World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/1007-9327office
wjg@wjgnet.com
doi:10.3748/wjg.v17.i39.4421

World J Gastroenterol 2011 October 21; 17(39): 4421-4428
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

BRIEF ARTICLE

Comparative epidemiology of gastric cancer between Japan and China

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Supported by Grant-in-Aid from the Third Term Comprehensive Control Research for Cancer, the Ministry of Health, Labour and Welfare, Japan
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Received: February 21, 2011 Revised: June 9, 2011
Accepted: June 16, 2011
Published online: October 21, 2011

Abstract

AIM: To clarify the similarities and differences in gastric cancer epidemiology between Japan and China.

METHODS: A comprehensive literature search of the PubMed database was performed. The relevant literature published in China was also been cited. Data on incidence and mortality rates in 2008 were obtained from the Cancer Mondial database, published by International Agency for Research on Cancer at http://www-dep.iarc.fr/.

RESULTS: Gastric cancer remains a significant public health burden in both Japan and China. The prevalence of *Helicobacter pylori* (*H. pylori*) colonization is high in the adult populations of both countries. Accumulating evidence from intervention studies in both countries has shown the effectiveness of *H. pylori* eradication in reducing gastric cancer incidence. There are differences, however, in many aspects of gastric cancer, including patterns of incidence and mortality, trends in the prevalence of *H. pylori* infection, *H. pylori* strains, the magnitude of risk of gastric cancer related to *H. pylori* infection, and associations with dietary habits. Compared with China, Japan has seen a more rapid decline in *H. pylori* infection among adolescents. While Japanese cohort studies have dominated the literature concerning the associations between gastric cancer and dietary habits, numerous case-control studies in China suggest a positive association between a high intake of preserved fish and vegetables and gastric cancer risk. There is a need for a multidisciplinary research approach to understand the interactions between various strains of *H. pylori*, host factors, and other lifestyle and environmental factors in gastric carcinogenesis in both countries.

CONCLUSION: The shared high incidence of gastric cancer and high prevalence of *H. pylori*, as well as differences in many aspects of gastric cancer, provide an excellent opportunity to establish Sino-Japanese collaborations.

Key words: Gastric cancer; Risk factor; *Helicobacter pylori*; Epidemiology

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Lin Y, Ueda J, Kikuchi S, Totsuka Y, Wei WQ, Qiao YL, Inoue M. Comparative epidemiology of gastric cancer between Japan and China. *World J Gastroenterol* 2011; 17(39): 4421-4428 Available from: URL: http://www.wjgnet.com/1007-9327/full/v17/i39/4421.htm DOI: http://dx.doi.org/10.3748/wjg.v17.i39.4421

INTRODUCTION

Gastric cancer is a heterogeneous, multifactorial disease. The incidence and mortality vary geographically, with the highest rates in East Asia (Japan, China and Korea)[1]. Although a trend of declining incidence has been observed in Japan and China, gastric cancer still represents a tremendous burden in each country. According to the vital statistics released by the Ministry of Health, Welfare and Labor in Japan, approximately 50 000 Japanese men and women die from gastric cancer annually, representing approximately 15% of annual cancer-related deaths over the past four decades[2]. No systematic national vital statistics exist in China, but a retrospective sampling survey on malignant tumors from 2004 to 2005 found that the mortality rate from gastric cancer ranked third in overall cancer mortality[3]. Notably, China alone accounts for 42% of all gastric cancer cases worldwide, at least in part because of its large population[1].

Numerous epidemiologic studies have been conducted in Japan and China to identify environmental and lifestyle factors that contribute to the development of gastric cancer; these studies have identified *Helicobacter pylori* (*H. pylori*) infection as an important risk factor for gastric cancer[4]. Additionally, high salt intake and exposure to *N*-nitroso compounds significantly increase the risk among *H. pylori* infected individuals[5]. It is noteworthy that Japan has a strong tradition of gastric cancer research, not only in basic science but also in epidemiology and clinical trials. Seminal papers published during the last three decades have greatly contributed to our understanding of gastric cancer etiology and prevention[6-9]. However, an increasing number of case-control studies in different regions of China have examined risk factors for gastric cancer, and cohort studies are ongoing to investigate the role of lifestyle in urban and rural areas[10-12].

