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Review article

Diet and the risk of gastric cancer: review of epidemiological evidence

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Abstract

There are geographic and ethnic differences in the incidence of gastric cancer around the world as well as with its trends for each population over time. The incidence patterns observed among immigrants change according to where they live. All of these factors serve to indicate the close association of gastric cancer with modifiable factors such as diet. This review presents epidemiological evidence on the association between dietary factors and gastric cancer based on previous systematic reviews and subsequent updates. Infection with *Helicobacter pylori* is a strong and established risk factor of gastric cancer but is not a sufficient cause for its development. Substantial evidence from ecological, case-control, and cohort studies strongly suggests that the risk may be increased with a high intake of various traditional salt-preserved foods and salt per se and decreased with a high intake of fruit and vegetables, particularly fruit. However, it remains unclear which constituents in fruit and vegetables play a significant role in gastric cancer prevention. Among them, vitamin C is a plausible candidate supported by a relatively large body of epidemiological evidence. Consumption of green tea is possibly associated with a decreased risk of gastric cancer, although the protective effects have been, for the most part, identified in Japanese women, most of whom are nonsmokers. In contrast, processed meat and *N*-nitroso compounds may be positively associated with the risk of gastric cancer. In conclusion, dietary modification by reducing salt and salted food intake, as well as by increasing intake of fruit and vitamin C, represents a practical strategy to prevent gastric cancer.

Key words Stomach neoplasms · Diet · Salt · *Helicobacter pylori* · Fruit and vegetables · Epidemiological studies

Introduction

In 2000, gastric cancer was the second most frequent cause of cancer death worldwide and the fourth most common cancer, with an estimated 650 000 deaths and 880 000 new cases per year. Almost two-thirds of these new cases occurred in developing countries [1]. In Japan, gastric cancer accounted for 51 000 deaths in 2004, or 16% of all cancer deaths (Vital Statistics: Ministry of Health, Labor and Welfare, Japan); a total of 103 000 new cases were detected in 2000, or 19% of all incident cancers [2]. The prevention of gastric cancer therefore represents one of the most important aspects of any cancer control strategy in Japan and around the world.

There are geographic and ethnic differences in gastric cancer incidence in the world and in its trends for each population with time. The incidence patterns observed among immigrants change according to where they live. These factors indicate the close association of gastric cancer with modifiable factors such as diet. Substantial evidence from ecological, case-control, and cohort studies strongly suggest that the risk of cancer increases with a high intake of various traditional salt-preserved foods as well as salt per se and that this risk could be decreased with a high intake of fruit and vegetables [3,4]. A recent report of a joint World Health Organization (WHO)/Food and Agriculture Organization (FAO) Expert Consultation concluded that salt-preserved food and salt "probably" increase the risk of gastric cancer, whereas fruit and vegetables "probably" decrease the risk [5]. Other established nondietary factors include cigarette smoking [6] and infection with the bacterium *Helicobacter pylori* (*H. pylori*) [7]. In addition, there is some evidence that the intake of green tea and vitamin C is associated with the risk of gastric cancer.

In this review, we present epidemiological evidence for the association between dietary factors and gastric cancer, with particular reference to our recent work as well as related articles.

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Salt-preserved food and salt

In experimental studies in rats, ingestion of salt is known to cause gastritis and, on co-administration, to enhance the carcinogenic effects of known gastric carcinogens such as *N*-methyl-*N*-nitro-*N*-nitrosoguanidine (MNNG) [8,9]. A high salt concentration in the stomach destroys the mucosal barrier and leads to inflammation and damage such as diffuse erosion and degeneration. Furthermore, the induced proliferative change may act to promote the effect of food-derived carcinogens. It is therefore biologically plausible that high salt intake increases the risk of gastric cancer in humans.

