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Alcohol consumption and the risk of Barrett's esophagus: A meta-analysis

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Abstract

AIM: To evaluate the possible association between alcohol consumption and Barrett's esophagus (BE).

METHODS: We performed a systematic literature search of multiple online electronic databases. Inclusion criteria entailed studies about alcohol and BE. Meta-analysis was conducted to evaluate odds ratio (OR) and 95%CIs for the association between alcohol consumption and BE.

RESULTS: Twenty studies comprising 4758 patients with BE were included in the meta-analysis. The risk of BE in patients with alcohol consumption was increased compared with control groups (OR = 1.01; 95%CI: 1.00-1.02), especially in case-control and cohort, European and Asian, and hospital studies, but there was a decreased risk of BE associated with alcohol consumption from American studies (OR = 0.86; 95%CI: 0.77-0.96). At the same time, there was no significant association between BE and alcohol consumption in community studies (OR = 0.97; 95%CI: 0.84-1.12) and the type of alcohol (wine, beer and liquor) studies.

CONCLUSION: Our meta-analysis found that alcohol consumption was associated with an increased risk of BE, especially for European and Asian drinkers.

Key words: Barrett's esophagus; Alcohol consumption; Risk factors; Meta-analysis

Core tip: Barrett's esophagus (BE) is an acquired condition in which specialized columnar epithelium replaces the usual stratified squamous epithelium lining the esophagus. Some studies have investigated the association between alcohol consumption and BE, with conflicting conclusions. We performed a meta-analysis of the possible association between alcohol consumption and BE and found that alcohol consumption was associated with an increased risk of BE, especially for European and Asian drinkers.

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INTRODUCTION

Barrett's esophagus (BE) is an acquired condition in

Table 1 Characteristics of included studies

Ref.	Year	Country	Source	Study type	Number of BE patients
Levi *et al*[20]	1990	Switzerland	Hospital	Case-control	140
Gray *et al*[21]	1993	United Kingdom	Hospital	Case-control	58
Eloubeidi *et al*[22]	2001	United States	Hospital	Case-control	88
Gerson *et al*[25]	2002	United States	Hospital	Case-control	24
Conio *et al*[24]	2002	Italy	Hospital	Case-control	147
Avidan *et al*[23]	2002	United States	Hospital	Case-control	1189
Olliver *et al*[26]	2005	United Kingdom	Hospital	Case-control	50
de Jonge *et al*[27]	2006	The Netherlands	Hospital	Case-control	232
Kim *et al*[29]	2007	South Korea	Community	Cohort study	101
Anderson *et al*[28]	2007	Ireland	Community	Case-control	223
Akiyama *et al*[30]	2008	Japan	Hospital	Case-control	211
Anderson *et al*[17]	2009	Ireland	Hospital	Case-control	224
Fouad *et al*[32]	2009	Egypt	Hospital	Case-control	73
Kubo *et al*[18]	2009	United States	Community	Case-control	320
Akiyama *et al*[31]	2009	Japan	Hospital	Cohort study	374
Shi *et al*[39]	2010	China	Hospital	Case-control	179
Thrift *et al*[19]	2011	Australia	Community	Case-control	393
Steevens *et al*[16]	2011	The Netherlands	Community	Cohort study	370
Thrift *et al*[33]	2014	Australia	Hospital	Case-control	258
Yates *et al*[34]	2014	United Kingdom	Community	Cohort study	104

BE: Barrett's esophagus.

which specialized columnar epithelium replaces the usual stratified squamous epithelium lining the esophagus[1,2]. BE affects approximately 2% of the Western population and is most prevalent in white men aged over 50 years[3-6]. The prevalence of BE in other populations, such as Asian and African, is uncertain because many patients with BE are asymptomatic and do not accept a diagnostic endoscopy. Among patients with gastroesophageal reflux disease (GERD), the prevalence of BE increases to between 3% and 15%[7,8]. BE is an important risk factor for the development of esophageal adenocarcinoma (EAC)[9] and the incidence of EAC has significantly increased in Western countries over recent decades[10,11]. Moreover, survival for patients with EAC remains poor, with median survival less than 12 mo[12]. Understanding the causes of BE is a necessary step towards preventing EAC.

