



Meta-analysis of Barrett's esophagus in China

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Abstract

AIM: To investigate the epidemiology and characteristics of Barrett's esophagus (BE) in China and compare with cases in the west.

METHODS: Studies were retrieved from the China National Knowledge Infrastructure and PubMed databases using the terms "Barrett" and "Barrett AND China", respectively, as well as published studies about BE in China from 2000 to 2011. The researchers reviewed the titles and abstracts of all search results to determine whether or not the literature was relevant to the current topic of this research. The references listed in the studies were also searched. Inclusion and exclusion criteria for the literature were appropriately established, and the data reported in the selected studies were analyzed. Finally, a meta-analysis was performed.

RESULTS: The current research included 3873 cases

of BE from 69 studies. The endoscopic detection rate of BE in China was 1%. The ratio of male to female cases was 1.781 to 1, and the average age of BE patients was 49.07 ± 5.09 years. Island-type and short-segment BE were the most common endoscopic manifestations, accounting for 4.48% and 80.3%, respectively, of all cases studied. Cardiac-type BE was observed in 40.0% of the cases, representing the most common histological characteristic of the condition. Cancer incidence was 1.418 per 1000 person-years.

CONCLUSION: Average age of BE patients in China is lower than in Western countries. Endoscopic detection and cancer incidence were also lower in China.

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Key words: Barrett's esophagus; Epidemiology; Cancer incidence; China; Meta-analysis

Core tip: Barrett's esophagus (BE) is a precursor of esophageal adenocarcinoma. Western countries have published more research on BE than China has. Thus, epidemiological knowledge of BE in China is inadequate. Diagnosis and treatment of BE in China is based on western criteria, therefore, diagnosis, monitoring, and treatment of BE require more data based on the unique characteristics of patients and clinics in China. The current research analyzed 69 clinical studies to obtain a comprehensive understanding of BE in China. Results provide important guidelines that can help improve the treatment and follow-up of BE patients in China.

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INTRODUCTION

Barrett's esophagus (BE) is a pathological phenomenon that occurs when the stratified squamous epithelium in the lower esophagus is replaced by a metaplastic simple columnar epithelium. In some cases, BE is accompanied by intestinal metaplasia, which is considered a precursor of esophageal adenocarcinoma^[1]. Academics in Western countries have conducted more research on the subject than researchers in China. As such, despite the attention BE has drawn in recent years, epidemiological knowledge of BE in China is insufficient. The Digestive Disease Branch of the Chinese Medical Association drafted the Diagnosis and Treatment Consensus^[2] of BE in 2005 and amended it in 2011, when a consensus amongst clinicians was finally achieved^[1]. This consensus on BE, however, is based on western standards. Thus, the diagnosis, monitoring, and treatment of BE in China require more data based on Chinese clinics.

Although increasing numbers of researchers in China have focused on BE, the studies published thus far do not feature large samples or prospective designs. A systematic review^[3] of the clinical characteristics of BE in China was published in 2008. However, in this review, studies that used metaplasia as a necessary standard were not excluded, which contradicts the consensus. In addition, the sample sizes of some included studies are rather small, with reports featuring only one or two cases. The present study aims to obtain a comprehensive understanding of the characteristics of BE in China by conducting a meta-analysis on BE in China and comparing findings with cases in Western countries. Results will help improve the treatment and follow-up of Chinese BE patients.

MATERIALS AND METHODS

Sources of literature and retrieval methods

Information from the China National Knowledge Infrastructure (CNKI) and PubMed databases were used. Clinical studies on BE published in Chinese between 2000 and 2011 were retrieved from the CNKI database, and those published in English were obtained from the PubMed database using the keywords "Barrett" and "Barrett AND China", respectively. The researchers reviewed the titles and abstracts of all search results to determine whether or not the study was relevant to the current topic. The references listed in the studies obtained were also reviewed to locate additional studies.

