

A Survey of Esophageal Cancer in Cixian County of Hebei Province

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OBJECTIVE To characterize the histologic types of esophageal cardiac mucosa by endoscopic survey in a high-risk cancer area of China.

METHODS An endoscopic survey with Lugol's staining was carried out in Cixian County, Hebei Province from December 2001 to May 2002. The data were processed using computer SPSS 10.0 software.

RESULTS The incidences of mild esophagitis, moderate esophagitis, and severe esophagitis were for 2013 cases, 34.9%(703), 1.6%(33) and 0.1% (2) respectively; those with mild dysplasia, moderate dysplasia, severe dysplasia of the esophagus were 8.6% (172), 7.8% (157) and 2.6% (53) respectively; those with carcinoma in situ, intramucosal carcinoma, invasive squamous carcinoma of the esophagus were 2.5%(50), 0.2% (4) and 0.7%(14) respectively. The histologic-detecting rates of non-atrophic gastritis, and atrophic gastritis of the cardia were 36.3%(730), 11.5% (232) respectively; those with mild dysplasia, severe dysplasia of the cardia were 2.5%(51), 0.8%(17) respectively; those with intramucosal adenocarcinoma, invasive adenocarcinoma of the cardia were 0.1% (3), 0.8%(17) respectively. The early-detection rate of esophageal cancer was 79.4%(54/68). The survey rate(examined population to covered population) was 73.8% (2013/2725).

CONCLUSIONS Esophageal endoscopic screening with Lugol's solution staining has an advantage over esophageal balloon cytology, in that the histological diagnoses of esophageal cardiac diseases can be obtained, thus contributing to the prevention of subsequent disease. In using the staining method the detection rate of early esophageal cancer is higher than that revealed by balloon cytology.

KEYWORDS: esophageal neoplasms, cardiac neoplasms, dysplasia, endoscopy, screening.

Cixian County is one of the high incidence areas of esophageal cancer in China ^[1]. Over a period of almost 30 years of effort to prevent, esophageal cancer has resulted in a descending incidence trend, but it is still higher than many other areas ^[2]. Successful early detection, early diagnosis and early treatment are hard to achieve. In order to prevent and treat esophageal cancer, a large-scale endoscopic survey was carried out in Cixian in 2002 by Hebei Cancer Institute with satisfactory results.

MATERIAL AND METHODS

Survey population

In the National Tenth Five-Year Scientific Championship Project, people 40-69 years old in nine villages in the hilly part of Cixian were

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chosen as the survey population. The hilly part of the County has a higher incidence rate of esophageal cancer compared to the plain area. The total population of the nine villages was 12048. The incidence rate of esophageal cancer in this region during 1996–2000 was 176.0/100,000 and the mortality rate 126.2/100,000 per year. At the same time, 18,675 people from seven other villages were chosen as the control group, where the incidence rate and mortality rate were 171.1/100,000 and 139.2/100,000, respectively.

Survey Processing

The health professionals first prepared a printed list of 2000 people of ages 40–69 years in the nine villages. Two days prior to the survey, personal contacts with potential candidates to be examined were made by local physicians in order to arrange detailed procedures for the survey. At the beginning of the survey, those subjects were requested to fill out an epidemiological questionnaire and physical examinations were performed by physicians to exclude people with any serious contraindication to endoscopic examination. Then the endoscopic examination was performed by specialists using the method developed by Professor Wang Guoqing^[3]. The results were recorded in detail and the biopsy specimens fixed in 80% alcohol followed by staining with hematoxylin–eosin (HE). The diagnosis was determined by pathologists.

Data analysis

The data were computer processed to set up a survey information database which was handled by SPSS 10.0 software using a chi-square test, $\alpha=0.05$.

RESULTS

Survey rate

The total number of people from the nine villages who took part in the large-scale endoscopic survey was 12,048. The age of the 2,992 people examined was 40–69 years, excluding the contraindicative population of 267 (including 32 cancer patients, 22 heart disease patients, 29 cerebrovascular disease patients, 55 hypertension patients, 56 other kinds of disease patients, 59 deaths and 14 emigrants). The survey rate was 73.8% (2,013/2,725).

Age distribution

The number of people who were examined by endoscopy was 2,013, including 973 males and 1,040 females. The sex ratio (males to females) was 0.94:1

(Table 1).