Potential risk factors for BE in the general population include white race, older age, cigarette smoking, abdominal obesity and GERD[13,14], while use of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) may prevent the development of BE[15]. There is no meta-analysis about the association between alcohol consumption and BE. If the associations were shown to be causal, then alcohol would be a key target for early prevention of EAC. The results among these studies reporting the association between BE and alcohol consumption have been conflicting and the type of alcohol (wine, beer, liquor) can affect this association. For example, some studies have reported an inverse association with wine consumption, others have found lower risk associated with beer and some evidence for higher risk associated with liquor[16-19].

To confirm the relationship between alcohol consumption and BE, we conducted a meta-analysis of studies which calculated the prevalence of BE in an alcohol consumption population that also provided a quantitative estimate of the risk of BE in an alcohol consumption population. At the same time, we conducted further analyses to examine the association in different study types (case-control, cohort study), countries (Europe, America and Asia), sources (hospital, community) and alcohol type (wine, beer and liquor).

MATERIALS AND METHODS

Literature search

We conducted the meta-analysis with the standard protocol for study identification, inclusion, data abstraction and analysis. The PubMed, EMBASE, MEDLINE and Web of Science databases were used primarily to identify potentially relevant published studies. A search of studies in these databases from inception through to 30 October 2014 was performed using medical subject headings including "Barrett's esophagus", "BE", "risk factors", "alcohol", "wine", "beer" and "liquor". The search was not limited by language.

Study selection

Inclusion criteria were as follows: (1) case-control, cross-sectional and cohort study designs; (2) BE was diagnosed by endoscopy and confirmed that specialized columnar epithelium replaced the usual stratified squamous epithelium lining the esophagus; (3) the prevalence of BE in alcohol consumption groups and control groups was examined; and (4) the odds ratio (OR) and the 95%CI was reported or these data could be calculated.

The information collected from the studies included the publication year, country, source, study design and number of BE patients (Table 1). The outcome of the analysis was the OR of the prevalence of BE in an alcohol consumption group versus a control group and subgroup analysis was conducted in different study types (case-control, cohort study), countries (Europe, America

