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Review Article

Incidence of Gastric Cancer in the Patients with Schizophrenia: A Meta-analysis

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Abstract: Background: Several studies have reported the incidence of gastric cancer (GC) in the patients with schizophrenia, but the incidence of GC in schizophrenia patients remains controversy. It is necessary to perform a meta-analysis to detect the incidence of GC in schizophrenia patients. Methods: We search the relevant articles from PubMed, EMBASE, Web of Science, the Cochrane Library and Chinese electronic databases. The incidence of GC in schizophrenia patients and heterogeneity were analyzed with STATA10.0 software. Results: Our meta-analysis included total 283,422 patients with schizophrenia and 1,024 patients with GC in nine articles. The incidence of GC in schizophrenia patients was 0.62% (95%CI: 0.005-0.008; P<0.001), but there is obvious heterogeneity (I^2=98.7%). We next performed subgroup analysis to explore the incidence of GC in schizophrenia patients by gender and region. The GC incidence in male schizophrenia patients (0.28%, 95%CI: 0.001-0.003; P<0.001) was higher than that in female patients (0.23%, 95%CI: 0.002-0.004). In European countries, the GC incidence in schizophrenia patients (0.98%, 95%CI: 0.005-0.008) was higher than that in Asian countries (0.13%, 95%CI: 0.000-0.002; P<0.001). Conclusion: The incidence of GC in patients with schizophrenia was 0.62%. The GC incidence was higher in male and European countries schizophrenia patients, but large cohort studies are needed to confirm further.

Keywords: Schizophrenia, Gastric Cancer, Incidence, Meta-analysis

1. Introduction

Schizophrenia is a severe mental disease which is manifested by disruption in cognition and emotion. In the worldwide, approximately 1% of the population was suffered from schizophrenia [1]. In addition, many diseases are frequently comorbid with schizophrenia, such as cardiovascular, respiratory and metabolic diseases [2, 3]. Till now, schizophrenia has become a serious burden in public health care. Recently, an increasing number of researches have detected the incidence of different cancers in the schizophrenia patients, including colorectal cancer, melanoma, and gastric cancer (GC) [4, 5]. Several authors reported that schizophrenia patients had a low risk of GC [6]. But some authors reported that they did not find negative association, and maybe an increased risk of GC in schizophrenia patients [7, 8]. The incidence of GC in schizophrenia patients remains controversy. Therefore, it is vital to perform a meta-analysis to detect the incidence of GC in schizophrenia patients.

2. Method

2.1. Search Strategy

The databases of Web of Science, PubMed, the Cochrane Library, EMBASE and Chinese databases (WanFang and

CNKI) were used to search and collect the relevant articles. The date was limited to May 1, 2021. The following terms were used: 'schizophrenic' or 'schizophrenia' and 'gastric' or 'stomach' and 'tumor' or 'cancer'.

2.2. Inclusion and Exclusion Criteria

The inclusion criteria: (1) adult schizophrenia patients (the age more than18-year old). (2) schizophrenia identified as the exposure of interest at baseline. (3) record the number of cases of GC. (4) the cohort study (prospective or retrospective).

Exclusion Criteria: (1) studies of letter, review and comment. (2) studies without clinical data.

2.3. Data Extraction and Quality Evaluation

Firstly, two authors (J. G. and Y. W.) completed the literature search, and then they extracted data and accomplished the quality assessment independent. Discrepancies were discussed by another author (Z. J.). Data information included: first author, publication years, countries, number of GC and schizophrenia cases. We used the Newcastle-Ottawa Scale (NOS) score to evaluate the quality of the researches, and NOS score ≥6 was regarded as high quality.

2.4. Statistical Analysis

We used the STATA statistics software (version 10.0) to complete the meta-analysis.

Data of schizophrenia patients and GC patients were extracted to calculate incidence. We evaluate the heterogeneity by Q test and the I^2. I^2>50% indicated the presence of heterogeneity. The fixed effect model are applied to low heterogeneity. Random-effect model are applied to high heterogeneity. Funnel plots and Egger's test or Begg's test were used to assess bias. P<0.05 was considered as statistically significant.

