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Review

Prevention of gastric cancer: diet modifications

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SUMMARY

According to the available evidence a probable protective role of vegetables, especially allium vegetables, and fruit consumption against gastric cancer risk probably exist. It also seems probable that high salt intake increases gastric cancer risk. Furthermore, the available evidence, though limited, is suggestive of a protective role of pulses and foods containing selenium. Limited, but still suggestive evidence exists concerning an inverse association between chilli, processed meat, smoked foods and grilled or barbecued animal foods with gastric cancer risk. A great number of other dietary factors are being investigated, but it is still not safe to reach any conclusions concerning them.

Key words: Gastric cancer, diet, prevention

INTRODUCTION

It has been well documented that, during the last fifty years, the overall rates of incidence and mortality of gastric cancer are decreasing.[1,2] On the other hand, it should also be stressed that two types of gastric cancer have been examined. The first is the distal gastric cancer which is more common in African and in low-to-middle income countries and the other includes the proximal tumours, which are the ones located at the gastro-oesophageal junction and, in most of the cases, are examined along with oesophageal adenocarcinomas. The latter is more common among white people and in high income countries.

Apart from the fact that some people are genetically predisposed to gastric cancer, it is also well known that infection with H. pylori plays in important role in the aetiology of distal stomach cancers.[2] Furthermore it has also been well documented that other environmental factors, a great part of which are dietary habits, play an important role in gastric cancer aetiology.[3] A review of the relevant available evidence of the last decade has been attempted in order to identify the lifestyle and dietary factors, the anthropometric characteristics, the dietary patterns and the selected food item consumption that seem to play a role in gastric cancer aetiology. At this point it should be stressed that, when trying to identify such associations, it should be taken into consideration that the multifactorial nature of such diseases, along with the complexity of the human diet, sometimes make it difficult to identify the relative importance of each nutrient in each food item.

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Evidence concerning lifestyle factors

Tobacco smoking

More recently stomach cancer has been associated tobacco smoking. However, the association remains unclear. From the findings of a recent study using extended follow-up of the original Whitehall prospective cohort study a positive association between cigarette smoking and gastric cancer occurred.[4] Furthermore, from the findings of a hospital-based case-control study that was held in Mizoram, a state of India with high stomach cancer incidence, it was proposed that any form of tobacco use increases stomach cancer risk.[5] Finally, from a recent systematic review of epidemiology evidence, a moderate increase in gastric cancer risk by tobacco smoking in the Japanese population has been found.[6]

Concerning the observed association between cigarette smoking and gastric cancer risk, it should be stressed that there seems to be a combined influence of cigarette smoking and infection with H. pylori on gastric cancer risk.[7] Finally it has also been proposed that cigarette smoking associates differently with certain subtypes of stomach cancer.[8]

The evidence concerning the association between cigarette smoking and stomach cancer suggests a positive association, but needs further investigation.

Physical activity

The association between physical activity and stomach cancer is still not fully understood, but from the available evidence it seems that increased physical activity protects against gastric cancer,[9] especially women.[10] However, it should be noted that there is lack of evidence concerning the underlying biological mechanisms related to the hypothesized association and that the latter does not seem to be due to the impact of physical activity on body weight.[9]

Obesity

Over the last few years it has clearly been proposed that obesity increases gastric cardia cancer risk. However, it should be noted that there is inconsistency in the evidence concerning the association between BMI and non-cardia gastric cancer risk and that the existing evidence is, generally, of poor quality. From a recent population-based cohort study that was held in Norway it was proposed that BMI does not seem to be associated with non-cardia gastric cancer.[9]

The association between obesity and cancer has mainly been investigated among populations of Europe and the United States. From the findings of the Korea National Health Insurance Corporation study, it was proposed that gastric adenocarcinoma was increased only among obese Korean men who never smoked, but no dose-dependent relationship was found.[11] Furthermore, from a recent prospective cohort study held on the participants of the Netherlands Cohort Study it was proposed that higher BMI was strongly associated in a dose-dependent manner with gastric cardia adenocarcinoma. Despite the fact that the underlying biological mechanism of this association is still not fully understood, it has been proposed that it might be related to the observed effect of obesity on gastro-oesophageal reflux.[12-13]