Evidence from ecological studies

There are substantial geographic differences in the incidence of and mortality associated with gastric cancer worldwide, as well as nationwide in Japan. Using data from the INTERSALT study, in which randomly selected 24-h urine samples from 39 populations were sampled from 24 countries (n = 5756), Joossens and colleagues analyzed median sodium levels in samples from subjects aged 20–49 years in relation to the national gastric cancer mortality rates [10]. For the 24 countries, the Pearson correlation of gastric cancer mortality with sodium was 0.70 in men and 0.74 in women (both $P < 0.001$). In an ecological study of 65 rural counties in China, the consumption of salt-preserved vegetables was correlated with gastric cancer mortality ($r = 0.26$ in men, 0.36 in women) [11].

Approximately threefold differences in age-standardized mortality rates have been identified in Japan, with higher rates in Akita and Yamagata prefectures, lower rates in Kyushu district prefectures such as Kagoshima and Miyazaki, and an especially low rate in Okinawa (Vital Statistics: Ministry of Health, Labor and Welfare, Japan). Our ecological study of five selected areas in Japan showed an almost linear correlation between the cumulative mortality rate for gastric cancer in subjects up to 75 years of age and the urinary salt excretion level in 24-h urine samples [12,13].

Both age-adjusted mortality and incidence rates have been decreasing for several decades in Japan. In the United States [14] and Europe [15], gastric cancer used to be one of the most common cancers; however, mortality rates have fallen dramatically over the last 50 years in all Western countries without any specific intervention taken, and gastric cancer is now rare. This worldwide decline in incidence is likely attributable to the spread of refrigeration, the use of which would inversely correlate with salting and other salt-based methods of preservation such as curing and smoking, and with the overall volume of salt in the diet [3].

Studies in migrants offer clues about the relative importance of genetic and environmental factors in the etiology of cancer and are particularly useful when large differences exist between the original and host countries in incidence and lifestyle. Age-adjusted (world population) incidence rates of gastric cancer among Japanese residents in Hawaii (USA) were significantly lower than in Japan among both men and women, whereas rates in São Paulo, Brazil, were relatively similar to those in Japan [16]. These differences in incidence among three Japanese populations suggest that lifestyle changes, mainly dietary, are associated with a decreased risk of gastric cancer depending on the degree of westernization and the individual incidence rate in the respective host country (United States or Brazil).

According to cross-sectional studies of randomly selected Japanese Brazilians in the city of São Paulo (1989) and Japanese living in five prefectures across Japan (1989–1991), the dietary habits of Japanese Brazilians have shifted toward the pattern seen in Western countries [17]. However, Japanese Brazilians still consumed traditional and salted Japanese foods: 15% of Japanese Brazilian men aged 40–49 years consumed miso soup almost daily, and 4% consumed pickled vegetables [18]. The degree of westernization was not striking when compared with that of Japanese Americans. For example, only 2% of Japanese American men aged 45–69 years in Hawaii consumed miso soup almost daily during the 1960s [19]. Furthermore, salt excretion levels in 24-h urine samples among Japan-born male residents aged 40–59 years in São Paulo were 14.0 g/day for 21 volunteers originally from Iwate, Akita, and Nagasaki prefectures and 8.7 g/day for 12 volunteers from Okinawa Prefecture (unpublished data). These levels were closely comparable with those seen in each prefecture in Japan.

The substantial decrease in the incidence of gastric cancer among Japanese immigrants in the United States and the minimal decrease among Japanese immigrants in Brazil can be explained on the basis of the manner in which they continue to maintain Japanese dietary habits, which are typically high in salt.

Evidence from case-control studies

Many but not all case-control studies have found a positive association between gastric cancer and the intake of highly salted foods such as salted fish, cured meat, and salted vegetables or the use of table salt [4]. Several studies have quantitatively estimated total salt intake and found a strong positive association with the risk of gastric cancer, and several others evaluated its association with the intake of salted food such as salted fish and vegetables. In an evaluation performed by the

World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) in 1997 [3], 16 case-control studies reported an association between salt or salted food and the risk of gastric cancer. Eight of these estimated overall dietary salt or sodium intake; four showed strong statistically significant increases in risk [odds ratio (OR) = 2.1–5.0 for the highest intake level], whereas the remaining four showed no substantial association. Six of sixteen studies specifically examined the use of table salt, with three reporting statistically significant increased risks (OR = 1.6–6.2 for highest intakes) and two nonsignificant ORs. Several recent case-control studies have also revealed an association between salted food and the risk of gastric cancer [20–23].

