Meat intake and risk of inflammatory bowel disease: A meta-analysis

ABSTRACT

Background/Aims: This meta-analysis is designed to determine the association between meat consumption and the risk of inflammatory bowel disease.

Materials and Methods: Search relevant literature published in PubMed, Cochrane before July 2015 without restrictions. Studies were included if relative ratios and the corresponding 95% confidence intervals of the risk of inflammatory bowel disease were reported with respect to meat consumption.

Results: Nine studies were included in this meta-analysis. Relative to those who did not or seldom eat meat, meat consumers had a significantly greater risk of inflammatory bowel disease (pooled relative ratio: 1.50, 95% confidence interval: 1.15–1.95). The funnel plot revealed no evidence for publication bias.

Conclusion: Meat consumption may increase the risk of inflammatory bowel disease. Additional large prospective studies are warranted to verify this association.

Keywords: Case-control study, cohort study, inflammatory bowel disease, meat consumption, meta-analysis

INTRODUCTION

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn’s disease (CD), has significantly increased globally over the past several years, particularly in Europe and Asia. This increase in incidence is likely because of both the genetic and environmental causes, including infectious gastroenteritis (1), diet (2), medications (3), and smoking and drinking habits (4,5). For example, it is considered that a diet high in saturated fats and refined sugars changes the intestinal microenvironment and increases the risk for developing IBD (6,7).

Although diet and IBD have been investigated in many epidemiological studies, the association between meat consumption and IBD risk remains controversial. In contrast, a number of studies and meta-analyses have demonstrated that meat consumption is associated with an increased risk of coronary artery disease, hyperlipidemia, and prostate, esophageal, colorectal, and pancreatic cancers (8-10). With respect to IBD, some studies have suggested that meat intake is the causative factor, whereas other studies have suggested that the type of meat and cooking process may increase IBD risk (2,5). This meta-analysis was designed to assess the true association existing between IBD risk and meat consumption.

MATERIALS AND METHODS

Literature review and sources of data

We reviewed relevant studies from Pubmed and EMBASE databases that were published from July 1966 to July 2015 without language limitations. The inclusion criteria of the studies were as follows: inflammatory bowel disease, ulcerative colitis, Crohn’s disease,
and meat consumption (including red meat, processed meat, white meat, poultry, beef, pork, lamb, and goat). Red meat was defined as darker-colored meat from mammals, such as cows, sheep/lambs, pigs, and horses. White meat was defined as lighter-colored meat from poultry, such as chickens, and rabbits. The term "processed meat" referred to bacon, poultry sausage, luncheon meats (red and white meat), ham, hot dogs, etc.

Two investigators independently screened the results. Moreover, the reference lists of retrieved articles were reviewed to identify additional relevant studies. If the same data was present in different studies, the largest or latest study met the inclusion criteria.

**Inclusion and exclusion criteria**
Studies with the following criteria were included:
1) A case–control or cohort design; 2) an evaluation of the association between meat consumption (including total meat, red meat, processed meat, and white meat) and IBD risk; and 3) the availability of odds ratio, relative risk (RR), and hazard ratio estimates with 95% confidence interval (CI) statistical data.

**Quality evaluation of included studies**
The Newcastle–Ottawa Scale was adopted for quality assessment (11). A study is judged on three broad perspectives: the selection of the study groups, comparability of the groups, and ascertainment of either the exposure or outcome of interest for case–control or cohort studies, respectively. The maximum score is nine, and all studies included in this meta-analysis scored six or higher.

**Statistical analysis**
The $\chi^2$-based Q statistic (12) was used to estimate the heterogeneity among the included studies; a significant $\chi^2$ statistic means heterogeneity ($p<0.10$). Fixed or a random effect model (using the Mantel–Haenszel method or the DerSimonian and Laird method) was used to calculate the pooled OR. Using Begg’s funnel plot and Egger’s test, we evaluated publication bias ($p<0.05$ means statistically significant) (13). Analyses were performed using Stata software, version 12.0 (Stata Corp LP; College Station, TX, USA). A two-sided $p$ value of $<0.05$ was considered statistically significant (14).