From a recent systematic review and meta-analysis of observational studies investigating the hypothesised association between BMI and gastric cardia adenocarcinoma a weak association was found.[14]

It is known that abdominal obesity increases cancer risk, sometimes independently of BMI, and certain biological mechanisms have been proposed to support the observed association. However, from the findings of a recent case-control study held at the participants of the Kaiser Permanente Multiphasic Health Check Up Cohort, no association was found between abdominal obesity and gastric cardia adenocarcinoma

Risk.[15] As long as it concerns the impact of abdominal obesity on gastric cancer risk further research is needed in order to draw final conclusions.[16]

Adiponectin is an adipocyte-secreted hormone and its circulating levels are determined by genetic factors, adiposity and nutrition.[17] At this point it should be noted that it has been proposed that adiponectin circulating levels are inversely associated with BMI[16] and they have been found lower in patients with certain cancer types. Adiponectin's influence on cancer risk could be mediated through its effects on insulin resistance, although some direct actions on tumour cells have also been proposed.[17]

From a relatively recent study it has been proposed that low plasma adiponectin levels are associated with increased risk of gastric cancer and the association seems to be stronger for cancer of the upper stomach.[16]

Height

From a recent cohort study held on the participants of the Netherlands Cohort Study, height was not found to be associated with gastric cardia adenocarcinoma, but in general there is still a lack of evidence concerning the association between height and gastric cancer risk.[12]

Evidence concerning food intake and selected dietary factors

Vegetables

A large number of case-controled, cohort and ecological studies have examined the impact of vegetable consumption on gastric cancer risk.[3,1] Most of them have found that increased vegetable intake reduces gastric cancer risk, with the case-controled data being, generally, more consistent.[3,18]

Furthermore, a close-response relationship has also been found in these data. Finally, when examining specific vegetable categories green and yellow vegetables seem to have greater impact on gastric cancer risk.

When it comes to the underlying biological mechanisms of this association, it should be noted that a great number of vegetable constituents with potential antioxidant activity could exert a protective role against gastric cancer.[3]

Allium vegetables

A relatively small number of cohort and ecological and a greater number of case-control studies have investigated the association between allium vegetables intake and gastric cancer risk. Even fewer studies investigated the as-

sociation between garlic consumption and gastric cancer risk. In general, it has been found that increased intake of those food items reduces gastric cancer risk.[3]

A meta-analysis of the available epidemiologic evidence concerning the consumption of raw, and/or cooked garlic and stomach cancer found that high intake of raw and cooked garlic may exert a protective effect against stomach cancer.[19] However, a very recent analysis made with the use of the Food and Drug Administration's evidence-based review system for the scientific evaluation of health claims led to the conclusion that the available evidence is not supportive of an association between garlic intake and reduced gastric cancer risk.[20]

Concerning the underlying biological mechanism of the hypothesized association between allium vegetable consumption and gastric cancer risk, it is known that allium vegetables and garlic, in particular, have antibiotic properties and it is possible that they could exert a direct action against *H. pylori*. However the findings of relevant studies held in humans do not seem to support this hypothesis.[3]

Fruits

Many case-control, cohort and ecological studies have examined the impact of fruit consumption on gastric cancer risk. Most of them found that increased fruit intake decreases gastric cancer risk, with the case-control data being, generally more consistent and showing a dose-response relationship.[3] However, a meta-analysis of the cohort data found no significant association between fruit consumption and gastric cancer risk.[18]

Finally, it should be noted that fruit consumption has been found not to be associated with gastric cardia cancer risk, but it was inversely associated with gastric noncardia cancer risk among male smokers participants of the a-Tocopherol, b-Carotene Cancer Prevention Study.[21]