Evidence from cohort studies

Prospective data are scarce, and only two studies were evaluated in the 1997 report by the WCRF and AICR [3]. One reported no association with the intake of table salt or soy sauce, although the second found an association between salted fish intake and an increased risk of gastric cancer in white American men, largely of Scandinavian and German descent [relative risk (RR) = 1.9 for the highest intake level].

Four more recent studies have also reported this association. Ngoan and colleagues examined 13000 Japanese men and women and identified 116 gastric cancer deaths during a 10-year follow-up. Higher consumption of pickled foods and traditional soups were associated with increased risk, although without statistical significance [24].

The Netherlands Cohort Study examined 120852 men and women and identified 282 gastric cancer cases at a 6.3-year follow-up [25]. Salt intake was measured by calculating the mean daily sodium intake (dietary salt) from 150 food items and by specific questions related to the consumption of salt. The intake of dietary salt and several types of cured meat showed a weak positive association with the risk of gastric cancer.

The Hisayama study examined 2476 men and women and identified 93 gastric cancer cases during a 14-year follow-up [26]. Dietary salt intake from a 70-item food frequency questionnaire was significantly associated with the risk of gastric cancer after considering *H. pylori* infection.

Our population-based prospective study examined a total of 18684 men and 20381 women aged 40–59 years and documented 358 men and 128 women with histologically confirmed gastric cancer during the 12 years of follow-up [27]. After adjustment for potential confounding factors, the category salt intake by quintile was dose-dependently associated with the risk of gastric cancer in men (for trend, $P < 0.001$), whereas no clear trend was seen in women ($P = 0.48$). The weak association between salt intake and gastric cancer in women may have been due to the relatively low validity of the estimated salt intake: the Spearman rank correlation with a 2-day urinary excretion level was only 0.12 for women but 0.38 for men. Although the association was less clear for miso soup, pickled vegetables, and dried fish, the frequency categories of highly salted food (e.g., salted fish roe and salted fish preserves) were strongly associated with gastric cancer risk in both sexes.

These findings imply that either the intake of highly salted food increases the risk of gastric cancer or that it is merely a good marker of a preference for salted food or salt intake in general. An alternative explanation for the strong association between highly salted food and gastric cancer might involve the presence of chemical carcinogens such as *N*-nitroso compounds, which are formed by the reacting nitrate or nitrite during the process of preservation and during digestion in the stomach. A recent meta-analysis based on six prospective and nine case-control studies showed that the consumption of processed meat was associated with an increased risk of gastric cancer [28]. Of note, processed meat often contains chemical carcinogens such as the *N*-nitroso compounds as well as high amounts of salt.

Salt, salted food intake, and Helicobacter pylori infection

Infection with *H. pylori* is an established risk factor of, but not a sufficient cause for, the development of gastric cancer [7,29]. It is important to elucidate the role salt and salted food play in the causal link between *H. pylori* infection and gastric cancer.

We previously tested the association between lifestyle factors and *H. pylori* infection in a cross-sectional study of 634 men aged 40–49 years selected randomly from five areas in Japan. A total of 474 of the 628 men evaluated were positive for immunoglobulin G antibody against the bacterium [30]. Intake of pickled vegetables was positively associated with the prevalence of *H. pylori* (ORs against men who consume <1 day/week = 1.19 for 1–2 days/week, 1.92 for 3–4 days/week, and 1.90 for 5–7 days/week; for trend, $P = 0.02$), as was the daily consumption of miso soup [OR against non-daily consumers = 1.60, 95% confidence interval (CI) = 1.03–2.49]. In contrast, occupation, number of siblings, education, smoking, alcohol consumption, and other dietary habits were not significantly associated with the prevalence of infection in this population. Although there are limitations to cross-sectional studies such as this one, the consumption of salted food appears to increase the risk of *H. pylori* infection.