Table 1. Age Distribution of the Population

age	40–	45–	50–	55–	60–	65–	total
Male	364	220	139	120	86	44	973
Female	428	238	183	105	63	23	1040
Total	792	458	322	225	149	67	2013

Results of the endoscopic examinations

Detection rates of esophageal histologic types and age distribution

The histologic–detection rates were as follows of the 2,013 cases: carcinoma in situ was 2.5% (50); intramucosal carcinoma was 0.2% (4); invasive squamous carcinoma was 0.7% (14); early cancer was 2.7% (54), which made up 79.4% of the total esophageal cancer.

As noted in Table 2, as the age increased by 5-year intervals, the histologic–detection rates of esophageal cancer and dysplasia all increased from the 40-year-old group to the highest for the 65-year-old group ($\chi^2=135.943$, $P_1=0.000$; $\chi^2=182.782$, $P_2=0.000$). The histologic–detection rates of esophagitis between different age groups showed significant difference ($\chi^2=12.475$, $P=0.029$). The rates of dysplasia in different age groups displayed significant differences between them ($\chi^2=141.184$, $P=0.000$). The rates of esophageal cancer between different age groups showed significant differences ($\chi^2=74.855$, $P=0.000$).

Gender distribution of histologic types in the esophagus

The histologic–detection rates were as follows: esophagitis was 35.9% (349/973) in males and 37.6% (391/1,040) in females respectively, with no significant difference between them ($\chi^2=0.645$, $P=0.422$); dysplasia was 23.1% (225/973) in males and 15.1% (157/1,040) in females respectively, with a significant difference between them ($\chi^2=21.072$, $P=0.000$); esophageal cancer was 3.3% (32/973) in males and 3.5% (36/1,040) in females respectively, with no significant difference between them ($\chi^2=0.001$, $P=0.98$).

The incidence rate of esophageal cancer and precancerous lesions

We found 74 cases including 68 cases of esophageal cancer and 6 previously known cases (Table 3).

The outcome of the cardiac endoscopic survey

The histologic detection rate of cardiac cancer and age distribution

As is shown in Table 4, the histologic–detection rate of cardiac cancer was much lower than that of esophageal cancer ($\chi^2=26.767, P=0.000$), and early cardiac cancer only comprised 15% (3/20) of cardiac cancers. Histologic–detection rates were as follows: gastritis in the cardia was 44.5% (433/973) in males and 50.8% (529/1,040) in females respectively, showing a significant difference between them ($\chi^2=8.159, P=0.004$); dysplasia was 4.9% (48/973) in males and 1.9% (20/1,040) in females respectively, with a significant difference between them ($\chi^2=13.955, P=0.000$); cardiac cancer

was 1.3% (13/973) in males and 0.7% (7/1,040) in females, with no significant difference between them ($\chi^2=2.246, P=0.134$).

Age distribution: cardiac cancer is common in people over 50 years, and also at this age, the detection rate of carditis was 51.7% (409/792), also high in the 40–year–old group. The histologic–detection rates of cardiac cancer and dysplasia all increased with age ($\chi_1^2=84.875, P_1=0.000; \chi_2^2=36.209, P_2=0.000$).

The incidence rate of cardiac cancer and dysplasia

In this survey, we found 20 cases of cardiac cancer, 1 prevalence case, totally 21 cases, the incidence rate was lower than that of esophageal cancer (Table 5), and 2 cases of gastric cancer.

Table 2. Age distribution of detection rates of histologic types in the esophagus

Type	Age(%)					
	40~	45~	50~	55~	60~	65~
Normal squamous epithelium	355(44.8)	176(38.4)	92(28.6)	56(24.9)	14(9.4)	7(10.4)
Squamous epithelium acanthosis	11(1.4)	4(0.9)	10(3.1)	7(3.1)	5(3.4)	1(1.5)
Squamous epithelium atrophy	1(0.1)	1(0.2)	1(0.3)	—	—	—
Basal cell hyperplasia	6(0.8)	6(1.3)	3(0.9)	1(0.4)	2(1.3)	—
Mild esophagitis	304(38.4)	167(36.5)	90(28.0)	71(31.6)	53(35.6)	18(26.9)
Moderate esophagitis	17(2.1)	2(0.4)	9(2.8)	4(1.8)	1(0.7)	—
Severe esophagitis	1(0.2)	2(0.6)	1(0.4)	—	—	—
Mild dysplasia	37(4.7)	36(7.9)	41(12.7)	26(11.6)	21(14.1)	11(16.4)
Moderate dysplasia	19(2.4)	30(6.6)	43(13.4)	26(11.6)	26(17.4)	13(19.4)
Severe dysplasia	12(1.5)	12(2.6)	12(3.7)	6(2.7)	9(6.0)	2(3.0)
Carcinoma in situ	3(0.4)	8(1.7)	10(3.1)	14(6.2)	8(5.4)	7(10.4)
Intramucosal carcinoma	—	2(0.4)	—	—	2(1.3)	—
Invasive carcinoma	—	2(0.4)	3(0.9)	4(1.8)	3(2.0)	2(3.0)
Others	27(3.4)	11(2.4)	6(1.8)	9(4.0)	5(3.4)	6(9.0)
Total	792(100.0)	458(100.0)	322(100.0)	225(100.0)	149(100.0)	67(100.0)