In this article, we first summarize the current understanding of gastric cancer etiology on the basis of existing literature. We then compare the burden of gastric cancer between Japan and China in terms of trends in incidence and mortality. Next, we address three of the principal risk factors, based on epidemiologic studies conducted in each country: *H. pylori* infection, cigarette smoking and diet. Finally, we propose three potential avenues for Sino-Japanese collaboration.

MATERIALS AND METHODS

We performed a comprehensive literature search of the PubMed database using the search terms "risk factors", "*H. pylori*", "smoking", "diet", "gastric cancer", "China", and "Japan". In addition, relevant literature published in China was also cited. Data on incidence and mortality in 2008 were obtained from the Cancer Mondial database, published by International Agency for Research on Cancer (IARC) at http://www-dep.iarc.fr/.

RESULTS

Current knowledge about gastric carcinogenesis

Gastric cancer is a multifactorial disease with a complex interplay between genetics and both lifestyle and environmental factors. Gastric cancer can be classified as intestinal or diffuse. While the triggering factor and the histopathologic changes in the progression of diffuse gastric cancer remain incompletely understood, the progression of intestinal gastric cancer is well characterized[13]. An individual develops intestinal cancer through a series of histological changes beginning with the transition from normal mucosa to chronic superficial gastritis, which then leads to atrophic gastritis, intestinal metaplasia, and finally dysplasia and adenocarcinoma[13]. Before the discovery of *H. pylori* in 1983, epidemiologic studies had already suggested an important role for lifestyle in the etiology of gastric cancer. In particular, a high-salt diet and foods rich in *N*-nitroso compounds appeared to be major inducers of gastric cancer. Since the discovery of *H. pylori,* its close association with peptic ulcers and gastric cancer has been supported by numerous studies. Asia-Pacific consensus guidelines on gastric cancer prevention define *H. pylori* infection as necessary but not sufficient for the development of non-cardia gastric adenocarcinoma[4]. From an epidemiologic perspective, the synergistic interaction between *H. pylori* and diet plays an overriding role in gastric carcinogenesis[14].

However, current studies have not provided a clear answer as to why only a minority of individuals with *H. pylori* infection develop gastric cancer. One reason is that the interactions of *H. pylori* strains, host factors, and other lifestyle and environmental factors in gastric carcinogenesis are not well defined. Another reason is that few causally linked genes have been found, and the role of genetic and epigenetic changes in gastric carcinogenesis is poorly understood. These two issues need to be addressed in future studies.

Descriptive epidemiology of gastric cancer in Japan and China

Patterns of gastric cancer incidence, mortality and trends: According to Globocan 2008, gastric cancer is the third most frequently diagnosed cancer and the second leading cause of cancer deaths in Japan, with an estimated 102 040 new cases and 50 156 cancer deaths in 2008. The overall estimated age-adjusted incidence rate (standardized for world population) in 2008 was 31.1 per 100 000 people. However, gastric cancer is the second most frequently diagnosed cancer and the third lead-

Table 1 Comparisons of crude and age-standardized incidence rates of gastric cancer between Japan and China (1993-1997)

	Men		Women	
	Crude	ASR	Crude	ASR
Japan				
Hiroshima	113.1	85.5	55.1	33.9
Miyagi	109.2	69	52.2	27.1
Nagasaki	119.9	65.4	56.5	25.6
Osaka	87.7	59.9	42.9	23.8
Saga	115.8	63.6	57	24.9
Yamagata	178.5	91.6	94.1	38.9
China				
Beijing	27.8	19.8	13	8.7
Changle	103.5	145	29.6	34.5
Cixian	55.9	78.1	28	31.9
Jiashan	45.8	38.9	20.3	15.7
Qidong	39.5	37.8	24.2	19
Shanghai	54.6	32.3	29.8	17.6
Tianjin	33.5	26.9	13.9	10
Wuhan	29.3	29.8	17.1	14.5

Source: Cancer incidence in five continents Vol. Ⅷ, IARC scientific publications No. 155. ASR: Age standardized rate, per 100 000 population.

ing cause of cancer death in China, with an estimated 464 439 new cases and 352 315 cancer deaths in 2008. The overall estimated age-adjusted incidence rate in 2008 was 29.9 per 100 000 people in China.