Inclusion criteria of studies

The selected studies met the following criteria: (1) all of the cases described were from China; (2) diagnosis of BE conformed to standards set by the Digestive Disease Branch of the Chinese Medical Association in 2011; (3) BE was diagnosed through endoscopy and pathology; and (4) the number of cases included in the sample was > 10.

Exclusion criteria of studies

Studies were excluded if they featured any of the following criteria: (1) only published as an abstract; (2) intestinal metaplasia was used as a necessary diagnostic criteria; (3) the clinical aspects of BE were insufficient; that is, the study lacked at least three of the following aspects: endoscopic detection rate, sex, age, endoscopic manifestations, or histological type; (4) only a short segment of the study focused on BE; or (5) duplicate publication.

Data extraction and statistical analysis

Four researchers independently extracted data from every study, and any ensuing disagreements were resolved through discussion. The following data were extracted: name of the first author; year of publication; region of study; total number of cases; male to female ratio of the patients; average age, endoscopic detection rate; proportion of each endoscopic and histological type; follow-up cases and follow-up duration; and occurrence of esophageal adenocarcinoma during follow-up.

Data were analyzed using SPSS version 17.0. Proportions were evaluated using standard formulas. A mean difference demonstrating a 95% confidence rate was used for continuous data. The total number of person-years during follow-up was calculated by multiplying the number of follow-up cases with the follow-up duration. Cancer incidence was calculated by dividing the number of occurrences of esophageal adenocarcinoma among the follow-up cases by the total number of person-years.

RESULTS

Sources of studies

A total of 1121 studies were found in the CNKI database, and 108 of these studies met the inclusion criteria. Among these studies, 42 were rejected on the basis of the exclusion criteria; seven^[4-10] for using intestinal metaplasia as a necessary diagnostic standard; 28^[11-38] for having insufficient data on the clinical aspects of BE; four^[39-42] for providing only a small study on BE; and one each for inconsistent data^[43], doubts about plagiarism^[44] and duplicate publication^[45]. A total of 65 studies were found in the PubMed database; five of which met the inclusion criteria. Among these studies, one^[46] was excluded because of its duplicate publication in Chinese, and another^[47] was excluded for its use of intestinal metaplasia as a necessary diagnostic standard. A total of 69^[48-116] studies were included in the present research. The screening process is summarized using the flow diagram shown in Figure 1.

Characteristics of included studies

The 69 studies included in the present research were conducted in 25 provinces. The total number of samples in these studied was 12404, and the total number of cases was 3873 (Table 1).

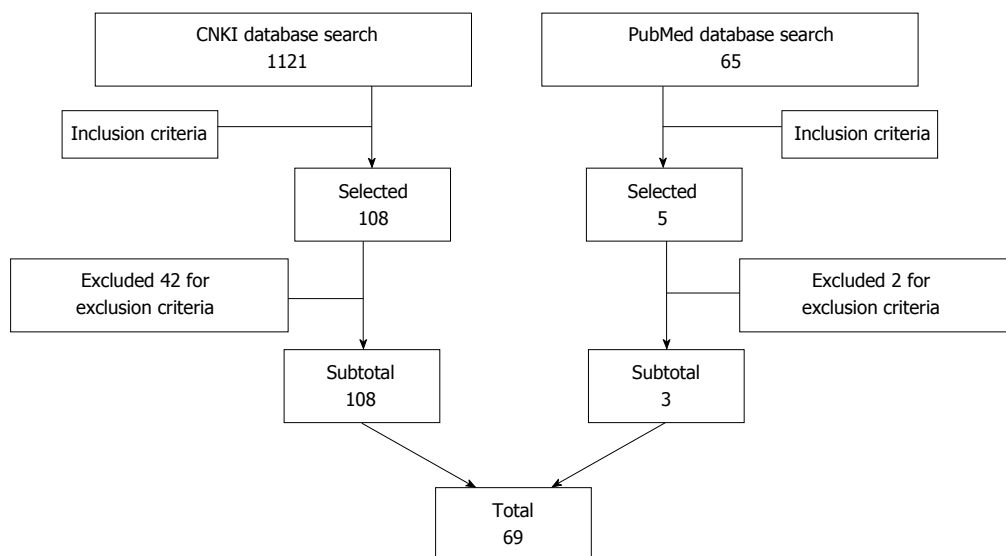


Figure 1 Flow diagram for the literature search. CNKI: China National Knowledge Infrastructure.

