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Meta-Analysis

A meta-analysis of the association between poultry and egg consumption and the risk of brain cancer

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Abstract: Poultry consumption, as well as egg consumption for brain cancer risk remains an important topic. The objective of this meta-analysis is to investigate the role of poultry and egg consumption for brain cancer risk. All articles about poultry and egg consumption for brain cancer were retrieved from PubMed, Web of knowledge and Wan Fang Med Online. The data was analyzed using Stata 12.0 software. Ten articles (6 articles for poultry and 5 articles for egg) were included. For poultry consumption, the summarized relative risk (RR) was 0.901 (95%CI= 0.703-1.154) for brain cancer risk, with high between-study heterogeneity (I^2= 60.7%, P=0.018). Four studies reported the association between poultry consumption and glioma risk, yielding a RR of 0.873 (95%CI= 0.737-1.034, I^2= 0.0%, P=0.838). The association between egg consumption and brain cancer risk was not significant (RR= 0.998, 95%CI= 0.552-1.805), with significant heterogeneity (I^2= 82.6%, P< 0.001). The pooled RR for glioma risk was 1.472 (95%CI= 0.935-2.316). In summary, our results concluded that poultry and egg consumption may be not associated with the risk of brain cancer. Due to the limited quality of evidence currently available, more studies related to poultry and egg consumption for brain cancer is necessary.

Key words: Poultry; Egg; Consumption; Brain cancer; Meta-analysis.

Introduction

Brain cancer is the neoplasms primary central nervous system, the incidence of brain cancer is approximately 14.4 per 100,000 persons annually (1), among which glioma is the most common brain cancer of the primary central nervous system and it has a relative poor prognosis (2, 3). However, its etiology and pathogenesis remains unclear. Furthermore, glioma accounts for about 50% of primary tumors of the central nervous system (4, 5). Epidemiology studies have indicated that genetic factor is an established risk factor for brain cancer patients (6, 7). Furthermore, external environment, such as long-term mobile phone use (8) could increase the risk of glioma. Furthermore, dietary intake such as vitamins C (9) and vitamin A (10) could reduce the risk of glioma.

Eggs provide roughly 1.2% of available food energy worldwide. It is rich in cholesterol, protein, folate, and B group vitamins. Poultry consumption has surpassed beef consumption during the last four decades (11). Some publications articles involving different sample size have assessed poultry and egg consumption for the risk of brain cancer, yielding inconsistent results (12-14). The objective of this meta-analysis was to explore the potential association between poultry and egg consumption and brain cancer risk.

Materials and Methods

Data sources and search strategy

We searched the relevant studies by electronic databases of Web of Knowledge, PubMed, and Wan Fang Med Online, with the strategy of 'poultry' OR 'chicken' OR 'turkey' OR 'egg' OR 'diet' combined with 'brain cancer' OR 'brain tumor' OR 'glioma' up to June 1st, 2018. Moreover, the references of the retrieved articles were checked to identify additional studies. The search process is shown in Figure 1. Two investigators (HFL and PS) independently conducted this systematic search.

Inclusion criteria

The inclusion criteria for studies in this meta-analysis were: (1) observational studies; (2) studies investigating the association between poultry and egg consumption and risk of brain cancer; (3) the relative risk (RR) with the corresponding 95% confidence interval (CI) in the relation was available, or could be calculated basing on relevant data; (4) humans studies; (5) poultry consumption included chicken, turkey, ground poultry, as well as the processed poultry components of turkey or chicken cold cuts.

Data extraction

The following required data were extracted by two independent individuals (HFL and PS): the first author's name; publication years; region for the study; study