Mucosal damage induced by salt and salted food may increase the possibility of persistent infection with

H. pylori [31]. Although salted food intake may increase the risk of *H. pylori* infection, salt per se was shown to act synergistically and dose-dependently to promote the development of gastric adenocarcinoma in Mongolian gerbils treated with *N*-methyl-*N*-nitrosourea (MNU) [32,33]. A synergistic exacerbatory effect of *H. pylori* infection and salted food intake has also been reported in case-control studies in Japan [34] and Korea [23].

Infection with *H. pylori*, however, is by itself unlikely to increase the intake of salted food, and *H. pylori* infection therefore cannot act as a confounder in the causal link between salt and salted food intake and gastric cancer. Restricting salt and salted food intake can, at the least, reduce the risk of gastric cancer.

In summary, a large body of evidence from descriptive and analytical epidemiological studies on the association between salt and salted food intake and the risk of gastric cancer indicates that dietary modification to reduce salt and salted food intake is probably protective against gastric cancer even after considering *H. pylori* infection.

Fruit and vegetables

Fruit and vegetables are rich sources of carotenoids, vitamin C, folate, and phytochemicals, which may have a protective role in the carcinogenesis process. It is likely that modulation of xenobiotic-metabolizing enzymes, in particular phase II enzymes, contributes to this putative preventive mechanism. The mechanisms of antioxidant activity may be also possible.

In 1997, an expert panel assembled by the WCRF and AICR concluded that diets high in fruit and vegetables "convincingly" protect against gastric cancer [3]. This evaluation was based mainly on reports of case-control studies. Since then, however, several cohort studies have reported conflicting results. The joint WHO/FAO Expert Consultation in 2003 concluded that fruit and vegetables "probably," but not "convincingly," decrease the risk of gastric cancer [5].

A subsequent report by the International Agency for Research on Cancer (IARC) determined that higher intake of fruit "probably" and higher intake of vegetables "possibly" reduce the risk of gastric cancer [35]. For fruit, the association has been evaluated in 10 cohort studies, most of which reported an inverse association with a summary value of 0.85 (95% CI = 0.77–0.95). Inverse associations were more striking in the 28 evaluable case-control studies, with summary ORs of 0.63 (95% CI = 0.58–0.69). For vegetables, the association has been evaluated in five cohort studies, most of which reported RRs below 1.0. However, none of these RR values were statistically significant, and the summary value was 0.94 (95% CI = 0.84–1.06). In contrast, most of the 20 evaluable case-control studies provided statistically significant ORs below 1.0 and a summary value of 0.66 (95% CI = 0.61–0.71). The reason case-control studies were more likely to show an inverse association is not clear, although one explanation might be the recall bias inherent to case-control studies. Furthermore, people with preclinical symptoms of gastric cancer or stomach disorders may change their dietary habits months or years before diagnosis.

A meta-analysis of cohort studies published up to 2004 reported nonsignificant summary estimates (RR for the highest versus the lowest consumption category) of 0.89 (95% CI = 0.78–1.02) for fruit (13 studies) and 0.98 (95% CI = 0.86–1.13) for vegetables (8 studies) [36]. However, the inverse associations became clearer when the studies were limited to those with incidence data (seven studies for fruit: RR = 0.82, 95% CI = 0.73–0.93; five studies for vegetables: RR = 0.88, 95% CI = 0.69–1.13) and with follow-up periods of 10 years or longer (three studies for fruit: RR = 0.66, 95% CI = 0.52–0.83; two studies for vegetables: RR = 0.71, 95% CI = 0.53–0.94).

