ESOPHAGEAL CANCER

An analysis of esophageal cancer incidence in Cixian county from 1974 to 1996

Yu-Tong He, Jun Hou, Cui-Yun Qiao, Zhi-Feng Chen, Guo-Hui Song, Shao-Sen Li, Fan-Shu Meng, Hong-Xin Jin, Chao Chen

Yu-Tong He, Jun Hou, Zhi-Feng Chen, Hebei Cancer Institute, Shijiazhuang 050011, Hebei Province China
Cui-Yun Qiao, Guo-Hui Song, Shao-Sen Li, Fan-Shu Meng, Hong-Xin Jin, Chao Chen, Cixian Cancer Institute, Cixian county 056500, Hebei Province China
Supported by The National Ninth-Five-Year Scientific Championship Project No.96-906-01-01
Correspondence to: Dr Jun Hou, Hebei Cancer Institute, Jiankanglu 5, Shijiazhuang 050011, Hebei Province China. hytong69@yahoo.com
Received: 2002-09-13 Accepted: 2002-10-21

Abstract

AIM: To describe the incidence of esophageal cancer (EC) in Cixian, a county of Hebei province during 1974-1996. We analyzed the sex and age characteristics as well as the geographic distribution of EC, in order to determine the impact so that methods of preventing and controlling EC in Cixian can be put in place.

METHODS: Since the early 1970s, the cancer registry system has been established, which collects the cancer incidence in Cixian county. The malignant tumors were coded according to International Classification of Disease IX (ICD-9). All the data were checked and analyzed using EPIINFO.

RESULTS: The trend of the incidence rate of EC from 1974 to 1996 had declined, (229.9/100 000 vs 178.5/100 000, Odds ratio=1.47, 95 % CI:1.32–1.63, χ²=52.89, trend χ²=26.54, P<0.001). The incidence rate of males declined significantly (281.81/100 000 vs 157.96/100 000, Odds ratio=1.61, 95 % CI: 1.41–1.84, χ²=47.85. Trend χ²=44.86, P<0.001), whereas, the females remained steady (157.96/100 000 vs 133.41/100 000, odds ratio=1.28, 95 % CI:1.17–1.49, χ²=9.26. trend χ²=2.69, P>0.05). Male average annual incidence rate was 142.80/100 000 and the female's was 95.18/100 000. The sex ratio (males to females) was 1.50:1. The incidence rate was increasing along with the age. As to the geographic distribution, the incidence rate in mountainous areas and hilly areas showed a significantly declining trend (mountainous areas, trend χ²=149.93, P<0.001; hilly areas, trend χ²=42.70, P<0.001). The incidence rate of EC in plain areas had increased (trend χ²=22.39, P<0.001).

CONCLUSION: The incidence rate of EC in Cixian county shows a trend and has declined after two decades, especially in mountainous area. But compared to other regions in the world, Cixian county still had a high incidence rate of EC.

INTRODUCTION

Cixian county is one of the highest incidence rates of esophageal cancer (EC) in China, as well as in the world[1-7]. At the start of the 1970s, a field study of EC prevention and treatment was set up[8]. At the same time the population-based cancer registry system, so called the three-level prevention web, was established. Each clinic doctor in every township was required to report each new case of cancer occurring in the township using a standard card, then the cards were sent to the clinic of the rural administration unit. The unit sorted the cards and sent them to the Cixian Cancer Registry. To this day the Cixian Cancer Registry continues to collect incidence data. This present report came from “A study of incidence, mortality and surveillant method of risk factors of common carcinoma” carried out in the Cixian county of Hebei province, which is adjacent to the Linxian county of Henan province. This study was one of The National Ninth-Five-Year Scientific Championship Project.