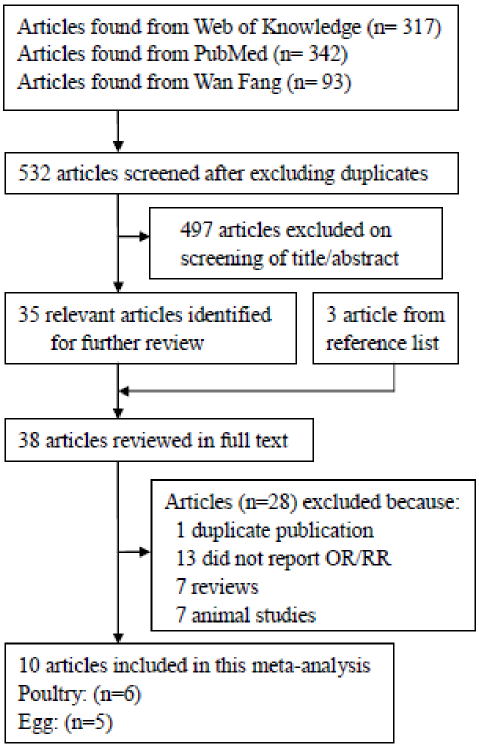

Figure 1. Flow chart of meta-analysis for exclusion/inclusion of studies.

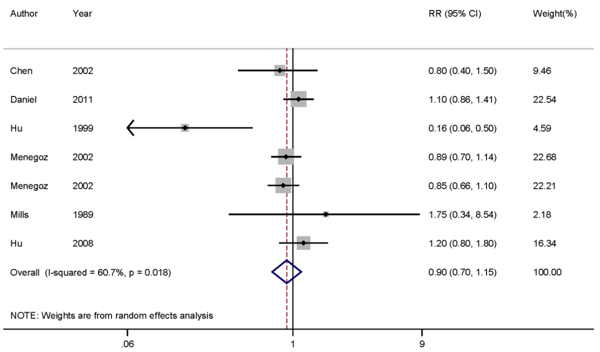

Figure 2. Flow chart of meta-analysis for exclusion/inclusion of studies.

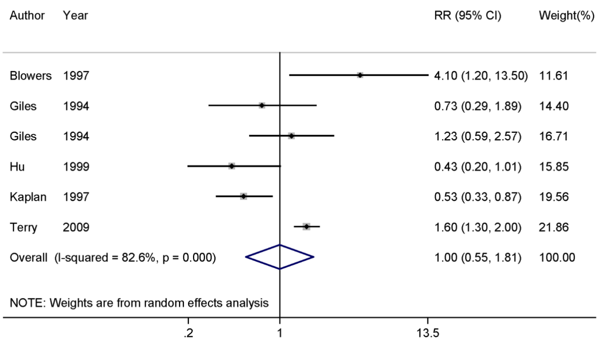

Figure 3. The forest plot of the relationship between egg consumption and brain cancer risk.

type; mean age or age range; cases and participants; RR with 95%CI for highest category compared with lowest category of poultry and egg consumption on brain cancer risk and adjustment for covariates. Disagreements were resolved through discussion.

Statistical analysis

RR with 95% CI was used to calculate the summary results (15). To evaluate heterogeneity between studies, we adopted I^2 statistic test and Q test (16). Between-study heterogeneity was considered to be significant if I^2 was greater than 50% or the p value of Q test was less than 0.1 (17). A random effects model was used for this analysis. Potential publication bias was examined via the Begg's funnel plots (18) and Egger's test (19). All analyses were two sided, with $P< 0.05$ indicating statistical significance, except for heterogeneity and publication bias testing, which has a boundary level of 0.10. All above statistical data were conducted by Stata software (version 12.0, Stata Corporation, College Station, TX).

Results

Search results

Overall, 317 articles from Web of Knowledge, 342 articles from PubMed and 93 articles from Wan Fang Med Online. The final analysis in this report includes a total of 10 articles (12-14, 20-26). Six articles (13, 14, 20, 22, 24, 25) were included for the analysis between poultry consumption and brain cancer risk. Menegoz et al. reported men and women independently. Therefore, 7 independent studies were suitable for poultry consumption. Five publications (12, 13, 21, 23, 26) were conducted to assess the association between egg consumption and brain cancer risk. Similarly, one article reported male and female, respectively. Thus, 6 independent studies were used. Two articles were prospective design and the remaining articles were case-control design. Characteristics of the included studies are summarized in Table 1.

Poultry consumption and brain cancer risk

Pooled RR for highest category of poultry consumption versus lowest category was 0.901 (95%CI=0.703-1.154, I^2= 60.7%, P=0.018; Figure 2). Four studies reported the association between poultry consumption and glioma risk, yielding a RR of 0.873 (95%CI= 0.737-1.034, I^2= 0.0%, P=0.838). In the stratified analysis by study design, similar results were found both in prospective studies (RR=1.112, 95%CI= 0.871-1.420) and case-control studies (RR= 0.817, 95%CI=0.593-1.126). Detailed results are showed in Table 2.