Although China's overall incidence rate is comparable to that of Japan, a wider variation in both crude and age-standardized rates is apparent when cancer registry data (1993-1997) from the 2 countries are compared (Table 1). For example, the incidence in Changle was 145 per 100 000 people, approximately 7 times higher than in Beijing. The highest rates were often found in economically undeveloped rural areas in China, including Gansu, Henan, Hebei, Shanxi, and Shaanxi Provinces[15]. Although gastric cancer incidence is declining in both rural and urban areas in China[16-18], the rate of decline may be slower than in developed countries[19]. The number of new gastric cancer cases has been projected to increase continuously over the next 40 years because of population growth and aging[19].

Risk factors for gastric cancer in Japan and China

From the large body of literature on gastric cancer etiology in Japan and China, we cite selected epidemiologic studies conducted in each country. Three major risk factors, namely *H. pylori* infection, cigarette smoking and high intake of salt/salty food, are addressed in detail.

H. pylori colonization: Prevalence of H. pylori colonization in the general population

Japan: Gastric *H. pylori* infection is common among middle-aged and elderly Japanese people. A seroepidemiological study of *H. pylori* infection among apparently healthy residents of Sapporo found a prevalence of 70%-80% for individuals born before 1950[20]. For those residents born after 1950, the frequency of *H. pylori* infection increased at approximately 1% per birth year[20]. The prevalence of *H. pylori* infection, however, has been decreasing over the past several decades. The overall *H. pylori* seropositivity was 72.7% in 1974, 54.6% in 1984, and 39.3% in 1994, based on an assay of serum samples from 1015 healthy people living in several prefectures in central Japan[21]. As in other developed countries, a clear birth cohort effect has been observed for *H. pylori* infection in Japan, with younger generations experiencing a more rapid decline than older generations[22,23]. In a 2007 study involving 777 university students with a mean age of 19.6 years, *H. pylori* prevalence was only 14.7%[24].

China: The Chinese population has a high prevalence of *H. pylori* infection. A 2003 meta-analysis, based on studies published between 1990 and 2002, concluded that the prevalence of *H. pylori* infection for the entire Chinese population was approximately 58%[25]. Since 2003, numerous studies have also been conducted to examine the prevalence of *H. pylori* in healthy people in different regions of China, with reported prevalence ranging from 40% to 81%[26-29]. Generally, studies in rural areas found a higher prevalence of *H. pylori* than studies in urban areas. Furthermore, areas with high gastric cancer incidence generally have a higher prevalence of *H. pylori* infection than low-incidence areas.

Because *H. pylori* is acquired during childhood, some surveys of *H. pylori* prevalence in China have focused on children. One recent study reported a prevalence of 37.7% in children aged 10-19 years in Beijing and 25.5% in the same age group in Shandong[30]. Some studies suggest a downward trend in *H. pylori* seroprevalence in some regions; for example, a significant decrease was observed across age groups in Guangzhou[31]. Evidence on this subject, however, is fragmentary and inconclusive. In particular, it remains unclear whether the rate of decline is accelerating, especially in the younger segments of the population.

H. pylori colonization: Findings from observational epidemiologic studies addressing the association between H. pylori and gastric cancer risk

Japan: Both case-control and cohort studies have been conducted to estimate the degree of gastric cancer risk associated with *H. pylori* infection in the Japanese population. To date, all four prospective studies have shown a positive association, with relative risks (RRs) ranging from 1.0 to 5.1[32-35] (Table 2). In the prospective study that used the largest dataset (511 cases and 511 control subjects), Sasazuki *et al*[35] showed that the adjusted odds ratio (OR) of gastric cancer associated with *H. pylori* infection was 5.1, which is quite similar to the estimate of 5.9 for non-cardia gastric cancer in a combined analysis of 12 case-control studies nested within prospective cohorts[36]. Based on the substantial evidence from both case-control and cohort studies, it is clear that *H. pylori* infection is causally linked to gastric cancer in the Japanese population.