**RESULTS**

**Literature review and study characteristics**
A flow chart depicting the selection of eligible studies from the literature review using the inclusion criteria is shown in Figure 1. The characteristics of the final nine studies selected for analysis are shown in Table 1 (15-23). Two cohort and seven case–control studies were included. The nine studies reported a total of 2,019 cases of UC, 683 of CD, and 160 of IBD. Data was obtained from Asian (n=4) (15-17,21) and European (n=5) populations (18-20, 22, 23). Of the nine studies, five examined total meat consumption (15-17,19,21,23), three only examined red meat consumption (18,20,22), two examined processed meat consumption (22,23), and two only examined white meat consumption (18,20). Four studies divided meat consumption into lowest intake, medium intake, and high intake (15,18,20,22); two studies defined high intake as meat consumption for $>7$ times/week, medium consumption as 3–5 times/week, and low consumption as $<1$ time/month (18,20). Two studies classified meat consumption into three groups by quartiles (T1–T3) of energy-adjusted intake among controls (19,23), and one study classified consumption into four groups by quartiles (Q1–Q4) (17). Among these studies, the confirmation of outcome was obtained from the cancer registry. Potential confounders (at least for age) were controlled in all studies.

**Meta-analysis**
The summary RRs for esophageal cancer in the highest versus lowest consumption groups were 1.50 (95% CI: 1.15–1.95) for total meat, 2.37 (95% CI: 1.40–3.99) for red meat, 1.60 (95% CI: 0.53–4.78) for processed meat, and 1.20 (95% CI: 0.73–1.97) for white meat (Table 2). There was significant evidence of heterogeneity among studies ($Q=45.31, p<0.001, I^2=60.3\%$).

Subgroup meta-analyses were conducted using geographic area, study design, and type of meat consumed. The summary RRs (95% CI) of the association between total meat consumption and IBD risk were 2.92 (1.59–5.34) in cohort studies and 1.33 (1.02–1.72) in case–control studies (Figure 2, Table 2). Significant heterogeneity existed among the case–control studies ($Q=30.51, p=0.010, I^2=50.8\%$) but not among the cohort studies ($Q=3.44, p=0.179, I^2=41.9\%$).

Stratification of data by geographic area (Figure 3) identified a significant association between total meat consumption and IBD risk in studies that were conducted in European populations (summary RR: 1.61; 95% CI: 1.16–2.21) with statistical heterogeneity among studies ($Q=28.71, p=0.007, I^2=54.7\%$) and
### Table 1. Characteristics of the nine studies included in this meta-analysis

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>No. of cases</th>
<th>Controls or cohort size (n)</th>
<th>Meat type</th>
<th>Meat consumption</th>
<th>Risk estimate (95% CI)</th>
<th>Adjustments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jowett et al. (22)</td>
<td>2004</td>
<td>UK</td>
<td>UC: 191</td>
<td>463</td>
<td>Meat and meat products Red and processed meat</td>
<td>Lowest intake Medium intake High intake</td>
<td>Meat and meat products 1.0 1.37 (0.60–3.13) 3.20 (1.31–7.79) Red and processed meat 1.0 2.16 (0.93–4.98) 5.19 (2.09–12.93)</td>
<td>Age, sex, smoking, triglycerides, alcohol consumption</td>
</tr>
<tr>
<td>Jantchou et al. (23)</td>
<td>2010</td>
<td>France</td>
<td>IBD: 77</td>
<td>67,581</td>
<td>Meat</td>
<td>T1</td>
<td>1.0</td>
<td>Age, sex, smoking, HR for energy</td>
</tr>
<tr>
<td>Higashi et al. (15)</td>
<td>1991</td>
<td>Japan</td>
<td>UC: 50</td>
<td>50</td>
<td>Meat</td>
<td>Lowest intake</td>
<td>1.0</td>
<td>Age, sex</td>
</tr>
<tr>
<td>Akihiro et al. (16)</td>
<td>1994</td>
<td>Japan</td>
<td>UC: 101</td>
<td>143</td>
<td>Meat</td>
<td>1–2 times/week</td>
<td>1.0</td>
<td>Age, sex, smoking</td>
</tr>
<tr>
<td>Sakamoto et al. (17)</td>
<td>2004</td>
<td>Japan</td>
<td>UC: 111 CD: 128</td>
<td>219</td>
<td>Meat</td>
<td>Q1</td>
<td>1.0</td>
<td>Age, sex, smoking, study area</td>
</tr>
<tr>
<td>Bernstein et al. (18)</td>
<td>2006</td>
<td>Canada</td>
<td>UC: 217 CD: 364</td>
<td>433</td>
<td>Pork (red meat) Chicken (white meat)</td>
<td>Lowest intake Medium intake High intake</td>
<td>Pork UC 1.0 2.62 (1.37–5.03)</td>
<td>Age, sex, smoking, drinking</td>
</tr>
<tr>
<td>Maconi et al. (20)</td>
<td>2010</td>
<td>Italy</td>
<td>IBD: 83 UC: 41 CD: 42</td>
<td>160</td>
<td>Red meat</td>
<td>Lowest intake Medium intake High intake</td>
<td>Red meat UC 1.22 (0.45–3.32) 0.63 (0.20–1.94) 2.42 (0.85–6.85)</td>
<td>Age, sex</td>
</tr>
<tr>
<td>Magoni et al. (21)</td>
<td>2013</td>
<td>China</td>
<td>UC: 1308</td>
<td>1308</td>
<td>Meat-eaters</td>
<td>1.0</td>
<td>1.10 (0.50–2.52) 0.27 (0.05–1.47) 2.04 (0.69–6.05) 1.33 (0.50–3.52) 0.25 (0.05–1.27)</td>
<td>Age, sex</td>
</tr>
</tbody>
</table>