Endoscopic detection rate

A total of 15 studies reported the endoscopic detection rate of BE, which was obtained from all patients who had undergone endoscopy. However, the detection rate varied significantly, with rates ranging from 0.06% to 17.65%. The total endoscopic detection rate was 1.0% (95%CI: 0.1%-1.8%).

Sex

All studies reported the sex of BE patients (Table 1). One study^[85] was not included in this analysis because the sum of male and female patients was inconsistent with the reported total number of cases. The remaining 68 studies showed a total of 3829 cases with 2452 male patients, accounting for 64.0% of the sample (95%CI: 61.1%-67.0%), and 1377 female patients, accounting for 36.0% of the sample (95%CI: 33.0%-38.9%). The male to female ratio was 1.781 (95%CI: 1.552-2.009).

Age

A total of 58 studies reported the age of the BE patients (Table 1), and the average age of the patients was 49.07 ± 5.09 years.

Endoscopic manifestations

The endoscopic patterns of BE in 49 studies could be categorized into several types based on Herlihy criteria^[117]: island, tongue, circumferential, and mixed. On the basis of the columnar epithelial length reported in 29 studies, BE was divided into long-segment BE (LSBE) (*i.e.*, columnar epithelial metaplasia cells were involved in the entire circumference of the esophagus and the length of the segment was ≥ 3 cm) and short-segment BE (SSBE) (*i.e.*, columnar epithelial metaplasia cells were not involved in the entire circumference of the esophagus or the whole circumference of esophagus was involved but the length of the segment was < 3 cm)^[11] (Table 2).

Histological type

The histological type of BE was divided into the gastric-fundic, cardiac, and intestinal metaplasia types^[11] (Table 3).

Cancer incidence of BE

Thirty-one studies reported follow-up information. The total number of follow-up cases was 1283, with a follow-up duration ranging from 3 mo to 3 years. The mean follow-up duration was 1.099 years. Three studies^[80,91,95] focused only on the follow-up of atypical hyperplasia of BE; thus, these studies were not included in this analysis. The total number of person-years during follow-up was 1410. Among 1283 cases, only two developed esophageal adenocarcinoma during the follow-up period; these cases were reported in two studies^[91,103]. Four cases were also detected with esophageal adenocarcinoma during follow-up, but the number of follow-up cases and follow-up times were not provided. Studies with these cases were excluded from this analysis. The cancer incidence of BE was 1.418 per 1000 person-years.

DISCUSSION

The present research included 69 studies. The total endoscopic detection rate of BE was 1.0%, consistent with the total BE morbidity rate in Asia (0.9%-1.2%) reported by Hou *et al.*^[118]. The endoscopic detection rate of BE in the reviewed studies ranged from 0.06% to 17.65%. Tseng *et al.*^[90] reported that the endoscopic detection rate of BE in Taiwan was 0.06%, which is much lower than the total detection rate observed in China. This variation may be attributed to their inclusion of upper gastrointestinal tract endoscopy in routine health maintenance programs, which can yield more reliable data on the prevalence of BE in local populations. The endoscopic detection rate of BE in most studies is based on patients who have undergone upper gastrointestinal tract endos-