Begg's funnel plots (Supplementary figure 1) and Egger's test (P= 0.456) indicated that no publication was detected in the analysis. There is no single study had potential effects to the whole result when removed a study at time (Supplementary figure 2).

Egg consumption and brain cancer risk

The association between egg consumption and brain cancer risk was not significant (RR= 0.998, 95%CI= 0.552-1.805), with significant heterogeneity (I^2= 82.6%, $P< 0.001$) (Figure 3). The pooled RR for glioma risk was 1.472 (95%CI= 0.935-2.316). Upon a stratified analysis based on number of cases, we found significant association in the subgroup of number of cases ≥200 (RR= 1.567, 95%CI= 1.274-1.927). Detailed results are showed in Table 2.

Egger's test (P= 0.399) and Begg's funnel plots (Supplementary figure 3) indicated that no publication was detected in the report. There is no single study had potential effects to the whole result when removed a study at time (Supplementary figure 4).

Table 1. Characteristics of the included studies on poultry and egg consumption and brain cancer risk.

Study, year	Country	Study design	Participants (cases)	Age (years)	Exposure	Outcome	RR (95%CI) for highest versus lowest category	Adjustment for covariates
Blowers et al, 1997	United States	PCC	188 (94)	25-74	Egg	Brain glioma	4.1 (1.2-13.5)	Adjusted for age (within five years), gender and race (Black or White).
Chen et al. 2002	United States	PCC	685 (236)	≥21	Poultry	Brain glioma	0.8 (0.4-1.5)	Adjusting for age, age squared, gender, total energy intake, respondent type, education level, family history, and farming experience.
Daniel et al. 2011	United States	Cohort	492186 (749)	50-71	Poultry	Brain cancer	1.10 (0.86-1.41)	Adjusted for red meat intake, age, sex, education, marital status, family history of cancer, race, body mass index, smoking status, frequency of vigorous physical activity, menopausal hormone therapy in women, and intake of alcohol, fruit, vegetables, and total energy; mutually adjusted for intake of fish or poultry.
Giles et al. 1994	Australia	PCC	818 (409)	20-70	Egg	Brain glioma	Females: 0.73 (0.29-1.89) Males: 1.23 (0.59-2.57)	Adjusted for alcohol and tobacco.
Hu et al. 1999	China	HCC	331 (73)	20-74	Poultry Egg	Brain cancer	Poultry: 0.16 (0.06-0.50) Egg: 0.43 (0.20-1.01)	Adjusted for income, education, cigarette smoking, alcohol intake, selected occupational exposures and total energy intake.
Kaplan et al. 1997	Israel	HCC	417 (139)	18-75	Egg	Brain cancer	0.53 (0.33-0.87)	Adjusted for age, sex and ethnic origin.
Menegoz et al. 2002	France	PCC	3152 (1177)	20-80	Poultry	Brain glioma	Females: 0.85 (0.66-1.10) Males: 0.89 (0.70-1.14)	Adjusted for age (six levels), centre (eight centres for men, seven centres for women) + years of schooling + exposure + (centre exposure).
Milles et al.1989	United States	Cohort	34,000 (19)	≥25	Poultry	Brain glioma	1.75 (0.34-8.54)	Adjusted for age and sex.
Terry et al. 2009	Europe, Northern American and Australia	PCC	3671 (1185)	20-80	Egg	Brain cancer Brain glioma	Brain cancer 1.6 (1.3-2.0) Brain glioma 1.6 (1.3-2.0)	Adjusted for age, sex, center and the following food groups: leafy green vegetables, yellow-orange vegetables, cured meat, non-cured meat, fresh fish, dairy eggs, grains, and citrus fruit.
Hu et al. 2008	Canada	PCC	6048 (1009)	20-76	Poultry	Brain cancer	1.2(0.8-1.8)	Adjusted for age group, province, education, body mass index, sex, alcohol use, pack-year smoking, total of vegetable and fruit intake, and total energy intake.