Table 2 Summary of findings on the associations between *H. pylori* carriage and risk of gastric cancer in prospective studies from Japan and China

Author[Ref.], yr	Country	Study design	Case patients /control subjects	Seroprevalence of *H. pylori* in cases *vs* controls (%)	ELISA kit used for measuring seroprevalence of *H. pylori*	OR (95% CI)
Watanabe *et al*[32], 1997	Japan	Nested case-control study	45/225	91.1 *vs* 75.6	Pirikaplate G *Helicobacter* enzyme immunoassay (Fujirebio Inc., Tokyo)	3.4 (1.2-9.9)
Sasazuki *et al*[35], 2006	Japan	Nested case-control study	511/511	93.5 *vs* 74.5	E Plate, produced by Eiken Kagaku Co.Ltd., Tokyo	5.1 (3.2-8.0)
Yamagata *et al*[33], 2000	Japan	Cohort study	1070 men and 1532 women at baseline	71.5 among men *vs* 62.4 among women	HM-CAP, Enteric Products Inc, Westbury, NY	Men: RR = 2.9 (1.1-7.4) Women: RR = 1.0 (0.3-3.0)
Yatsuya *et al*[34], 2004	Japan	Nested case-control study	202/394	88.6 *vs* 79.2	HM-CAP, Enteric Products Inc, Westbury, NY	Men: 1.7 (0.5-5.1) Women: 5.1 (1.6-16.5)
Yuan et al[38], 1999	China	Nested case-control study	188/548	86 *vs* 85	Locally Developed and Validated Assay	1.8 (1.1-3.1), but 3.7 (1.5-9.3) for subjects followed for 5 or more years
Limburg *et al*[39], 2001	China	Nested case-control study	181/192	62.0 *vs* 52.0	Antibodies to the whole cell antigen	1.6 (1.1-2.5)
Kamangar *et al*[12], 2007	China	Case-cohort study	Cardia 582/992 Noncardia 343/992	Cardia 81.0 *vs* 73.0 Noncardia 80.0 *vs* 73.0	IgG antibodies to whole-cell antigen	Cardia 1.6 (1.3-2.1) Noncardia 1.6 (1.2-2.1)

OR: Odds ratio; RR: Relative risk; CI: Confidence interval.

China: The majority of epidemiologic studies that examined the association between *H. pylori* infection and gastric cancer in China are retrospective case-control studies. Of 11 case-control studies included in a 2001 meta-analysis, all studies showed a positive association. The ORs ranged from 2.1 to 5.6, with a combined OR of 3.0[37].

This positive association was also observed in two prospective cohort studies. Yuan *et al*[38] reported that the OR was 3.7 for individuals seropositive for *H. pylori* who were followed for 5 or more years, on the basis of a nested case-control study within a cohort of Shanghai residents. A prospective, nested case-control study in Linxian, one of the highest-incidence regions in China, found that *H. pylori* seropositivity results in an approximately 2-fold increased risk of gastric cancer[39]. This result was confirmed by a 2007 case-cohort study, in which *H. pylori* was associated with a 1.6-fold increased risk of both cardia and non-cardia gastric adenocarcinomas[12].

H. pylori colonization: Findings from clinical studies, including both non-intervention and intervention studies

Japan: Several recent clinical studies have greatly improved our understanding of the role of *H. pylori* in the development of gastric cancer. Umemura *et al*[7] (2001) found that gastric cancer developed in 36 of 1246 *H. pylori*-infected patients but none of the 280 uninfected patients in a prospective study involving 1526 Japanese patients with peptic ulcers, gastric hyperplasia or non-ulcer dyspepsia. The results are convincing because *H. pylori* colonization was confirmed by a combination of tests, including endoscopy, biopsy, histology, a rapid urease test, and serologic testing. This seminal study thus offers compelling evidence that *H. pylori infection* is associated with the development of both intestinal and diffuse gastric cancers. Another important study, a multicenter, open-label randomized controlled trial followed 544 patients who underwent endoscopic resection of early gastric cancer, half of whom underwent eradication of colonizing *H. pylori*[8]. Eradication decreased the risk of developing metachronous gastric cancer by approximately 65%, even though these patients had already been diagnosed with early gastric cancer.

China: To determine whether *H. pylori* eradication reduces the incidence of gastric cancer at the population level in high-risk areas in China, Wong *et al*[40] (2004) conducted a randomized, placebo-controlled trial, using subjects without precancerous lesions. Unfortunately, however, this study was restricted by a short follow-up period and did not address whether those subjects with precancerous lesions experience a similar reduction in gastric cancer risk.