Table 1 Characteristics of the selected studies

Ref.	Year of publication	Region (province)	Cases	Male	Female	Mean age (yr)
Chen <i>et al</i> ^[48]	2011	Henan	150	60	90	45.42
Chen <i>et al</i> ^[49]	2011	Hubei	52	31	21	49
Guo <i>et al</i> ^[50]	2011	Hebei	42	27	15	48
Han <i>et al</i> ^[51]	2011	Jilin	30	21	9	45
Hao <i>et al</i> ^[52]	2011	Guangdong	76	58	18	50.6
Lin <i>et al</i> ^[53]	2011	Zhejiang	41	28	13	58.9
Lv <i>et al</i> ^[54]	2011	Zhejiang	108	80	28	61
Su <i>et al</i> ^[55]	2011	Hubei	23	13	10	40.3
Wang <i>et al</i> ^[56]	2011	Fujian	113	67	46	54.5
Zou <i>et al</i> ^[57]	2010	Guangxi	23	16	7	50.3
Xia <i>et al</i> ^[58]	2010	Hubei	56	34	22	45.85
Wu <i>et al</i> ^[59]	2010	Shanghai	84	50	34	36.3
Liu <i>et al</i> ^[60]	2010	Chongqing	62	35	27	51
Li <i>et al</i> ^[61]	2010	Anhui	32	18	14	48.6
Li <i>et al</i> ^[62]	2010	Guangdong	45	18	27	43
Hao <i>et al</i> ^[63]	2010	Henan	144	98	46	NA1
Yao <i>et al</i> ^[64]	2010	Sichuan	21	15	6	40.1
Tang <i>et al</i> ^[65]	2010	Jiangxi	63	43	20	45
Shi <i>et al</i> ^[66]	2010	Fujian	57	36	21	53
Jia <i>et al</i> ^[67]	2010	Shanxi	26	21	5	49
Gao <i>et al</i> ^[68]	2010	Hubei	32	21	11	NA
Tian <i>et al</i> ^[69]	2009	Shandong	59	43	16	49.14
Li <i>et al</i> ^[70]	2009	Guangxi	38	27	11	47.56
Dai <i>et al</i> ^[71]	2009	Hunan	23	18	5	50.3
Bai <i>et al</i> ^[72]	2009	Chongqing	67	41	26	50.7
Yang <i>et al</i> ^[73]	2009	Shaanxi	87	58	29	53.3
Yang <i>et al</i> ^[74]	2009	Ningxia	51	29	22	49.14
Tan <i>et al</i> ^[75]	2009	Liaoning	48	31	17	58.4
Qiu <i>et al</i> ^[76]	2009	Fujian	404	238	166	44.2
Lu <i>et al</i> ^[77]	2009	Jiangsu	12	9	3	NA
Liu <i>et al</i> ^[78]	2009	Liaoning	23	18	5	49
Gao <i>et al</i> ^[79]	2009	Liaoning	42	25	17	NA
Peng <i>et al</i> ^[80]	2009	Guangdong	27	14	13	48.18
Wu <i>et al</i> ^[81]	2008	Henan	25	16	9	48.3
Wang <i>et al</i> ^[82]	2008	Henan	12	10	2	49.5
Wang <i>et al</i> ^[83]	2008	Ningxia	109	64	45	50.11
Lu <i>et al</i> ^[84]	2008	Guangxi	32	22	10	52.5
Gao <i>et al</i> ^[85]	2008	Shandong	44	22	20	50
Zhang <i>et al</i> ^[86]	2008	Jiangxi	84	51	33	46
Yang <i>et al</i> ^[87]	2008	Hebei	74	40	34	52.6
Jian <i>et al</i> ^[88]	2008	Yunnan	68	51	17	52
Ji <i>et al</i> ^[89]	2008	Jiangsu	51	38	13	52.5
Tseng <i>et al</i> ^[90]	2008	Taiwan	12	9	3	61.6
Zhang <i>et al</i> ^[91]	2007	Shandong	30	24	6	52
Meng <i>et al</i> ^[92]	2007	Liaoning	21	13	8	54.6
Duan <i>et al</i> ^[93]	2007	Henan	54	38	16	51.6
Zhou <i>et al</i> ^[94]	2007	Zhejiang	13	7	6	NA
Wang <i>et al</i> ^[95]	2007	Hubei	88	61	27	47.46
Li <i>et al</i> ^[96]	2007	Fujian	75	45	30	45.42
Jin <i>et al</i> ^[97]	2007	Zhejiang	37	22	15	53
Zhou <i>et al</i> ^[98]	2006	Hubei	128	93	35	NA
Yang <i>et al</i> ^[99]	2006	Shaanxi	86	58	28	46
Wu <i>et al</i> ^[100]	2006	Fujian	13	10	3	48
Wang <i>et al</i> ^[101]	2006	Shaanxi	73	29	44	45.6
Suo <i>et al</i> ^[102]	2006	Fujian	37	24	13	50
Li <i>et al</i> ^[103]	2006	Liaoning	54	35	19	49
Li <i>et al</i> ^[104]	2006	Tianjin	37	25	12	58.3
Dou <i>et al</i> ^[105]	2006	Guizhou	89	57	32	46.3
Wang <i>et al</i> ^[106]	2006	Hubei	33	22	11	48
Shu <i>et al</i> ^[107]	2006	Hubei	13	12	1	NA
Zheng <i>et al</i> ^[108]	2005	Hubei	45	31	14	NA
Liang <i>et al</i> ^[109]	2005	Xinjiang	20	14	6	NA
Zhang <i>et al</i> ^[110]	2004	Shaanxi	69	54	15	56.2
Zhao <i>et al</i> ^[111]	2003	Shandong	55	38	17	46.8
Dong <i>et al</i> ^[112]	2003	Zhejiang	32	23	9	48.8
Zhang <i>et al</i> ^[113]	2001	Anhui	14	11	3	NA
Wang <i>et al</i> ^[114]	2001	Guangdong	21	16	5	67.3