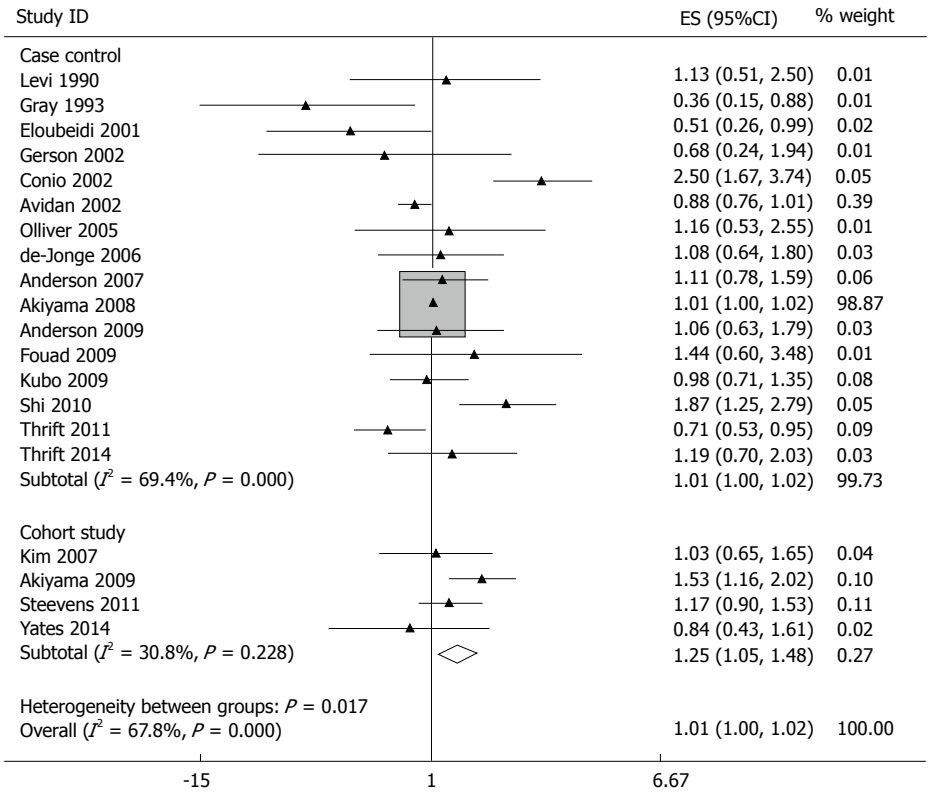

Figure 1 Forest plot of the prevalence of Barrett's esophagus in alcohol consumption groups *vs* control groups and subgroup analysis by study type (case-control and cohort study).

and Asia), sources (hospital, community) and alcohol type (wine, beer and liquor). Included studies were collected in EndNote X4 software. Two investigators browsed the titles and abstracts of the studies and studies that met the criteria were further analyzed for eligibility. For studies that met the inclusion criteria of the meta-analysis, we extracted the data using standard operating norms. Information about qualifying studies included the publication year, country, source, study design and number of BE patients. Inconsistent results were determined by the senior investigator. The consistency rate among the authors was 0.994. The methodological quality of each trial was assessed by the following criteria: study design, method of BE diagnosis and method of patient enrollment.

Data synthesis and analysis

The inconsistency index (I^2) was calculated to assess the inter-study heterogeneity and significant difference was set at the $P < 0.10$ level. We chose the random-effects model to calculate the pooled OR if there was heterogeneity among these studies and the fixed-effects model to calculate the pooled OR if there was homogeneity. Summary OR and 95%CI were calculated to describe the relationship between alcohol consumption and the risk of BE. We chose a funnel plot analysis to estimate publication bias. The meta-analyses were done using STATA 12.0 software.

RESULTS

Our systematic review identified 38 studies. After we carefully reviewed these studies, twenty met the inclusion criteria. Information regarding the author, year, country, source, study type and number of BE patients of the included studies can be found in Table 1. There are two types of studies, case-control and cohort. The studies come from different geographical regions, with 10 European, 6 American and 4 Asian studies. The number of the study population ranged from 97 to 4736 and BE patients ranged from 24 to 1189.

Twenty studies were included in our meta-analysis for the prevalence of BE in comparing alcohol consumption groups with control groups. BE patients were more likely to be in alcohol consumption groups than control groups (OR = 1.01; 95%CI: 1.00-1.02) (Figure 1). There was significant heterogeneity (P = 0.017). The funnel plot (Figure 2) is generally symmetrical, showing no evidence of publication bias (Begg's Test, Z = 0.36, P = 0.721). The subgroup analysis of sixteen case-control studies showed an increased risk of BE associated with alcohol consumption (OR = 1.01; 95%CI: 1.00-1.02) (Figure 1) and the four cohort studies also showed an increased risk of BE associated with alcohol consumption (OR = 1.25; 95%CI: 1.05-1.48) (Figure 1).

The subgroup analysis of ten European studies showed an increased risk of BE associated with alcohol consumption (OR = 1.21; 95%CI: 1.04-1.41) (Figure 3), six American studies showed a decreased risk of BE associated with alcohol consumption (OR = 0.86; 95%CI: 0.77-0.96) (Figure 3) and the four Asian studies showed an increased risk of BE associated with alcohol con-