Cigarette smoking

Japan: Numerous epidemiologic studies over the past several decades have examined the association between cigarette smoking and gastric cancer risk in Japan, with the majority showing a significantly increased risk in current smokers when compared with those subjects who have never smoked. According to a systematic review and meta-analysis conducted by the Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan in 2006, the summary RR for current smokers were estimated to be 1.8 (95% CI: 1.5-2.1) in men and 1.2 (1.1-1.4) in women[41]. Based on these results, the research group concluded that there is convincing evidence that tobacco smoking moderately increases the risk of gastric cancer in the Japanese population. Approximately 28.4% of gastric cancers are related to cigarette smoking, according to data from the Hisayama Study, a population-based prospective study of the combined influence of cigarette smoking and *H. pylori* infection[42]. That study found that cigarette smoking is sig-

nificantly associated with increased risk of gastric cancer independent of *H. pylori* infection.

Although cigarette smoking is associated with an increased risk of gastric cancer, it remains unclear whether the observed positive association is homogeneous in terms of histologic type or anatomic location; such information has not been included in most previous studies. A cohort study was designed to address this question, incorporating complete histologic data. The results suggest that smoking significantly increases the risk of differentiated, but not undifferentiated, distal gastric cancer[43].

China: The association between cigarette smoking and gastric cancer has been investigated in a number of epidemiologic studies, including both case-control and cohort studies, but the results are inconsistent[44]. No association was found in a cohort study involving 9351 middle-aged adults in urban Shanghai[45]. Another cohort study showed a non-significant increase in risk, with an RR of 1.4 for current smokers[46]. In contrast, a recent prospective study of men in Shanghai showed that among nondrinkers, smokers have an 80% greater risk of gastric cancer, suggesting that cigarette smoking and alcohol consumption exert independent effects on gastric cancer risk[47].

High intake of salt/salty food and food sources of nitrosamines

Japan: Collective evidence from epidemiologic and experimental studies over the past several decades strongly suggests that high intake of salt/salty food is associated with an increased risk of gastric cancer in Japanese populations[9]. Japanese cohort studies dominate the published literature on gastric cancer epidemiology; of the 11 cohort studies included in a recent meta-analysis of salt consumption and gastric cancer risk, six of these studies came from Japan[10]. In four of these Japanese studies, a statistically significant association was observed, with the RR ranging from 2.2 to 5.4 at the highest intake level.

The positive association observed between salt/salty food intake and gastric cancer risk in epidemiologic studies is also supported by experimental evidence. Using chemical carcinogens such as *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine (MNNG), Tatematsu *et al*[6] reported the first experimental model of gastric carcinogenesis in *H. pylori*-infected Mongolian gerbils. Experiments with this model demonstrated that sodium chloride (NaCl) enhances the carcinogenic effects of MNNG and 4-nitroquinoline-1-oxide. Another notable finding is that salt and *H. pylori* act synergistically to promote the development of gastric cancer in Mongolian gerbils[48].

No cohort or case-control studies in Japan have published results on nitrite or nitrosamine intake in relation to gastric cancer risk; however, the association between gastric cancer and dietary intake of exogenous and/or endogenous nitrosamine, including meat, processed meat, preserved fish, and preserved vegetables, was examined in 11 cohort studies published between 1985 and 2005[49]. The results are inconsistent, but most studies show no statistically significant association.

China: Of the 45 case-control studies and 11 cohort studies that were included in a 2009 meta-analysis of salt consumption and gastric cancer risk, 13 case-control studies, but no cohort studies, focus on Chinese populations[10]. The associations of gastric cancer with intake of salt, salty fish, salty vegetables, pickled vegetables, salted and fermented soya paste, and other salted foods have been examined, with ORs for individuals at the highest intake level ranging from 1.1 to 2.6. Overall, these findings indicate that high intake of salt and salty food increase the risk of gastric cancer.

Neither cohort nor case-control studies have been conducted to examine the risk of gastric cancer in relation to nitrite or nitrosamine intake in China. One cohort study, however, found no significant association between processed meat consumption and gastric cancer risk[49]. Additionally, a number of case-control studies have found that high intake of preserved fish and preserved vegetables is significantly associated with increased risk of gastric cancer[49].