Zhao <i>et al</i> ^[115]	2000	Shandong	35	26	9	NA
Yang <i>et al</i> ^[116]	2000	Beijing	29	22	7	50

NA: Not applicable (data were either unavailable or not reported).

Table 2 Endoscopic manifestations of Barrett's esophagus

Type	Proportion	95%CI
Island	0.448	0.375-0.521
Tongue	0.262	0.204-0.320
Circumferential	0.247	0.190-0.303
Mixed	0.043	-0.006-0.093
SSBE	0.803	0.771-0.835
LSBE	0.197	0.165-0.229

The island type of Barrett's esophagus (BE) accounted for 44.8% of all cases, the tongue type for 26.2%, the circumferential type for 24.7%, and the mixed type for 4.3%. Short-segment BE and long-segment BE accounted for 80.3% and 19.7% of the cases, respectively.

Table 3 Histological type of Barrett's esophagus

Type	Proportion	95%CI
Cardiac	0.400	0.310-0.491
Gastric-fundic	0.325	0.227-0.422
Intestinal Metaplasia	0.272	0.226-0.318
Mixed type	0.003	-0.002-0.008

The cardiac type accounted for 40.0% of the cases, the gastric-fundic type for 32.5%, the intestinal metaplasia type for 27.2%, and the mixed type for 0.3%.

copy in a local hospital. These patients mainly suffer from several gastrointestinal symptoms such as regurgitation, heartburn, epigastric discomfort, nausea, vomiting, and eructation. Reports of such symptoms increase the detection rate of BE, so this result cannot represent the prevalence of BE in the general population.

In this research, the total endoscopic detection rate was lower than that reported in a meta-analysis in 2008^[3] (2.39%), likely because of the increasing number of patients accepting endoscopy in recent years as a means of diagnosing and treating upper gastrointestinal tract diseases. Some patients opt to undergo endoscopic examination when experiencing upper gastrointestinal tract symptoms, while others choose endoscopy for routine health maintenance. Thus, the data do not provide sufficient evidence to conclude that the incidence of BE has declined in China.