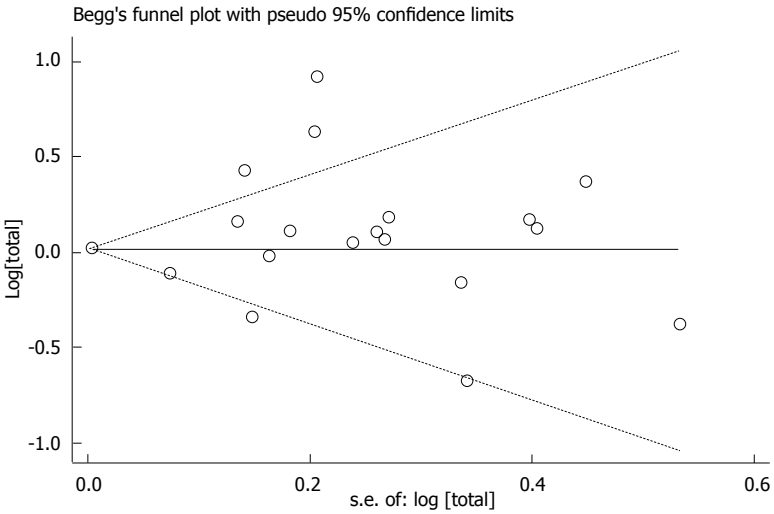

Figure 2 Begg's funnel plot analysis of each study.

sumption (OR = 1.01; 95%CI: 1.00-1.02) (Figure 3).

The subgroup analysis of fourteen hospital studies showed an increased risk of BE associated with alcohol consumption (OR = 1.01; 95%CI: 1.00-1.02) (Figure 4) and the six community studies did not show an increased risk of BE associated with alcohol consumption (OR = 0.97; 95%CI: 0.84-1.12) (Figure 4).

At the same time, the type of alcohol consumption is divided into wine, beer and liquor. The subgroup analysis of five studies about wine did not show an increased risk of BE associated with alcohol consumption (OR = 1.00; 95%CI: 0.85-1.17) (Figure 5), the five studies about beer did not showed an increased risk of BE associated with alcohol consumption (OR = 0.94; 95%CI: 0.79-1.12) (Figure 5) and the five studies about liquor did not show an increased risk of BE associated with alcohol consumption (OR = 1.10; 95%CI: 0.93-1.29) (Figure 5).

DISCUSSION

Lifestyle factors, such as cigarette smoking, alcohol consumption and exercise, are increasingly important for many diseases. Alcohol consumption is considered to be an important risk factor for gastric cancer, cirrhosis and liver cancer. Although there are many studies about the association between alcohol consumption and BE[17,18,20-34], there is no exact definition. Our meta-analysis identified numerous studies examining the relationship between BE and alcohol consumption. We found that BE patients were more likely to be in alcohol consumption groups than control groups. At the same time, we conducted further analyses to examine the association in different study types (case-control, cohort study), countries (Europe, America and Asia), sources (hospital, community) and alcohol type (wine, beer and liquor). We found that there was an increased risk of BE associated with alcohol consumption from case-control and cohort, European and Asian, and hospital studies, but there was a decreased risk of BE associated with alcohol consumption from American studies. At the same time, there was no significant association between BE and alcohol consumption in community studies and the type of alcohol (wine, beer and liquor) studies.

There are several potential mechanisms through which alcohol consumption may be associated with BE, an early event in the development of esophageal adenocarcinoma. First, gastroesophageal reflux (GER) is the main predisposing risk factor for BE. Alcohol, which has been shown to reduce gastroesophageal sphincter pressure, can lead to an increase in GER and the risk of developing BE. This is reflected in the 1.6 to 3.0-fold increased risk of GER symptoms in people who drink alcohol. However, cautious interpretation of this finding is advised because of the lack of internal consistency. Alcohol consumption was significantly lower in population controls reporting GER symptoms, suggesting that patients with GER symptoms may avoid or reduce their alcohol intake after the development of GER symptoms. Second, there are different results in drinking patterns of alcohol. Wine drinkers are more likely than liquor drinkers to consume their alcoholic beverage with food. Consumption of alcohol with food may reduce the direct damage of the lining of esophagus, reducing the carcinogenesis process. At the same time, red wine contains compounds, such as polyphenol, that have a significant protective effect on oxidative stress[35]. Some clinical and animal studies have demonstrated that anti-oxidants may decrease the risk of BE and prevent the development of esophageal adenocarcinoma[36-38]. Drinking wine may reduce the oxidative damage caused by GERD, thereby decreasing the risk of esophagitis and BE among GERD patients, and the protective effects of alcohol consumption may arise from reduction in insulin resistance or increased levels of lipoproteins. Our results showed that there was an increased risk of BE associated with alcohol consumption from European and Asian studies, but there was a decreased risk of BE associated with alcohol consumption from American studies. This is because Americans are more likely than Europeans and Asians to drink wine. However, our meta-analysis showed that there was no significant association between BE and alcohol consumption in the type of alcohol (wine, beer and