Subsequent to the evaluation by the IARC [35] and the meta-analysis of Lunet et al. [36], several cohort studies have reported the association with fruit and vegetables. In a study in Sweden (139 gastric cancer cases among 70000 men and women) [37], subjects who consumed 2.5 servings of vegetables or more per day had a hazard ratio of 0.56 (95% CI = 0.34–0.93) compared with those who consumed less than 1.0 serving per day. The respective hazard ratio for fruit consumption was 0.86 (95% CI = 0.52–1.43). In the European Prospective Investigation into Cancer and Nutrition (330 gastric cancer cases among 520000 men and women) [38], a protective role for vegetable intake was observed for the intestinal type of gastric cancer. Citrus fruit consumption may play a role in protection against gastric cardia cancer.

In our cohort study with 400 gastric cancer cases among 40000 men and women, the RR associated with intake 1 day or more per week compared with less than 1 day per week was 0.64 (95% CI = 0.45–0.92) for yellow vegetables, 0.48 (95% CI = 0.25–0.89) for white vegetables, and 0.70 (95% CI = 0.49–1.00) for fruit. RRs associated with the quintile of total vegetable consumption were 1.00, 0.86, 0.75, 0.90, and 0.75 (for trend, P = 0.17). This association became clearer for the differentiated type of gastric cancer, at 1.00, 0.96, 0.78, 0.88, and 0.53 (for trend, P = 0.03). These findings suggest that vegetable and fruit intake, even in relatively low amounts, is associated with a lower risk of gastric cancer.

In summary, consumption of fruit and vegetables, particularly fruit, is probably protective against gastric cancer. Nevertheless, it remains unknown which con-

stituents in fruit and vegetables play a significant role in gastric cancer prevention.

Vitamin C (ascorbic acid)

Fruit and vegetables are rich sources of vitamin C. Vitamin C acts as an antioxidant and can quench reactive oxygen species produced in the gastric environment [39]; it is also known to inhibit production of carcinogenic *N*-nitroso compound in the stomach [40]. A possible relation between *H. pylori* infection and ascorbic acid is under investigation, as some research has indicated that high-dose vitamin C is effective in inhibiting *H. pylori* infection [41,42].

The WCRF/AICR report [3] concluded that high dietary vitamin C intake probably decreases the risk of gastric cancer. This conclusion is based on 1 of 2 cohort studies and 12 of 13 case-control studies showing inverse associations between dietary vitamin C intake and the risk of gastric cancer. In addition, one prospective study showed that baseline plasma vitamin C levels among subjects who died from gastric cancer (n = 20) was 20% lower than those who remained cancer-free (n = 2421) during more than 12 years of follow-up [43].

Since then a limited number of prospective studies have directly tested the association between dietary intake or blood level of vitamin C and the risk of gastric cancer. Dietary intake from comprehensive food frequency questionnaires was inversely associated with the risk of noncardia gastric cancer (n = 179) during a median follow-up of 12 years in Finnish male smokers [44] and with the risk of gastric cancer (n = 282) over 6.3 years in a Dutch cohort [45], with an inverse association, albeit diminished, in the latter study after excluding cases diagnosed within 2 years of baseline.

A nested case-control study in the European Prospective Investigation into Cancer and Nutrition (EPIC) compared the levels of dietary and prediagnostic plasma vitamin C between 215 gastric cancer cases and 416 matched controls [46]. No association with gastric cancer risk was observed for dietary vitamin C, whereas an inverse association was seen in the highest versus lowest quartile of plasma vitamin C (OR = 0.55, 95% CI = 0.31–0.97; for trend, P = 0.04). This inverse association was more pronounced in subjects consuming high levels of red and processed meat, a factor that may increase endogenous *N*-nitroso compound production. In a nested case-control study in a cohort of 20000 Chinese men (191 cases and 570 matched controls), increased serum levels of vitamin C were significantly associated with a reduced risk of gastric cancer among never-smoker and non-heavy-alcohol drinking men (for trend, P = 0.02) [47].