Abbreviations: RR= relative risk; CI= confidence interval; PCC= Population-based case-control studies; HCC= Hospital-based case-control studies.

Table 2. Summary risk estimates of the association between poultry and egg consumption and brain cancer risk.

Sub-groups	Poultry consumption (Highest vs. lowest category)				Egg consumption (Highest vs. lowest category)			
	Studies, n	RR(95%CI)	I^2(%)	$P_{heterogeneity}$	Studies, n	RR(95%CI)	I^2(%)	$P_{heterogeneity}$
All studies	7	0.901(0.703-1.154)	60.7	0.018	6	0.998(0.552-1.805)	82.6	<0.001
Glioma	4	0.873(0.737-1.034)	0.0	0.838	4	1.472(0.935-2.316)	44.7	0.143
Study design								
Prospective	2	1.112(0.871-1.420)	0.0	0.577	0	-	-	-
Case-control	5	0.817(0.593-1.126)	67.6	0.015	6	0.998(0.552-1.805)	82.6	<0.001
Number of cases								
<200	2	0.488(0.047-5.065)	83.1	0.015	4	0.800(0.371-1.723)	71.8	0.014
≥200	5	0.960(0.841-1.097)	0.0	0.425	2	1.567(1.274-1.927)	0.0	0.501

Discussion

Our meta-analysis suggested that highest category of poultry and egg consumption had no significant association on the risk of brain cancer. Similarly, the association was not significant on glioma risk in poultry consumption or in egg consumption. Publication bias was not found in poultry consumption or in egg consumption.

We found significant between-study heterogeneity on the association between poultry and egg consumption and brain cancer risk. A paper had said that between-study heterogeneity in the meta-analysis is common (27), and it is an essential component to explore the heterogeneity existed in the between-study. Meta-regression was used to explore the causes of heterogeneity for covariates of publication year, pathology types, study design, ethnicity and number of cases. However, we did not find any covariate having a significant impact on between-study heterogeneity for the above mentioned covariates. For poultry consumption and brain cancer risk, we are concerned about the results from Hu et al. 1999, given the RR of 0.16 and huge confidence interval; this did not appear to be a plausible result and we then removed this study. The test of I^2 was reduced from 60.7% to 0.0%. However, the study by Hu 1999 did not have a notable impact on the overall estimate (overall RR=0.964, 95%CI= 0.845-1.101). Therefore, Hu et al. 1999 may be the main source of heterogeneity.

Previous meta-analysis suggested highest versus lowest categories of poultry consumption had lack of association on the risk of non-Hodgkin lymphoma (28), prostate cancer (29), esophageal cancer (30) and so on. Our results are consistent with the above mentioned studies. The factor that was thought to be responsible for the hazard was heme iron, because it contributed to endogenous formation of carcinogenic N-nitroso compounds. However, poultry was low in heme iron. Additionally, poultry contained higher amount of unsaturated fat and lower amount of saturated fat compared with red meat (31). This may be the potential reasons for the lack of an overall association between poultry consumption and cancer risk.

Publications had indicated that higher categories of egg intake had no significant association on the risk of non-Hodgkin lymphoma (28), prostate cancer (32) and so on. But, some papers concluded that highest versus lowest egg consumption could increase the risk of ovarian cancer (33), and breast cancer (34). Eggs are an important source of cholesterol and choline. Cholesterol homeostasis is disrupted in malignant cells, leading to accumulation of cholesterol, which is a precursor of androgens and can change signaling pathways to promote cancer progression (35, 36). Choline is essential for the cellular functions involved in cancer growth and development (37).

Some potential limitations should be required attention. First, only articles published in English were included, which may omit other languages studies. However, we did not detect any publication bias. Second, eight of the 10 studies were case-control studies. The selection bias, recall bias and some other confounding factors cannot be excluded; for example, some subjects may change their poultry and egg consumption after the baseline assessment. However, case-control design was a very important epidemiological approach in the observational study. Therefore, it is requirement for evidence from prospective cohort studies.

In summary, our results concluded that poultry and egg consumption may be not associated with the risk of brain cancer. Due to the limited quality of evidence currently available, more studies related to poultry and egg consumption for brain cancer is necessary.

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