fr.
2. Yang D, Hendifar A, Lenz C, et al. Survival of metastatic gastric cancer: significance of age, sex and race/ethnicity. J Gastrointest Oncol 2011;2:77–84.
3. Roshanaei G, Ghannad MS, Safari M, et al. Prediction of time to recurrence and influencing factors for gastric cancer in Iran. Asian Pac J Cancer Prev 2012;13:2639–2642.
4. Tural D, Selçukbiricik F, Serdengeçti S, et al. A comparison of patient characteristics, prognosis, treatment modalities, and survival according to age group in gastric cancer patients. World J Surg Oncol 2012;10:234.
5. Itoh H, Oohata Y, Nakamura K, et al. Complete ten-year post-gastrectomy follow-up of early gastric cancer. Am J Surg 1989; 158:14–16.
6. Noguchi Y, Yoshikawa T, Tsuburaya A, et al. Is gastric carcinoma different between Japan and the United States? Cancer 2000; 89:2237–2246.
7. Hwang JS, Wang JD. Monte Carlo estimation of extrapolation of quality-adjusted survival for follow-up studies. Stat Med 1999; 8:1627–1640.
8. Fang CT, Chang YY, Hsu HM, et al. Life expectancy of patients with newly-diagnosed HIV infection in the era of highly active antiretroviral therapy. QJM INT J MED 2007;100:97–105.
9. Lee WJ, Lee WC, Houng SJ, et al. Survival after resection of gastric cancer and prognostic relevance of systematic lymph node dissection: twenty years experience in Taiwan. World J Surg 1995; 19:707–713.
10. Wu CY, Yeh HZ, Shih TP, et al. A clinicopathologic study of mucinous gastric carcinoma including multivariate analysis. Cancer 1998; 83:1312–1318.
11. Hyatt BJ, Paull PE, Wassef W. Gastric oncology: an update. Curr Opin Gastroenterol 2009;25:570–578.

12. Everett SM, Axon ATR. Early gastric cancer: disease or pseudo-disease? Lancet 1998;351:1350–1352.
13. Sheu BS, Sheu SM, Yang HB, et al. Host gastric Lewis expression determines the bacterial density of *Helicobacter pylori* in *babA2* genopositive infection. Gut 2003;52:927–932.
14. Sheu BS, Odenbreit S, Hung KH, et al. Interaction between host gastric Sialyl-Lewis X and *H. pylori* SabA enhances *H. pylori* density in patients lacking gastric Lewis B antigen. Am J Gastroenterol 2006;101:36–44.
15. Chuang CH, Yang HB, Sheu SM, et al. *Helicobacter pylori* with stronger intensity of CagA phosphorylation lead to an increased risk of gastric intestinal metaplasia and cancer. BMC Microbiol 2011; 11:121–128.
16. Sheu BS, Yang HB, Yeh YC, et al. *Helicobacter pylori* colonization of the human gastric epithelium: a bug's first step is a novel target for us. J Gastroenterol Hepatol 2010;25:26–32.
17. Saito H, Fukumoto Y, Osaki T, et al. Distinct recurrence pattern and outcome of adenocarcinoma of the gastric cardia in comparison with carcinoma of other regions of the stomach. World J Surg 2006; 30:1864–1869.
18. Pinto-De-Sousa J, David L, Seixas M, et al. Clinicopathologic profiles and prognosis of gastric carcinomas from the cardia, fundus/body and antrum. Dig Surg 2001;18:102–110.
19. Deans C, Yeo MS, Soe MY, et al. Cancer of the gastric cardia is rising in incidence in an Asian population and is associated with adverse outcome. World J Surg 2011;35:617–624.
20. Chiu CT, Kuo CJ, Yeh TS, et al. Early signet ring cell gastric cancer. Dig Dis Sci 2011;56:1749–1756.
21. Maehara Y, Sakaguchi Y, Moriguchi S, et al. Signet ring cell carcinoma of the stomach. Cancer 1992;69:1645–1650.
22. Otsuji E, Yamaguchi T, Sawai K, et al. Characterization of signet ring cell carcinoma of the stomach. J Surg Oncol 1998;67: 216–220.
23. Sipponen P, Correa P. Delayed rise in incidence of gastric cancer in females results in unique sex ratio (M/F) pattern: etiologic hypothesis. Gastric Cancer 2002;5:213–219.
24. Adachi Y, Yasuda K, Inomata M, et al. Pathology and prognosis of gastric carcinoma: well versus poorly differentiated type. Cancer 2000;89:1418–1424.

Reprint requests

Address requests for reprints to: Bor-Shyang Sheu, MD, Department of Internal Medicine, National Cheng Kung University Hospital, #138 Sheng Li Road, Tainan, Taiwan 70428. e-mail: sheubs@mail.ncku.edu.tw; fax: +886-6-276-6175.

Acknowledgments

Drs Wang and Sheu contributed equally to this work.

Conflicts of interest

The authors disclose no conflicts.

Funding

Supported by grants NHRI-EX99-9908BI from the National Health Research Institute and DOH100-TD-C-111-003 from Department of Health, Taiwan.