3. Results

3.1. Literature Search Results

The search process of included articles was described in Figure 1. Firstly, 43 articles were chosen in the database according to search terms. 16 were excluded based on assessment of title and abstracts. Among the 27 articles, we exclude 18 articles, including animal experiment (N=11), other cancers (N=2), no statistical (N=3), meta-analysis (N=1), review (N=1). Finally, 9 articles were included in our study [7-15].

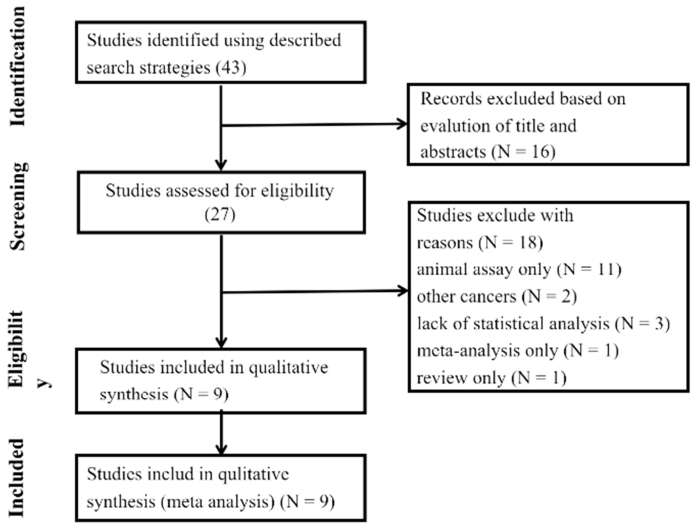

Figure 1. *Flow diagram of the literature review.*

3.2. Study Characteristics and Quality Evaluation

Our meta-analysis included 283,422 patients with schizophrenia and total 1,024 patients with GC. In the 9 articles, there are 3 articles from Asian countries and 6 articles from European countries. Based on relevant data, we listed the 9 articles in Table 1.

Table 1. *Main characteristics and results of the eligible studies.*

No	Author	Year	Journal	Country	Study-Period	GC	Schizophrenia	NOS
1 [9]	Saku M	1995	Int J Edpipemiol	Japan	1948-1982	7	2268	8
2 [10]	Lin CY	2013	Cancer sci	China (Taiwan)	1995-2007	157	102202	7
3 [11]	Ajdacic-Grossv	2014	Int J methphychres	Switzerland	1969-2007	156	17012	6
4 [7]	D.pettersson	2020	Edpipemiol psychiatrSci	Swedish	1990-2013	324	11306	8
5 [12]	Ji J	2013	Schzophr Bull	Swedish	1965-2008	184	59233	9
6 [13]	Barak Y	2005	Cancer	Italy	1993-2003	3	3226	6
7 [14]	Chou FH	2011	Schzophr res	China (Taiwan)	2000-2008	41	59257	6
8 [8]	Mortensen PB	1989	J Edpipemiol commun	Denmark	1957-1984	115	6152	7
9 [15]	Dalton	2005	Schzophr res	Denmark	1969-1993	37	22766	7

3.3. Schizophrenia and Incidence of GC

The included 9 studies detected the incidence of GC in schizophrenia patients. We found that GC incidence in patients with schizophrenia was 0.62% (95%CI: 0.005-0.008; *P*<0.001), but heterogeneity was high (I^2=98.7%) (Figure 2).