Table 3. The incidence rate of esophageal cancer and precancerous lesions (1/100,000)

Type	Dysplasia			Cancer
	Mild	Moderate	Severe	
Cases	355(44.8)	176(38.4)	92(28.6)	56(24.9)
Crude incidence rate	11(1.4)	4(0.9)	10(3.1)	7(3.1)
Standard rate in China	1(0.1)	1(0.2)	1(0.3)	—
Standard rate in the world	6(0.8)	6(1.3)	3(0.9)	1(0.4)

Table 4. Age distribution of detection rates of histologic types in cardia

Type	Age(%)					
	40~	45~	50~	55~	60~	65~
Normal adenoepithelium	295(37.2)	156(34.1)	81(25.2)	61(27.1)	27(18.1)	10(14.9)
Non-atrophic gastritis	319(40.3)	169(36.9)	116(36.0)	60(26.7)	47(31.5)	19(28.4)
Atrophic gastritis	90(11.4)	45(9.8)	38(11.8)	34(15.1)	14(9.4)	11(16.4)
Mild dysplasia I	13(1.6)	8(1.7)	10(3.1)	8(3.6)	8(5.4)	4(6.0)
Severe dysplasia	—	8(1.7)	2(0.6)	3(1.3)	4(2.7)	—
Intramucosal adenocarcinoma	—	—	1(0.3)	1(0.7)	1(1.5)	1(1.5)
Invasive adenocarcinoma	—	1(0.2)	1(0.3)	3(1.3)	5(3.4)	7(10.4)
Others	75(9.5)	71(15.5)	73(22.6)	56(24.9)	43(28.9)	15(22.4)
Total	792(100.0)	458(100.0)	322(100.0)	225(100.0)	149(100.0)	67(100.0)

Table 5. The incidence rate of cardiac cancer and precancerous lesions per 100,000

Type	Mild dysplasia	Severe dysplasia	Cancer
Cases	51	17	21
Crude incidence rate	2533.5	844.5	1092.8
Standard rate in China	361.7	119.2	165.3
Standard rate in the World	490.0	161.4	249.7

DISCUSSION

In order to prevent and treat esophageal cancer, systematic research including clinical, laboratory and field investigations has been carried out in China in high-risk areas since the 1950's [4-8]. A variety of detecting methods have been developed by Chinese scientists such as exfoliative balloon cytology (EBC), occult blood bead detector (OBB), conventional endoscopy combined with smear preparation or biopsy, deficient hydrochloric acid preliminary screening, serum total salicylic acid detection (TSA), ear information diagnostic examination, and so on. One of the often-used methods for clinical diagnosis in a high-incidence area is exfoliative balloon cytology, which was created by Professor Shen Qiong. Large scale screening with the population of 126,187 in Cixian was carried out in 1992 and 16,748 high-risk participants aged 40 years and older were screened with exfoliative balloon cytology. The survey rate was 71.4%. The results were 179 cases of esophageal cancer (EC), 172 of near esophageal cancer (NEC), 866 of stage-two severe esophageal epithelial dysplasia (SEED II), 3,179 cases of stage-one severe esophageal epithelial dysplasia (SEED I) and 5,346 cases of mild esophageal epithelium dysplasia [9] (MEED). Exfoliative balloon cytology technology was used resulting in the detection rates of MEED, SEED I, SEED II, NEC and EC as fol-

lows: 31.92%, 18.98%, 5.17%, 1.03% and 1.07% respectively. Most studies indicated that exfoliative balloon cytology detection was an effective, economical and practical method, with a higher detection rate for esophageal cancer than conventional endoscopy, but only cytological data could be acquired and a further endoscopic biopsy and histopathologic examination was necessary to confirm the diagnosis. This method is now insufficient for esophageal cancer screening because of patient discomfort and a lower detection rate. Esophageal chromoendoscopy with multi-point biopsy and histopathologic examination has developed rapidly since the 1970's. The detection rate for esophageal cancer and/or precancerous lesions has increased greatly [10], and at the same time the character and scope of the lesions have been identified, directing treatment and follow-up, thus providing a new strategy for the prevention of subsequent esophageal cancer [11,12].