CI: confidence interval; IBD: inflammatory bowel diseases; UC: ulcerative colitis; CD: Crohn's disease; NA: not applicable; Lowest intake: <1 times/month; Medium intake: 1–3 times/month or 1–2 times/week; High intake: 3–6 times/week or every day.
Asian populations (summary RR: 1.15, 95% CI: 0.85–1.56) with no statistical heterogeneity among studies (Q=5.23, p=0.265, I²=23.5%). Only red meat consumption was associated with IBD risk (RR: 2.37, 95% CI: 1.40–3.99). No significant association between white meat (RR: 1.20, 95% CI: 0.73–1.97) or processed meat (RR: 1.60, 95% CI: 0.53–4.78) and IBD risk was found. A significant association between total meat intake and UC risk was found (summary RR: 1.47; 95% CI: 1.01–2.15), whereas no association was detected between total meat intake and CD risk (summary RR: 1.50, 95% CI: 0.98–2.28). However, there was significant heterogeneity among studies conducted on UC (Q=29.98, p=0.001, I²=66.6%) and CD (Q=11.51, p=0.074, I²=47.9%).

Publication bias
As shown in Figure 4, there was no publication bias as determined by either the Egger’s test (p=0.245) or Begg’s funnel plot (p=0.327).

DISCUSSION
The results suggest that high meat intake increases IBD risk, and this association varies by the type of meat consumed. Summary associations for red meat consumption are slightly greater compared with processed meat and white meat consumption.

Several possible underlying mechanisms exist linking the consumption of meat, particularly red meat, and the incidence of IBD. Research has revealed that cooking meat at high temperatures creates chemical by-products with mutagenic or carcinogenic properties.
genic properties that may influence the digestive tract once ingested (24). Other postulated mechanisms involve heme iron and N-nitroso compounds. Heme iron, derived from red meat, can promote the formation of N-nitroso compounds, which influence cell proliferation in the digestive tract. Under acidic gastric conditions, nitrates, which are mainly found in processed meats (25), create nitrosylating agents that react with amines or amides (8). Fat intake from animal sources has also been hypothesized to increase IBD risk (6,7). Indeed, a high intake of meat correlates with UC incidence and relapse (26). Furthermore, studies have demonstrated that a high intake of linoleic acid, a polyunsaturated omega-6 fatty acid present in meat, increases IBD risk (26,27). Previous meta-analyses have also revealed that consumption of processed meat increases cancer risk (7,9,10). However, this meta-analysis found no correlation between processed meat and IBD; to confirm this, additional studies are required.

Heterogeneity is a common concern in meta-analysis. A certain degree of heterogeneity was observed in this study, which is not surprising given the inter-study variation in factors, such as race and study type. In this analysis, one source of heterogeneity may have been the inclusion of both cohort and case–control studies. The degree of heterogeneity was slightly attenuated among the studies conducted in Asian populations, suggesting that race is an influential factor. However, meta-regression analysis did not detect any variables as potential contributors to heterogeneity.

The results from this study may have been confounded by the influence of several environmental risk factors, such as aging and smoking. However, the analyses determined that risk was only marginally attenuated after adjustment for a wide range of potential confounders. Moreover, there was no evidence of publication bias as determined by either the Egger’s test or Begg’s funnel plot.

This meta-analysis has potential limitations that should be taken into consideration. First, many of the analyzed studies did not extensively describe the study characteristics; some studies categorized meat consumption on the basis of amount ingested, whereas others did not specify consumption levels. Consequently, dose-response analysis was not possible. Many studies did not analyze the type of meat consumed. Third, the number of analyzed studies requires to be increased. The inclusion of additional cohort studies is required to confirm the results obtained in this study.

In conclusion, the results of this meta-analysis indicate that high intake of meat is associated with an increased IBD risk. Further cohort studies are warranted to confirm this association.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Shandong Pro vincial Hospital, Shandong University.

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