Concerning the underlying biological mechanisms of this association, it should be noted that fruits, like vegetables, are rich in dietary factors with potential antioxidant activity.[3]

At this point it should be noted that the impact of fruit and vegetable intake has been investigated in common in many studies. A prospective investigation of the association between fruit and vegetable consumption and gastric cancer incidence among the participants of the Swedish Mammography Cohort and the Cohort of Swedish Men found a statistically significant association between vegetables consumption, mainly green leafy and root vegetables, and gastric cancer risk, while, when it comes to fruits no statistical association was found.[1]

The association between fruit and vegetable consumption and gastric cancer risk was also investigated among the participants of the European Prospective Investigation into Cancer and Nutrition. The findings of this study are not supportive of an association between fresh fruit or total vegetable intake and gastric cancer. Furthermore, from the same study it was proposed that infection with Helicobacter pylori did not seem to modify the association between fruit and vegetable intake and gastric cancer risk.[22]

Finally the impact of yellow and green vegetables and fruit consumption on gastric cancer has been investigated among the participants in the Hiroshima/Nagasaki Life Span Study and it was found that fruit consumption significantly reduced stomach cancer risk.[23]

Salt

An important amount of cohort, case-control and ecological studies have investigated the association between sodium intake, as well as salt added at the table and gastric cancer risk. The findings of most of them showed that increased sodium intake is associated with a statistically significant increased risk of gastric cancer. On the other hand, when examining the association between total salt intake and gastric cancer risk, it seems in general, increased total salt intake that increases gastric cancer risk, but the association found is not statistically significant.[3]

However, the findings of a recent population-based cohort study held on the participants of the Nord-Trondenlag in Norway are not supportive of the hypothesis that salt intake increases gastric adenocarcinoma risk.[24]

It should also be said that there is evidence concerning the underlying biological mechanism of this association. First of all, it has been shown that in animal models high salt along with cyclooxygenase-2 overexpression, seem to promote gastric chemical carcinogenesis.[25]

Furthermore there is evidence supportive of the hypothesis that salt increases the formation of N-nitroso compounds. It is also known that *H. pylori* responds to salt concentrations. More specifically, it seems that *H. pylori* infection seems to be facilitated by high salt intakes.[3]

Soy and soy products

A relatively small number of cohort, case-control and ecological studies has investigated the association between soy and soy product intake and gastric cancer risk. A meta-analysis of the cohort data showed that soy and soy product consumption was inversely associated with gastric cancer risk, but the association was not statistically significant.

On the other hand, a meta-analysis of the case-control data found a statistically significant inverse association between soy and soy product intake and gastric cancer risk.[3]

The association between soy product intake and the risk of certain cancer types was investigated in an ecological study held in Japan. The findings of this study supported a modest prevention of soy product intake against stomach cancer risk. Although it is known that soy products are rich sources of isoflavones which are known to exert anticarcinogenic actions due to their antioxidant activity,[26] further research is needed in order to draw final conclusions. Furthermore, from a metaanalysis held in order to investigate the association between soy foods intake and stomach cancer risk, it has been proposed that until potential confounders, such as fruit, vegetables and salt intake are adjusted for, no safe conclusions can be reached.[27]

Selenium

A relatively small number of ecological, cohort and case-control studies have been held in order to investigate the association between selenium intake or serum, nails and blood selenium levels and gastric cancer risk. A meta-analysis of the available cohort data showed that selenium levels were inversely associated with gastric cancer risk, but the association was not statistically significant. A meta-analysis of the case-control data found a statistically significant inverse association between selenium levels and gastric cancer risk.[3] At this point it should be noted that from a prospective study held on the participants of the General Population Trial of Linxian, China, a significant inverse association was found between serum selenium levels and gastric cardia cancer, but no significant association was found between serum selenium levels and gastric noncardia cancer.[28]