The use of vitamin C supplements was inversely and nonsignificantly associated with the risk of gastric cancer mortality (n = 1725; RR = 0.83, 95% CI = 0.68–1.01) among a million U.S. adults followed for 16 years (Cancer Prevention Study II) [48]. However, the decrease in risk was observed among users of shorter duration only, not among those of longer duration.

A nutritional intervention trial in Linxian, China, showed that supplementation with β-carotene (15 mg), α-tocopherol (30 mg), and selenium (50 μg) reduced the risk of gastric cancer mortality by approximately 20% after 5.25 years [49]. Other micronutrients, including vitamin C (120 mg), however, were associated with no reduction. In contrast, a chemoprevention trial of gastric dysplasia in Colombia in which vitamin C supplementation at 2 g/day for 6 years was tested as one of three treatment regimens showed that vitamin C as well as 30 mg β-carotene and anti-*H. pylori* therapy increased the regression rate of gastric precancerous lesions [50].

In our population-based, double-blind, randomized controlled trial to examine the effect of 5 years of vitamin C supplementation, a statistically significant difference was seen between the high-dose group (500 mg/day) and the low-dose group (50 mg/day) (P = 0.046) in the change in the pepsinogen I/pepsinogen II ratio, a marker of mucosal atrophic change in the stomach. This finding suggests that vitamin C supplementation may protect against the progression of gastric mucosal atrophy [51].

In summary, when the relatively consistent epidemiological evidence and biological plausibility are considered, dietary or supplemental vitamin C intake probably decreases the risk of gastric cancer.

Green tea and other beverages

Green tea

Green tea contains polyphenols, more commonly known as catechins. Major green tea catechins include (–)-epigallocatechin-3-gallate (EGCG), (–)-epigallocatechin (EGC), (–)-epicatechin-3-gallate (ECG), and (–)-epicatechin (EC). Antioxidant activities and the ability to inhibit the nitrosation of polyphenols have been isolated from green tea in both in vitro and in vivo studies [52–54]. In addition, recent research has proposed many other possible mechanisms for the cancer-inhibitory effects of green tea, including modulation of signal transduction pathways, leading to the inhibition of cell proliferation and transformation, induction of apoptosis and cell cycle arrest, and inhibition of tumor invasion and angiogenesis [55–57].

The WCRF/AICR report [3] included five case-control studies investigating the relation between green

tea intake and gastric cancer risk. Among these studies, four suggested a protective effect. Although a Japanese study showed a significant decrease in risk only among those consuming 10 cups or more per day, a Chinese study identified a clear dose relation. In contrast, a case-control study in Japan observed no material associations for green tea. Based on these findings, the WCRF/AICR report concluded that high consumption of green tea "possibly" decreases the risk of gastric cancer. More recent case-control studies have also shown a reduction in the risk with green tea intake, most with statistical significance [58–61].

In contrast to laboratory studies and most case-control studies, however, all but one recent cohort study have shown no protective effect of green tea for gastric cancer [62–65]. In a population-based prospective study conducted in Miyagi Prefecture in northern Japan, the RRs associated with drinking one or two, three or four, and five or more cups of green tea per day, as compared with less than one cup per day, were 1.3 (95% CI = 0.8–1.9), 1.2 (95% CI = 0.8–1.8), and 1.5 (95% CI = 1.0–2.1), respectively, in men (for trend, $P = 0.03$), and 0.8 (95% CI = 0.5–1.5), 0.7 (95% CI = 0.4–1.3), and 0.8 (95% CI = 0.5–1.3), respectively, in women (for trend, $P = 0.46$) [62]. In a nationwide multicenter prospective study, no inverse association was found between green tea consumption and gastric cancer death, with the risks associated with drinking 1 or 2, 3 or 4, 5–9, and ≥ 10 cups of green tea per day, relative to those of drinking less than 1 cup per day, of 1.6 (95% CI = 0.9–2.9), 1.1 (95% CI = 0.6–1.9), 1.0 (95% CI = 0.5–2.0), and 1.0 (95% CI = 0.5–2.0), respectively, in men (for trend, $P = 0.669$), and 1.1 (95% CI = 0.5–2.5), 1.0 (95% CI = 0.5–2.5), 0.8 (95% CI = 0.4–1.6), and 0.8 (95% CI = 0.3–2.1), respectively, in women (for trend, $P = 0.448$) [63]. Furthermore, green tea consumption was virtually unrelated to the incidence of any cancer, including gastric cancer, in a follow-up study of atomic bomb survivors in Hiroshima and Nagasaki [64].