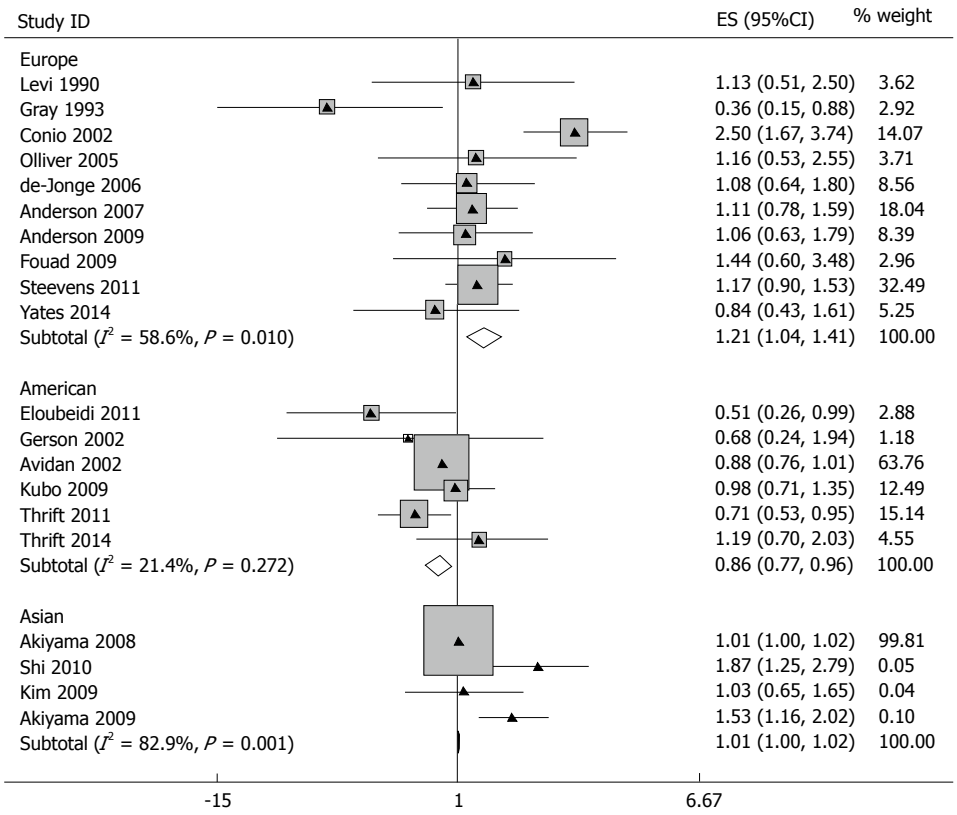

Figure 3 Forest plot of the prevalence of Barrett's esophagus in alcohol consumption groups *vs* control groups in different geographical regions (Europe, America, Asia).