MATERIALS AND METHODS

Materials

Cixian is located at latitude 36° 30’ North and longitude 114° 40’ East. It is situated on the east side of the Taihang Mountain, along the Zhanhe River and it lies in the south of the Handan City. Across the Zhanhe River to the south is the Anyang City of Henan Province. Cixian county occupies an area about 951 square kilometers, composed of 35 districts, and its population is 574 828, consisting of 289 391 males and 285 437 females. There is a remarkable variation in the earth stratum of the county, with mountainous, hilly, and level land each constituting about one-third of its total area. The climate is influenced mainly by the warm mainland seasonal winds. The temperature range is between 18-25 °C and the rainfall range is between 600-700 millimeters. The major soil there is brown and light colored weed earth. Farm products include wheat, corn, millet, rice, red potato and beans. Iron and coal are the main minerals, and coal is the main local fuel of the county.

Cixian Cancer Registry is a population-based registry that has been established, which collects the cancer incidence in Cixian county. The malignant tumors were coded according to International Classification of Disease IX (ICD-9). At the same time the population-based cancer registry system, so called the three-level prevention web, was established. Each clinic doctor in every township was required to report each new case of cancer occurring in the township using a standard card, then the cards were sent to the clinic of the rural administration unit. The unit sorted the cards and sent them to the Cixian Cancer Registry. To this day the Cixian Cancer Registry continues to collect incidence data. This present report came from “A study of incidence, mortality and surveillant method of risk factors of common carcinoma” carried out in the Cixian county of Hebei province, which is adjacent to the Linxian county of Henan province. This study was one of The National Ninth-Five-Year Scientific Championship Project.

METHODS

The register was conducted by the three-level prevention web. Each clinic doctor in every township (prevention web I) was required to report each new case of cancer occurring in the township by a standard card, then the cards were sent to the clinic of the rural administration unit (prevention web II). They were sorted and sent to the Cixian Cancer Registry (prevention web III) once a month, these cards were checked, analyzed, coded and stored there. At the end of each year, a sample survey was conducted, to check the quality of the registration.

The carcinoma were coded according to International Classification of Disease IX (ICD-9)[9]. All the data was checked and analyzed by EPIINFO software. Age-standardized...
rates (ASR) were standardized to the world population using
the direct method and the statistical analysis was carried out
by using χ² and U-test, a probability value of less than 0.05
was considered statistically significant.

RESULTS

Incidence of esophageal cancer

Between the years 1974 and 1996 there were 14 207 cases
of EC in the county. The annual average incidence rate was
119.43/100 000, the ASR was 167.22/100 000. In 1974, the
incidence rate of EC was 165.81/100 000. It declined to
113.49/100 000 in 1996, representing a decline of 31.5 percent.
From Table 1 and Figure 1, we can see that the incidence rate
of EC in Cixian had a trend of gradual decline. The trend test
revealed that χ² = 26.54, P < 0.001. The incidence rate among
males declined significantly (χ² = 44.86, P < 0.001), whereas,
the females remained steady (χ² = 2.69, P > 0.05). In total, the
incidence rate between 1970s and 1990s showed significant
differences (U test: P < 0.01). While the difference between
1980s and 1990s was not significant.

The sex and age distribution

During the period there were 8 559 males and 5 648 females
with EC. The incidence rate among males was 142.80/100 000,
while females was 95.18/100 000. The sex ratio was 1.50
: 1.

The sex ratios (males to females) in 1970s, 1980s and 1990s
respectively was 1.57:1, 1.56:1 and 1.35:1.

The minimum age group of incidence was 1-year group
over 23 years. The incidence rate of EC increased with age
after 30 years old. It reached the highest at 80 years old group.
In females at the 60-year-old group it declined a little and reached
the highest at 80-year-old group. In 1990s the minimum
incidence group was 60-year-old group. The male incidence rate reached
the highest at 80 years old group, while the female declined
little at 60-year-old group and reached the highest at 80-year-
old group.