In our cohort study, among 73 000 subjects with 890 gastric cancers, although no association between green tea consumption and gastric cancer was observed among men, decreased risk was suggested in women, with RRs and 95% CI for one or two, three or four, and five or more cups per day compared to less than one cup per day of 0.85 (95% CI = 0.53–1.38), 1.04 (95% CI = 0.68–1.58), and 0.67 (95% CI = 0.43–1.04), respectively (for trend, $P = 0.08$) [65]. This association was further strengthened when cancer was restricted to the distal portion, with a RR of 0.51 (95% CI = 0.30–0.86) for consumption of five or more cups of green tea (for trend, $P = 0.01$). These results are consistent with those of previous prospective studies in that decreased risk was more apparent in women.

In summary, consumption of green tea is possibly associated with decreased risk of gastric cancer, especially in Japanese women, most of whom are nonsmokers. Further prospective studies with detailed information are needed to clarify the role of green tea on gastric carcinogenesis.

Black tea and coffee

Although catechin levels in black tea are only about 30% of those in green tea, the inhibitory activity of black tea against tumorigenesis has been shown to be comparable to that of green tea in several animal models [66]. Most of three prospective studies and 12 case-control studies showed no association with the risk of gastric cancer. Thus, the WCRF/AICR found that high consumption of black tea "probably" has no association with the risk of gastric cancer [3]. Only one prospective study in Japan has been conducted since then, and it showed a nonsignificant increase in the risk of gastric cancer among women who drink black tea more than several times per week [67]. It is possible that lifestyle, which was not investigated in this study, was associated with the increased risk of gastric cancer. Thus, the evidence is less clear for black tea than for green tea.

Caffeine, kahweol, and cafestol in coffee may contribute to a protective effect against cancer [68]. Based on the evaluation of two prospective and eight case-control studies, which showed no statistically significant association between coffee consumption and gastric cancer, the WCRF/AICR concluded that high consumption of coffee "probably" has no relation with the risk of gastric cancer [3]. In a more recent systematic review and meta-analysis of 23 studies (7 cohort studies and 16 case-control studies) [68], coffee intake showed no effect on gastric cancer when all studies were combined (OR = 0.97, 95% CI = 0.86–1.09), with a combined risk estimate of 1.02 (95% CI = 0.76–1.37) for cohort studies, 0.90 (95% CI = 0.70–1.15) for population-based case-control studies, and 0.97 (95% CI = 0.83–1.13) for hospital-based case-control studies. Notwithstanding that risk estimates differed significantly according to country of origin, with North American studies presenting a significantly higher risk, this meta-analysis showed no overall effect of coffee consumption on gastric cancer risk.

In summary, there is no apparent evidence that black tea or coffee consumption has any effect on the risk of gastric cancer.

Conclusions

Although the eradication of *H. pylori* may be a promising strategy for gastric cancer prevention, most middle-

aged and elderly Japanese are already infected with this pathogen [30]. The worldwide decrease in the age-adjusted incidence of gastric cancer over the last 50 years occurred without any intentional *H. pylori* infection eradication program. Rather, and perhaps more importantly, it can be related to decreased intake of salt and salted food and increased intake of fresh fruit and vegetables, which arose subsequent to the mass availability of refrigeration. Dietary modification to reduce salt and salted food intake and to increase intake of fruit, particularly vitamin C — as well as quitting smoking — represents an effective, practical, low-cost means of preventing gastric cancer.

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