This study was a part of The National Tenth Five-Year Scientific Championship Project. A large-scale esophageal chromoendoscopic survey in a high-risk area was conducted. Compared with exfoliative balloon cytology, the advantages and disadvantages are: first, there is a high detection rate. Compliance to the survey was high after the people had understood the advantages of esophageal chromoendoscopic survey; (with the help of a forceful educational publicity cam-

paign). The detection rate in this survey reached 73.8% , while the previous rate was 71.4% in 1992. Second, histological and pathological diagnoses can be obtained, precancerous lesions and non -cancer diseases of esophageal and cardiac cancer can be detected, providing a basis for the prevention and treatment of possible diseases. Third, the detection rate of early esophageal cancer was 79.4% , higher than the 61.7% in 1992. Fourth, the detection rate of precancerous lesions was lower than that of cytological method, the detection rate of SEED is 2.6% , lower than that of cytology (5.17%); Fifth, The cost is higher than that of exfoliative balloon cytology. So it can be widely used in those area and units with appropriate conditions.

In this survey, the detection rates of cardiac cancer and gastric cancer were lower than that of esophageal cancer. The first reason is that the gastric mucosa chromoendoscopy may not take up iodine well as the esophageal mucosa; secondly, in this area, the incidence rates of cardiac cancer and gastric cancer are actually lower than those of esophageal cancer.

REFERENCES

- 1 China Institute of Cancer Prevention and Research, Statistic and Information Center Ministry of Health. The incidence and mortality of malignant tumors in experimental units in China. Beijing: Chinese Science Publishing House of Medicine, 2002;126-129.
- 2 Hou J, He YT, Qiao CY, et al. Analysis of Incidence of Esophageal Cancer in Cixian. *Oncology in China*, 2002;11: 394-396.
- 3 Wang GQ, Zhou MH, Cong QW. Lugol's solution in endoscopic diagnosis of early esophageal cancer. *China Med J*, 1995;75:417-418.
- 4 Hu SP, Yang HS, Shen ZY. Study on etiology of esophageal carcinoma: retrospect and prospect. *China Oncology*, 2001; 11:171-174.
- 5 Hou J, Qiao CY, Meng FS, Zhang GS, He YT, Chen ZF, Liu JB, Song GH, Li SS, Hao SM, Ji HX. A case-control study on risk factor of esophageal cancer in cixian county of Hebei Province. *Buletin of Chinese cancer*, 1999;8:252-255.
- 6 Jing DW, Gao F, Lin PZ, et al. Long term of effect of treating patients with precancerous lesion of the esophagus. *China J Oncology cancer*, 1999;21:275-277.
- 7 Hou J, Yuan FR, Li SS, et al. A clinical study on the treatment results of esophageal dysplasia by composite Dangshen pill. *Chinese Medicine and Pharmacy*, 1992;7:11-13.
- 8 Hou J, Yuan FR, Li SS, et al. A clinical study on the effect of Cangdouwan on esophageal precancerous lesion. *Chinese Journal of Integrated Traditional and Western Medicine*, 1992;12:604-606.
- 9 Hou J, Lin PZ, Chen ZF, Wang GQ, Liu TG, Li SS, Meng FS, Du CL. A study survey of esophageal cancer in Cixian of Hebei. *Cancer Research on Prevention and Treatment*, 1998;25:73-75.
- 10 Wang GQ, Wei WQ, Lu N, et al. Significance of screening by iodine staining of endoscopic examination in the area of high incidence of esophageal carcinoma. *Cancer*, 2003;22: 175-177.
- 11 Akaska Y, Okuda S, Ida K. Basic research and clinical application in esophagus copic lugol's staining. *Gastroenterol Endose*, 1974;18:84.
- 12 Wang GQ, Chang FB, Tian ZJ, et al. The use of in vivo staining by Toluidine Blue in the diagnosis of early esophageal carcinoma. *Nati Med J China*, 1980;60:93.