Geographic Distribution

In the mountainous area there were 2 106 EC cases from 1974
to 1996. The annual average incidence rate was 112.14/100 000.
The incidence rate of EC in 1974 was 213.60/100 000, which
dropped to 82.55/100 000 in 1996. Decreased by 131.05/100 000,
and the decline rate was 61.35 percent. From Table 2 and Figure
3 we could find that the incidence rate of EC in mountainous

| Year | Population | Case | Incidence rate | ASR | Population | Case | Incidence rate | ASR |
|------|------------|-----|----------------|-----|------------|-----|----------------|-----|
| 74   | 221842     | 450 | 202.85         | 281.81 | 217799     | 279 | 128.10         | 157.96 |
| 75   | 224063     | 392 | 174.95         | 244.74 | 220937     | 279 | 126.28         | 162.8 |
| 76   | 226098     | 407 | 180.01         | 247.68 | 222526     | 236 | 106.06         | 131.44 |
| 77   | 227998     | 335 | 146.93         | 195.17 | 224094     | 193 | 86.12          | 103.31 |
| 78   | 227677     | 320 | 140.55         | 186.94 | 228524     | 191 | 83.58          | 104.51 |
| 79   | 231485     | 302 | 130.46         | 197.31 | 229242     | 190 | 82.88          | 108.11 |
| 80   | 235881     | 323 | 136.93         | 199.38 | 232902     | 221 | 94.89          | 124.86 |
| 81   | 242181     | 301 | 124.29         | 193.06 | 239316     | 191 | 79.87          | 101.76 |
| 82   | 242211     | 334 | 137.90         | 210.05 | 244007     | 194 | 79.51          | 106.98 |
| 83   | 251237     | 348 | 138.51         | 220.67 | 249751     | 229 | 91.69          | 122.07 |
| 84   | 253097     | 367 | 145.00         | 240.89 | 251332     | 192 | 76.39          | 103.22 |
| 85   | 256616     | 324 | 126.26         | 217.06 | 254526     | 214 | 84.08          | 113.06 |
| 86   | 260149     | 374 | 143.76         | 250.52 | 257671     | 205 | 79.56          | 100.92 |
| 87   | 265498     | 331 | 124.67         | 202.98 | 261498     | 231 | 88.34          | 114.62 |
| 88   | 262726     | 404 | 153.80         | 250.76 | 264539     | 287 | 108.49         | 153.86 |
| 89   | 272643     | 401 | 147.10         | 237.16 | 285840     | 258 | 90.26          | 131.13 |
| 90   | 289391     | 443 | 153.10         | 248.1  | 285437     | 322 | 112.81         | 151.55 |
| 91   | 294993     | 446 | 151.20         | 260.53 | 287546     | 305 | 106.07         | 139.36 |
| 92   | 299306     | 430 | 143.70         | 240.72 | 291905     | 302 | 103.46         | 139.6 |
| 93   | 299498     | 408 | 136.20         | 216.73 | 296060     | 283 | 95.59          | 126.12 |
| 94   | 303761     | 379 | 124.80         | 197.96 | 295104     | 260 | 88.10          | 114.01 |
| 95   | 302782     | 359 | 118.60         | 192.95 | 294867     | 289 | 98.01          | 125.92 |
| 96   | 302538     | 381 | 125.90         | 203.65 | 298596     | 297 | 99.47          | 133.41 |

Total of 70’s 1595044    2529 158.55    — 1576024 1589 100.82    —
Total of 80’s 2595749    3627 139.73    — 2593737 2323 89.56    —
Total of 90’s 1802878    2403 133.29    — 1764078 1736 98.41    —
Total 5993671    8559 142.80    — 5933839 5648 95.18    —
area had significantly decreased. The result of trend test was \( \chi^2 = 149.93, P < 0.001 \). The incidence rates of EC in 1970s, 1980s, and 1990s were 150.44/100,000, 109.85/100,000 and 75.55/100,000, respectively. The U test result between 1970s and 1990s, between 1980s and 1990s was \( P < 0.01 \). Both of them had significant difference.