DISCUSSION

We aimed to clarify the similarities and differences in gastric cancer epidemiology in Japan and China by closely examining patterns of incidence, mortality rates and risk profiles. It can be difficult to compare data from two different countries because of differences in genetic susceptibility; environmental exposure; lifestyle; and the way each country defines, reports and interprets data. Commonalities emerge, however, when the data are carefully compared. First, gastric cancer still poses a tremendous health burden in both countries. Second, the prevalence of *H. pylori* remains high in adults, and *H. pylori* infection significantly increases the risk for gastric cancer. The magnitude of positive association may have been underestimated in studies from both countries if only conventional IgG enzyme-linked immunosorbent assay (ELISA) serology was used to detect past *H. pylori* exposure. Because atrophy of the gastric mucosa progresses with time, seroreversion may result from loss of infection. In an analysis restricted to early diffuse cancer, a very strong association with *H. pylori* infection was observed among all age groups[50]. In a 2001 Swedish study that combined IgG ELISA with CagA immunoblot to detect *H. pylori* exposure, the adjusted OR for noncardia gastric cancer was 21.0 (8.3-53.4) among *H. pylori*-positive subjects[51]. Third, almost all *H. pylori* strains are CagA-positive, and CagA plays a central role in *H. pylori*-induced gastric carcinogenesis[52]. Fourth, in addition to *H. pylori* infection, cigarette smoking and high intake of salt/salty food are two important risk factors for gastric cancer. Fifth, clinical studies have provided important insights into the effects of *H. pylori* eradication on the

development of gastric cancer.

Despite these similarities, there are significant differences in many aspects of gastric cancer epidemiology between Japan and China, including patterns in mortality and the prevalence of *H. pylori* infection, *H. pylori* strains, the magnitude of gastric cancer risk related to *H. pylori* infection, and associations with diet. Studies in China have found a wider variation in patterns of incidence and mortality than have studies in Japan. Because the highest rates of gastric cancer are often seen in economically undeveloped rural areas in China, reduction of the mortality rate in these high-risk areas should be given top priority. Because of the pivotal role of *H. pylori* infection in gastric carcinogenesis, trends in infection prevalence likely affect the incidence of gastric cancer. The decline in *H. pylori* prevalence may have occurred faster in Japan than in China. Furthermore, in Japan, the observed decrease in gastric cancer was more marked than in China, especially among 20-39 years old subjects, suggesting a clear cohort effect. Further research is required to determine whether such an effect has been or will be occurring in China. Although it is unclear why only a small percentage of individuals infected with *H. pylori* develop gastric cancer, differences in *H. pylori* strains (i.e., virulence factors), inflammatory responses, and environmental exposure may be important factors in determining individual susceptibility to gastric cancer. In an analysis of 419 *H. pylori* strains from Japanese subjects and 65 *H. pylori* strains from Chinese subjects, East Asian CagA type accounted for 94% and 93%, respectively, of the detected strains[51]. This result suggests that almost all Japanese and Chinese *H. pylori* strains are CagA-positive; however, differences in other virulence factors, such as VacA and OipA, also warrant further study.

Diet is commonly believed to play an important role in the development of gastric cancer[53]. Because of the complexity of diet and the limitations of questionnaire-based surveys, clarifying its precise role remains a major challenge in epidemiologic studies. Compared to China, Japanese cohort studies dominate the literature on the associations of gastric cancer with diet; in particular, salt/salty food and dietary *N*-nitroso compounds are associated with gastric cancer incidence. There is substantial evidence suggesting that high intake of salt/salty food significantly increases the risk of gastric cancer in the Japanese population. Similarly, numerous case-control studies in China strongly suggest a positive association between high intake of preserved fish and vegetables and gastric cancer risk. The role of *N*-nitroso compounds is also crucial in gastric carcinogenesis, but epidemiologic studies from both Japan and China do not provide a clear picture of this role, at least in part because the intake of *N*-nitroso compounds is notoriously difficult to measure.

There is a need to accelerate the reduction of gastric cancer incidence and mortality in both countries and to determine the most effective strategy for the prevention of gastric cancer. Cost-effective prevention strategies have been extensively discussed in Japan[54]; one difficult issue is whether to adopt a test-and-treat policy for asymptomatic individuals. The available data do not provide a clear picture of the optimal timing for *H. pylori* eradication to achieve the maximum benefit while doing the least harm. In China, tobacco control could confer substantial public health benefits. With 20% of the world's population, China produces and consumes about 30% of the world's cigarettes and suffers about a million deaths a year from tobacco[55]. Efforts to promote tobacco control and decrease salt consumption should effectively reduce incidence and mortality from gastric cancers.