The detection rate of BE in Western countries is 3%-8%^[119], which is higher than that in China. Variations observed may be due to the following reasons: (1) variations in genetic and environmental factors; (2) western lifestyle and diet-related factors, such as visceral obesity, high-fat diet, and tobacco and alcohol consumption, which are risk factors for BE^[118,120-133]; and (3) delayed recognition of BE in China, considering that current diagnostic standards are based on western practices and some Chinese doctors experience difficulties when diagnosing patients with BE.

In this research, the number of male BE patients was higher than that of female patients, which is similar to western reports^[133]. The average age of onset of BE in this study was 49.07 years, whereas the average age in Western countries is 60 years^[134,135]. Variations observed may be attributed to differences in the Chinese and western lifestyles.

The main types of endoscopic manifestations of BE include the island type and SSBE, which is similar to western reports^[136]. Experts in the United States believe that LSBE and SSBE represent two different pathological changes and that the former is related to severe gastroesophageal reflux disease, which is common in older people. Although LSBE tends to increase the risk of cancer, no evidence today correlates the length of BE and cancer risk^[137].

The number of cases of cardiac type BE was higher than that of other histological types in this research. Jankowski *et al*^[138] reported that intestinal metaplasia progresses to cancer, and the Diagnosis and Treatment Consensus of BE of China (2011) regards intestinal metaplasia as a precursor of esophageal adenocarcinoma. Unfortunately, the reviewed studies present limited clinical and pathological data on intestinal metaplasia related to BE, considering Chinese researchers' lack of knowledge on the topic. Some researchers believe that cancer formation is related to atypia of the epithelial instead of columnar epithelial metaplasia^[139].

An individual with BE is estimated to be at 25-30 times greater risk of developing esophageal adenocarcinoma^[140-143] than the general population. Cancer incidence was found to be 1.418 per 1000 person-years in the present study, which is lower than that in England (7.0 per 1000 person-years), United States (6.4 per 1000 person-years), and other European countries (5.6 per 1000 person-years)^[144]. Thus, the cancer incidence of BE in China is lower than that in Western countries. The spectrum of BE characteristics differs significantly between the two regions.

COMMENTS

Background

Barrett's esophagus (BE) is a precursor of esophageal adenocarcinoma. The Diagnosis and Treatment Consensus of BE in China is based on Western criteria. Epidemiological knowledge of BE in China is inadequate.

Research frontiers

A large number of clinical studies on BE have been conducted in China but they do not feature large sample sizes or prospective designs. A systematic review of the clinical characteristics of BE in China was published in 2008. However, in this review, studies that used metaplasia as a necessary standard were not excluded, which contrasts the consensus.

Innovations and breakthroughs

The Digestive Disease Branch of the Chinese Medical Association drafted the

Diagnosis and Treatment Consensus of BE in 2005 and amended it in 2011, when a consensus amongst clinicians was achieved. Based on this consensus, the present research analyzed existing clinical studies with the aim of obtaining a comprehensive understanding of the characteristics of BE in China.

Applications

This research analyzed existing clinical studies with the aim of understanding the characteristics of BE in China. The results obtained will help improve the treatment and follow-up protocols of BE patients in China.

Terminology

BE is a pathological phenomenon that occurs when the stratified squamous epithelium in the lower esophagus is replaced by a metaplastic simple columnar epithelium. In some cases, BE is accompanied by intestinal metaplasia, which is considered a precursor of esophageal adenocarcinoma.

Peer review

This research has a high degree of significance. The meta-analysis presented here reviews the characteristics of the BE cases in China, including patient demographics, endoscopic and histological features, and risks for developing adenocarcinoma. The inclusion and exclusion criteria are appropriate, and the information obtained from selected reports is sufficiently analyzed.

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