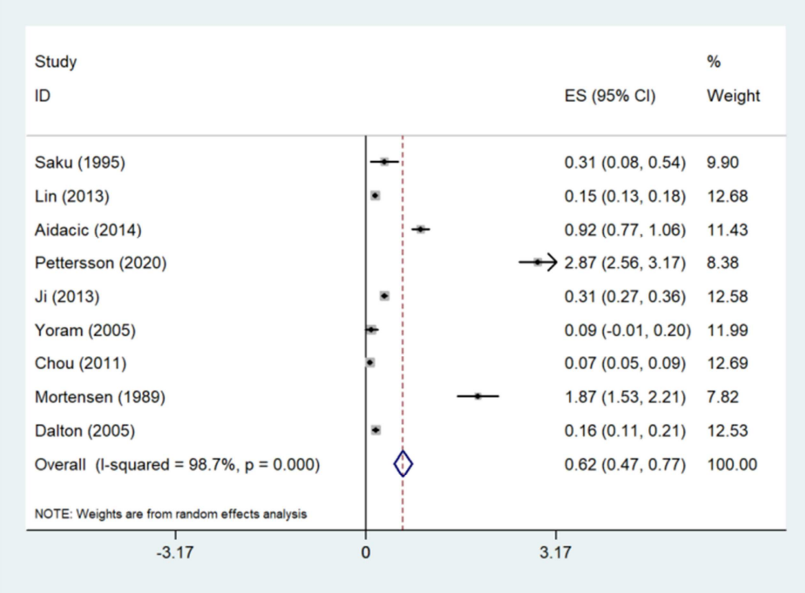

Figure 2. *Forest plot of overall risk ratio for incidence of GC in schizophrenia patients.*

3.4. Results of Subgroup Analysis

In order to explore the high heterogeneity of the incidence, we performed subgroup analysis between schizophrenia and incidence of GC by gender and region. We separately evaluated the incidence of GC in schizophrenia patients by gender (male and female) and region (Asian and European countries). We found that the GC incidence in male schizophrenia patients (0.28%, 95%CI: 0.001-0.003; *P*<0.001) was higher than that in female schizophrenia patients (0.23%, 95%CI: 0.002-0.004). In European countries, the GC incidence in schizophrenia patients (0.98%, 95%CI: 0.005-0.008) was higher than that in Asian countries (0.13%, 95%CI: 0.000-0.002; *P*<0.001) (Figure 3, Table 2). After subgroup analysis, we found that the heterogeneity were also high. Therefore the gender and region are not the source of high heterogeneity.

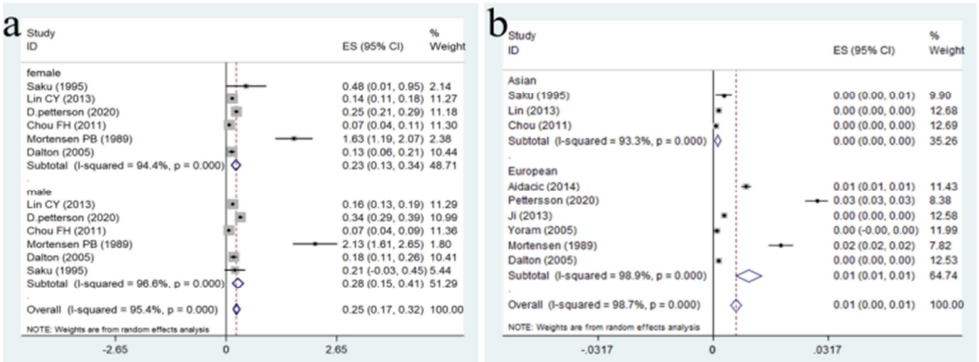

Figure 3. *Subgroup analysis for GC incidence in schizophrenia patients.*

Table 2. *Subgroup analysis for GC incidence in schizophrenia patients.*

Categories	N	Incidence	95%CI	Heterogeneity		Egger's test	Subgroup (*P* value)
				P value	I^2		
Gender					<0.001		
Male	7	0.23%	0.001-0.003	<0.001	94.4%	0.191	
Female	7	0.28%	0.002-0.004	<0.001	96.6%	0.141	
Countries					<0.001		
Asian	3	0.13%	0.000-0.002	<0.001	93.3%	0.761	
European	6	0.98%	0.005-0.008	<0.001	98.9%	0.051	

3.5. Assessment for Publication Bias

The funnel plot was used to assess publication bias. The graph was not completely symmetric on visual inspection. We found in the Egger's test that publication bias exists (P=0.013) (Figure 4). Thus the publication bias could not be ignored in this study, and further studies are needed to confirm the results.