We propose the following three avenues for potential collaborative work based on the comparison of gastric cancer epidemiology between Japan and China. First, data comparisons on *H. pylori* genotyping are useful for identifying those people at increased risk of neoplastic transformation. Second, because the prevalence of premalignant disease states in the general population is currently undefined, it is important to estimate the prevalence of precancerous lesions, such as chronic atrophic gastritis and gastric intestinal metaplasia, and their associations with *H. pylori* infection, on the basis of endoscopic findings and serologic tests. Third, a multidisciplinary study is needed to address the role of *N*-nitroso compounds in the development of gastric cancer because epidemiologic studies are limited by difficulties in the precise measurement of *N*-nitroso compound intake. It is a challenge to find common ground for international collaboration. However, the similarities between these two countries, namely a high incidence of gastric cancer and a high prevalence of *H. pylori* infection, along with differences in many aspects of gastric cancer epidemiology, provide an excellent opportunity for Sino-Japanese collaboration. Such collaborations will facilitate a more complete understanding of gastric cancer etiology and the development of more effective interventions to reduce the mortality and incidence of gastric cancers. Given the pivotal role of *H. pylori* in gastric carcinogenesis, screening strategies in both countries based on *H. pylori* infection status would be very powerful for developing appropriate and cost-effective screening programs.

COMMENTS

Background

Japan and China have the highest incidences of gastric cancer in the world. Although a trend of declining incidence has been observed over the past several decades, gastric cancer still poses a tremendous burden to populations in each country. Although numerous gastric cancer studies have been conducted in each country, this article is the first to clarify the similarities and differences in gastric cancer between Japan and China by closely examining both epidemiologic features, such as patterns of incidence and mortality rates, and risk profiles on the basis of extensive published literature.

Research frontiers

To address why only a minority of individuals with *Helicobacter pylori (H. pylori)* colonization develop gastric cancer, **the authors need to elucidate the interacting** roles of various strains of *H. pylori,* host factors, and other lifestyle/environmental factors in gastric cancer. **The authors also need more evidence on the optimal** timing for *H. pylori* eradication in the interest of preventing gastric cancer.

Innovations and breakthroughs

The authors found differences in many aspects of gastric cancer between Japan and China, including patterns of mortality, trends in prevalence of *H. pylori* infection, *H. pylori* strains, and risk profiles. Due to the pivotal role of *H. pylori* infection in gastric carcinogenesis, trends in its population prevalence are likely to affect gastric cancer incidence. The decline in *H. pylori* prevalence may have occurred faster in Japan than in China. In Japan, a more marked decrease in gastric cancer was observed, especially among those people aged 20-39 years old; this evidence suggests a clear cohort effect. It will therefore be intriguing to see whether such a cohort effect has occurred in China or will do in the future.

Applications

This article has implications for future collaborative studies between Japan and China. First, comparing data on *H. pylori* genotyping is useful for identifying those patients at increased risk of neoplastic transformation. Second, it is important to estimate the prevalence of precancerous lesions, such as chronic atrophic gastritis and gastric intestinal metaplasia, and to evaluate the distribution of *H. pylori* in high-risk populations, on the basis of endoscopic findings and serologic tests. Third, a multidisciplinary study is needed to address the role of *N*-nitroso compounds in the development of gastric cancer. Specifically, screening strategies based on *H. pylori* negativity or positivity in both countries would be very powerful in terms of developing appropriate and cost-effective screening programs.

Terminology

H. pylori colonizes the human stomach, and individuals with *H. pylori* infection have an increased risk of developing gastric cancer.

Peer review

This article compares factors associated with the risk for developing gastric cancer in *H. pylori*-infected individuals from China or Japan. It summarizes a large body of literature on the rates of *H. pylori* infection along with the links between smoking, high salt and nitrate diets and gastric cancer rates. This article should be well received, especially in Asian countries, where the prevalence of *H. pylori* infection and gastric cancer remains unacceptably high.

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