In the hilly area there were 4,633 EC cases. The annual average rate was 117.16/100,000. From 1974 to 1996, the incidence rate changed from 165.71/100,000 to 96.33/100,000. Decreasing in number was 69.38/100,000. And declining rate was 41.86 percent. The result of trend test was \( \chi^2 = 42.70, P < 0.001 \). From Table 2 and Figure 3, we could see that from 1970s to 1980s the incidence rate of EC declined significantly, from 141.62/100,000 to 106.30/100,000 (U test: \( P < 0.01 \)). While comparing the incidence rate of EC of 1980s with that of the 1990s', it increased from 116.14/100,000 to 130.09/100,000 (U test: \( P < 0.01 \)). We could see that the incidence rate of EC in level land was increasing steadily.

There are 35 townships in Cixian County. In the 1970s, Linfeng township had the highest incidence rate of EC, which was 211.90/100,000. While Dudang township had the lowest, which was 66.57/100,000. The highest male incidence rate existed in Linfeng and the number was 298.02/100,000. While the highest female incidence rate existed in Guanglu township and the number was 164.49/100,000. The lowest incidence rate of EC of both male and female existed in Dudang, which was 79.71/100,000 and 51.51/100,000, respectively. The highest rate was 3.18 times as much as the lowest. Cixian County had two high risk areas, one was the mountainous area, which was centered around Baitu district (128.23/100,000), the other was hilly area which was centered around Lintan district (128.64/100,000). Level land had the lowest incidence rate of EC (116.01/100,000). After 1980s, the highest incidence rate existed in Guanglu township (232.04/100,000) and the lowest existed in Dudang (55.08/100,000). Linfeng had the highest male incidence rate of EC (285.37/100,000), while Cizhou had the lowest (64.77/100,000). Guanglu had the highest female incidence rate of EC (214.28/100,000), while Dudang had the lowest (38.65/100,000). The highest EC incidence rate was 4.21 times as much as the lowest. There were 20 townships whose incidence rate were higher than the average of county wide, forming a high-risk hilly area, which was centered around Lintan district. After 1990s, Ducun township had the highest EC incidence rate of 275.80/100,000. While Dudang township
had the lowest whose number was 45.92/100 000. The highest male incidence rate existed in Ducun township which was 341.08/100 000. The highest female incidence rate existed in Guanglu which was 213.26/100 000. While the lowest male incidence rate lay in Wuhe township which number was 36.20/100 000. The highest EC incidence rate was 6.01 times as much as the lowest. There were 19 townships whose incidence rate were higher than the average of county wide, forming a high-risk level land area which was centered around Ducun township.

In the 1970s, the high incidence area existed in mountainous areas which are centered around Baitu district and in hilly area which was centered around Lintan district. After 1990s, the incidence rate of EC in Cixian declined significantly. But the hilly area still had high incidence rate, declining slowly. While the level land area had increasing trend, forming a high risk area which was centered around Ducun township.

**DISCUSSION**

Cixian county is one of the highest EC incidence rate areas in China, as well as in the world. Since the early 1970s, cancer registry system has been established where began to collected the cancer incidence in Cixian county[10-21]. Until now Cixian Cancer Registry have piled up the incidence data of more than twenty years. In this study we found the trend of the incidence rate of EC from 1974 to 1996 had declined after two decades. As for the possible causes of EC[22-27], we advocate the inhabitant to take follow prevention: (1) To improve the quality of the drinking water condition; (2) To administer the farm products storage, not to eat the food with mold; (3) Eating more vegetables and fruits, changing the bad life style; (4) Conducting screening survey to find the carcinoma in situ or intramucosal carcinoma especially esophageal epithelium dysplasia (EED). EED is a precancerous lesion which can either develop further into a more severe stage or cancer, stay unchanged, or reverse back to normal again for a period of several years or even a decade[28-34]. It is therefore very promising to detect patients with EED and treat the precancerous lesions before they transform into the irreversible malignant stage. There are several techniques and chemicals or nutrients that have been reported to be effective in blocking precancerous lesions from transforming into cancer[35-38].

The incidence rate among males declined significantly however, females remained steady. As to the geographic distribution, the incidence rate in mountainous area and hilly area showed a declining trend. The incidence rate of EC in level land area had increased. The reasons why these happened needs to be further studied and analysed.