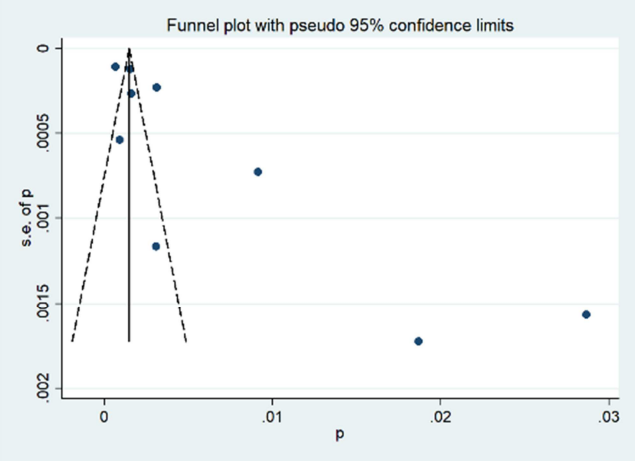

Figure 4. *Funnel plot estimated the publication bias of the included literature.*

4. Discussion

Recently, some articles reported the incidence of cancers in schizophrenia patients. Schizophrenia patients had a relatively higher incidence of pancreatic and lung cancers, increased incidence of breast tumor among the women, and decreased incidence of prostate cancer in men [7]. But the incidence of GC in schizophrenia patients remains controversy [7, 8]. In our meta-analysis, 9 studies included 283,422 patients were enrolled to detect the incidence of GC. We found that GC incidence in patients with schizophrenia was 0.62%. Subgroup analysis showed that the GC incidence was higher in female and European countries schizophrenia patients.

The incidence of GC in schizophrenia patients is controversial. Chou *et al*. reported that the incidence of GC is low in patients with schizophrenia [14]. However, Ajdacic-Gross *et al*. found that the incidence of GC is high in patients with schizophrenia [11]. It has been reported that many factors may be involved in the potential mechanisms underlying the association between GC incidence in schizophrenia patients. Firstly, epidemiological observations have indicated that schizophrenia patients exhibited low risk of cancer after long-term drug treatment, which has potential as anticancer agents. Some antipsychotic agents like chlorpromazine, thioridazine, aripiprazole and clozapine have been shown anticancer activity [16]. Secondly, Jahrami *et al.* found that a pro-inflammatory diet is associated with schizophrenia. Changes in dietary habits in patients with schizophrenia and other nutritional factors often showed lower incidence in GC [17]. Furthermore, helicobacter pylori increased the prevalence of schizophrenia patients, and suffer from the helicobacter pylori has been considered as a carcinogen for GC [18]. In our results, we found that GC incidence in patients with schizophrenia was 0.62%. But we need more researches to explore the potential mechanisms between GC incidence and schizophrenia.

Recently, several articles results revealed that schizophrenia patients had an increased incidence of lung cancer and pancreatic tumor, lower incidence of liver cancer, women with schizophrenia had an increased risk of breast cancer, and men with schizophrenia had a decreased risk of prostate cancer [19-22]. These indicated that the relationship is complicated between schizophrenia and cancer incidence, and the cancer site and gender may be the correlation factors. In our meta-analysis, we found that the GC incidence was higher in female schizophrenia patients. In European countries, the GC incidence in schizophrenia patients was higher than that in Asian countries. These may be because the difference of cancer screening in different areas, and low screening rates of cancers for people with schizophrenia in Asian countries [23]. In addition, we found that certain cancer risks are associated with gender in schizophrenia patients in previous researches, and found a significantly higher incidence of lung cancer and breast cancer in female with schizophrenia [7]. We found a significantly higher risk of GC in male with schizophrenia. But the heterogeneity and bias were obvious in our study, and further large studies are needed to confirm the results.

We explored GC incidence of schizophrenia patients in this meta-analysis, however, some limitations could not be ignored. Firstly, our article only included Chinese and English literature and a few Asian countries patients, and this may induce heterogeneity in our study. Secondly, the correlation factors were not uniform in our studies, and more factors should be included to perform the subgroup analysis. Furthermore, due to the less number and quality of our included articles, our conclusion is needed to further confirm.

5. Conclusion

In conclusion, we investigated the incidence of GC in schizophrenia patients through meta-analysis. Our results indicated that GC incidence in patients with schizophrenia was 0.62%. Subgroup analysis showed that the GC incidence in male schizophrenia patients was higher than that in female patients, and GC incidence in European countries was higher than that in Asian countries. Because of the heterogeneity and bias, the incidence of GC in the patients with schizophrenia should be determined by further large studies.

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