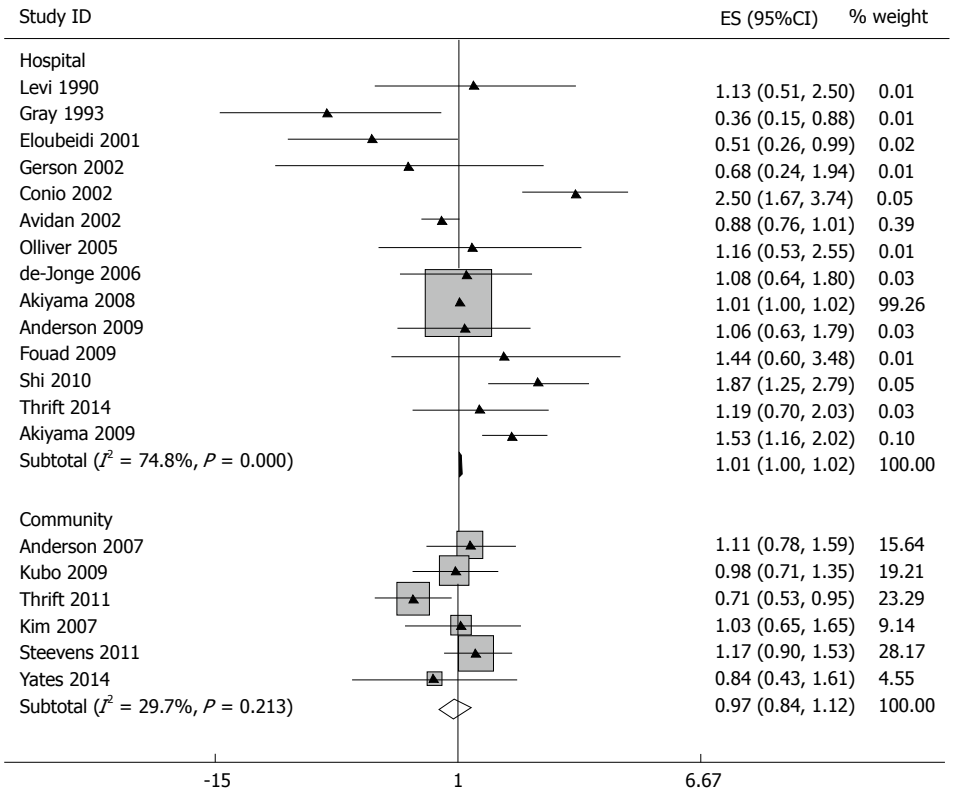

Figure 4 Forest plot of the prevalence of Barrett's esophagus in alcohol consumption groups *vs* control groups from different sources (hospital, community).

liquor) studies so we cannot use these theories to explain our results; perhaps this is due to the small sample size.

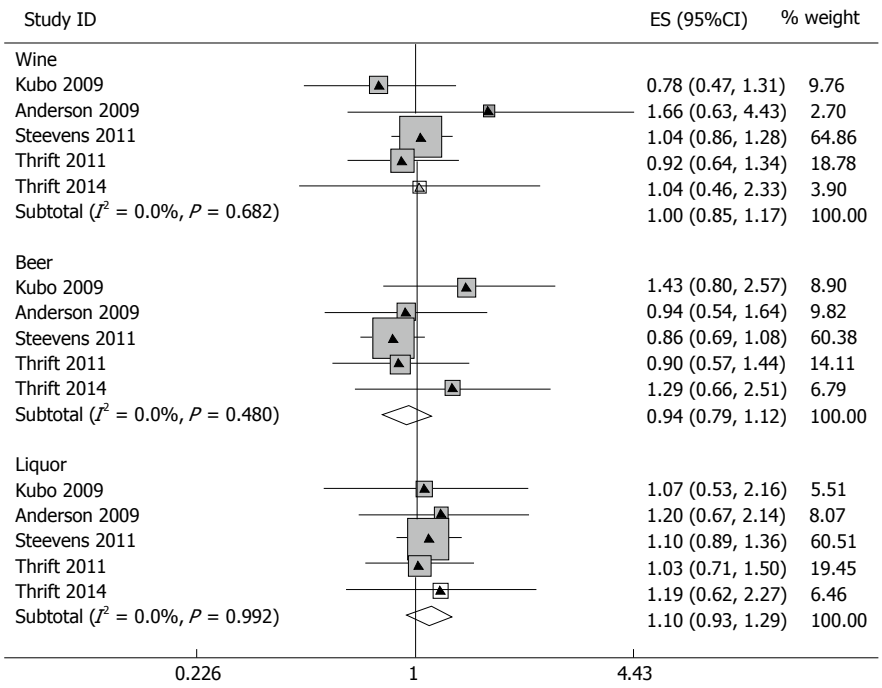

Figure 5 Forest plot of the prevalence of Barrett's esophagus in alcohol consumption groups *vs* control groups in different type of alcohol (wine, beer and liquor).