In conclusion, the trend of the EC incidence rate in Cixian county had declined after two decades, especially in mountainous areas. But compared to the other regions in the world Cixian county still had a high incidence rate of EC. By using a register the information can provide the scientific data for cancer prevention and control.

**REFERENCES**

1 Puttawibul P, Chanvitan A, Pornpatanarak C, Sangthong B. Esophageal carcinoma in Southern Thailand. J Med Assoc Thai 2001; 84: 1-5
2 Adanja B, Gledovic Z, Pekmezovic T, Vlajinac H, Jarebinski M, Zivjaljevic V, Pavlovic M. Mortality trends of malignant tumours of digestive organs in Belgrade, Yugoslavia, 1975-1997. Dig Liver Dis 2000; 32: 396-391
3 Vega KJ, Jamal MM. Changing pattern of esophageal cancer incidence in New Mexico. Am J Gastroenterol 2000; 95: 2352-2356
4 Martin IG. Gastro-esophageal malignancy in New Zealand: 1995-97. N Z Med J 2002; 115: 64-67
5 Corley DA, Buffler PA. Oesophageal and gastric cardia adenocarcinomas: analysis of regional variation using the Cancer Incidence in Five Continents database. Int J Epidemiol 2001; 30: 1415-1425
6 Aksel EM, Davydov MI, Ushakovu TI. Statistics of lung, stomach and esophageal cancer: status of oncological care, morbidity and mortality. Vestn Ross Akad Med Nauk 2001; 9: 61-65
7 Kocher HM, Linklater K, Patel S, Ellul JP. Epidemiological study of oesophageal and gastric cancer in south east England. Br J Surg 2001; 88: 1249-1257
8 Hou J, Lin PZ, Chen ZF, Ding ZW, Li SS, Men FS, Guo LP, He YT, Oiao CY, Guo CL, Duan JP, Wen DG. Field Population-based blocking treatment of esophageal epithelia dysplasia. World J Gastroenterol 2002; 8: 418-422
9 World health organization. International classification of diseases of the international statistical classification of diseases, injuries, and causes of death. Volume 1. Geneva 1977: 115-163
10 Zhang WH, Bailey-Wilson JE, Li WD, Wang XQ, Zhang CL, Mao XZ, Liu ZH, Zhou CN, Wu M. Segregation analysis of esophageal cancer in a moderately high-incidence area of northern
China. Am J Hum Genet 2002; 67: 110-119

11 Wang G, Hao C, Lai S. Endoscopic study on cancer of gastric cardia in the high incidence areas of China. Zhonghua Zongliu Zazhi 2002; 24: 381-383

12 Wu MY, Chen MH, Liang YR, Meng GZ, Yang HX, Zhuang CX. Experimental and clinicopathologic study on the relationship between transcription factor Egr-1 and esophageal carcinoma. World J Gastroenterol 2003; 7: 490-495

13 Tan LJ, Jiang W, Zhang N, Zhang XR, Qiu DH. Fas FasL expression of esophageal squamous cell carcinoma, dysplasia tissues and normal mucosa. Shijie Hua ren Xiaohua Zazhi 2003; 9: 15-19

14 Wu QM, Li SB, Wang Q, Wang DH, Li XB, Liu CZ. The expression of COX-2 in esophageal carcinoma and its relation to clinicopathologic characteristic. Shijie Hua ren Xiaohua Zazhi 2001; 9: 11-14

15 Liu HF, Liu WW, Fang DC. Study of the relationship between apoptosis and proliferation in gastric carcinoma and its precancerous lesion. Shijie Hua ren Xiaohua Zazhi 1999; 7: 649-651

16 Liu J, Su Q, Zhang W. Relationship between HPV-E6 P53 protein and esophageal squamous carcinoma. Shijie Hua ren Xiaohua Zazhi 2000; 8: 494-496