Concerning the potential underlying biological mechanisms of the hypothesized association between selenium levels and gastric cancer risk, selenium is known to be implicated in oxidative damage repair and prevention, immune response regulation and intracellular signalling.[29] However, there still is lack of evidence in order to draw final conclusions concerning the association between the consumption of foods containing selenium and gastric cancer risk.[3]

Chilli

A small number of case-control studies have examined the association between chilli intake and gastric cancer risk, but, in general, it has been shown that higher intake of chilli seem to increase gastric cancer risk, the findings are inconsistent. Despite the fact that it is known that the use of increased amount of chilli could irritate the stomach and cause inflammation, it still is not safe to reach conclusions concerning the hypothesized association.[3]

Processed meat

In general, most of the studies held in order to investigate the association between processed meat intakes with gastric cancer risk, showed a positive association. A meta-analysis of eight cohort studies found that increased processed meat intake was associated with increased gastric cancer risk, but the association was not significant. A meta-analysis of 21 case-control studies found this association to be statistically significant.[3]

Furthermore, a relatively recent meta-analysis of cohort and casecontrol studies examining the same association found a possible positive association. However, future research is needed in order to control for potential confounders, such as genetic polymorphisms, interactions with other dietary factors, as well as *H. pylori* infection. Finally, it should be found whether the anatomic subsite or the histological subtype of gastric cancer modifies the observed association.[30]

The underlying biological mechanisms, relevant to this association include nitrates, which are used in processed meat preservation and can lead to N-nitroso compound formation. Furthermore, it is known that processed meats are rich in salt.[3]

Meat

A recent study held on the participants of the European Prospective Investigation into Cancer and Nutrition found a positive association between total, processed and red meat intake and gastric noncardia cancer, which was statistically significant. Furthermore, the observed associations between total and processed meat intakes and gastric noncardia cancers seemed to be modified by *H. pylori* infection. In any case, total, processed and red meat intake were found not to be associated with gastric cardia cancer.

The biological mechanisms used to explain the observed association include the fact that red meats contain haem, fat and protein, nitrosamines, nitrites, salt, heterocyclic amines and polycyclic aromatic hydrocarbons.[31]

However, from a population-based case-control study which was held in order to investigate the association between heterocyclic amine intake and gastric cardia cancer no association was found. This finding, along with the lack of established biological mechanisms of the hypothesized association, supports the need of further research.[32]

Smoked foods

A small number of case-control and ecological studies has investigated the association between smoked food consumption and gastric cancer risk. In general a positive association was found, though it was not statistically significant. The biological mechanisms proposed to support the hypothesis include the formation of polycyclic aromatic hydrocarbons and the high content of salt in smoked foods.[3]

Tea

In general, the findings of most of the case-control studies held in order to investigate the association between green tea consumption and gastric cancer risk were supportive of a statistically significant inverse association. However, the relevant prospective studies do not seem to support the hypothesis.[33] Green tea is thought to exert an effect on gastric cancer risk due to its content in catechins, which are polyphenols with known antioxidant activity. From a recent case-control study it was found that plasma levels of tea polyphenols were inversely associated with gastric cancer risk in women only. From the same study it has been proposed that cigarette seems to modify the observed association.[34] Finally, a very recently published study showed a potential mechanism which explains the way tea catechins reduce gastric inflammation.[35]

Alcohol

A recent review of the epidemiologic studies held in order to investigate the association between alcohol consumption and gastric cancer risk among Japanese population, found that the available evidence is still insufficient to support a causal relationship.[36]

Other relevant evidence

From a recent study held in order to identify the association between certain dietary patterns and gastric cancer risk it was found that diets rich in vegetables, fruits and fish were inversely associated with gastric adenocarcinoma risk, while diet rich in soft drinks, refined grains, sugars and processed meats were positively associated with the same risk.[37] Furthermore, it has also been proposed that reducing the prevalence of smoking, obesity and gastroesophageal reflux and increasing the consumption of fruits and vegetables could decrease the incidence of gastric cancer.[38]

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