In addition, some unmeasured lifestyle factors are used to explain the association between alcohol consumption and BE. For example, wine drinkers were more likely to be educated and have other markers of a healthy lifestyle, such as a better diet and vitamin use, while beer and liquor drinkers were more likely to engage in unhealthier lifestyles, such as eating fewer servings of fruit and vegetables and having a higher body mass index (BMI).

Although demographic and lifestyle factors were associated with Barrett's esophagus, these factors did not appear to explain the association between alcohol consumption and Barrett's esophagus. The association between alcohol consumption and Barrett's esophagus should also consider other factors, such as income, education, smoking, BMI, Helicobacter pylori, fruit and vegetable intake, vitamin supplement intake, NSAIDs use and television watching. For example, *Helicobacter pylori* infection can increase the activity of alcohol dehydrogenase (ADH) in the gastric epithelium. Ethanol is metabolized in the esophageal mucosa to acetaldehyde mainly by the action of ADH, which has been shown to have strong carcinogenic potential. In addition, homozygosity for the ADH_3 gene has recently been reported in patients with BE and could increase the rate of conversion of ethanol to ADH in the esophageal mucosa.

At the same time, our meta-analysis has some limitations. First, there were some bias and confounders in the included studies. For example, some case-control studies were subject to recall and selection bias which are inherent to retrospective studies. However, the recall bias with regards to alcohol consumption in the included studies was not a significant bias as recall of alcohol consumption is reliable among study participants and our meta-analysis included four prospective cohort studies which can reduce the risk of recall and selection bias. The second is the lack of information of the presence of GERD and the use of medications for this disease. Consequently, we were not able to investigate the possible confounding effects of these factors or their possible intermediate role in the associations investigated. There is also the lack of information about the length of alcohol consumption time in the included studies.

In conclusion, our meta-analysis demonstrated that alcohol consumption is a risk factor for the development of BE. Since alcohol consumption is a modifiable risk factor, it is an important concept in terms of BE prevention. Future studies should investigate the risk factors for progression of BE to EAC.

COMMENTS

Background

Barrett's esophagus (BE) is an acquired condition in which specialized columnar epithelium replaces the usual stratified squamous epithelium lining the esophagus. The main clinical significance of BE is its association with an increased risk of developing esophageal adenocarcinoma (EAC). Survival for patients with EAC remains poor, with median survival less than 12 mo. Understanding the causes of BE is a necessary step toward preventing EAC.

Research frontiers

Potential risk factors for BE include white race, male sex, older age, cigarette smoking, abdominal obesity and gastroesophageal reflux disease, while use of aspirin and non-steroidal anti-inflammatory drugs may prevent the development of BE. To date, no meta-analysis of the relationship between alcohol consumption and BE has been performed. The results among these studies reporting the association between BE and alcohol consumption have been conflicting and the type of alcohol (wine, beer, liquor) can affect this association.

Innovations and breakthroughs

Alcohol consumption was associated with an increased risk of BE compared

with control groups (OR = 1.01; 95%CI: 1.00-1.02). Subgroup analysis showed an increased risk of BE associated with alcohol consumption from case-control and cohort, European and Asian, and hospital studies, but there was a decreased risk of BE associated with alcohol consumption from American studies (OR = 0.86; 95%CI: 0.77-0.96). At the same time, there was no significant association between BE and alcohol consumption in community studies (OR = 0.97; 95%CI: 0.84-1.12) and the type of alcohol (wine, beer and liquor) studies.

Applications

Alcohol consumption was associated with an increased risk of BE, especially for European and Asian drinkers.

Terminology

BE is an acquired condition in which specialized columnar epithelium replaces the usual stratified squamous epithelium lining the esophagus.

Peer review

This manuscript about alcohol consumption and BE is interesting for the readership and should be published.

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