17 Lin J, Deng CS, Sun J, Zhou Y, Xiong P, Wang YP. Study on the genetic susceptibility of HLA-DQB1 alleles in esophageal cancer of Hubei Chinese Hans. Shijie Hua ren Xiaohua Zazhi 2000; 8: 965-968

18 Ma QF, Jiang H, Feng YQ, Wang XP, Zhou YA, Liu K, Jia ZL. Detection of human papillomavirus DNA in squamous cell carcinoma of the esophagus. Shijie Hua ren Xiaohua Zazhi 2000; 8: 1218-1224

19 Dong Z, Tang P, Li L, Wang G. The strategy for esophageal cancer control in high-risk areas of China. Jpn J Clin Oncol 2002; 32 (Suppl): S10-12

20 Lu Z, Chen K, Guo M. Detection of HPV in human esophageal cancer in high-incidence area and its correlation with p53 expression. Zhonghua Zongliu Zazhi 2001; 23: 220-223

21 Chen KN, Xu GW. Diagnosis and treatment of esophageal cancer. Shijie Hua ren Xiaohua Zazhi 2000; 8: 196-202

22 Wang AH, Sun CS, Li LS, Huang JY, Chen QS. Relationship of tobacco smoking CYP1A1 GSTM1 gene polymorphism and esophageal cancer in Xi’an. World J Gastroenterol 2002; 8: 49-53

23 Su M, Lu SM, Tian DP, Zhao H, Li XY, Li DR, Zheng ZC. Relationship between ABO blood groups and carcinoma of esophagus and cardia in Chaoshan inhabitants of China. World J Gastroenterol 2001; 7: 657-661

24 Yu GQ, Zhou Q, Ivan D, Gao SS, Zheng ZY, Zou JX, Li YX, Wang LD. Changes of p53 protein blood level in esophageal cancer patients and normal subjects from a high incidence area in Henan, China. World J Gastroenterol 1998; 4: 365-366

25 Liu DW, Wanf BY, Zhou Y, Cui WF, Liu B, Zhou Q, Ying JY, Zheng S, Gao SS, Jin XX, Min FZ, Min NH, Hao ZZ, Yang CS, Min BY, Jun QY. Endoscopic screening and determination of p53 and proliferating cell nuclear antigen in esophageal multistage carcinogenesis: a comparative study between high- and low-risk populations in Henan, northern China. Dis Esophagus 2002; 15: 80-84

26 Bachmann MO, Alderson D, Edwards D, Wotton S, Bedford C, Peters TJ, Harvey IM. Cohort study in South and West England of the influence of specialization on the management and outcome of patients with oesophageal and gastric cancers. Br J Surg 2002; 89: 914-922

27 Li T, Lu ZM, Chen KN, Guo M, Xing HP, Mei Q, Yang HH, Lechner JF, Ke Y. Human papillomavirus type 16 is an important infectious factor in the high incidence of esophageal cancer in Anyang area of China. Carcinogenesis 2001; 22: 929-934

28 Zuo L, Lin P, Qi F, Zhang L, Guo J, Liu J. Quantitative detection of multi-gene expressions and DNA content in the precancerous cells of esophageal carcinoma. Zhonghua Zongliu Zazhi 2002; 24: 30-33

29 Griffin SM, Shaw IH, Dresner SM. Early complications after Ivor Lewis subtotal esophagectomy with two-field lymphadenectomy: risk factors and management. J Am Coll Surg 2002; 194: 285-297

30 Zhang J, Yan XJ, Yan QJ, Duan J, Hou Y, Su CZ. Cloning and expression of HPV16 L2 DNA from esophageal carcinoma in E. coli. Shijie Hua ren Xiaohua Zazhi 2001; 9: 273-278

31 Wei ZB, Wang LB, Tian BS, Wang JL, Sun XF, Wei JP, Liu N, Wang JH. Lugol’s staining with p53 oncoproteins in detecting early esophageal cancer. Shijie Hua ren Xiaohua Zazhi 2001; 9: 495-498

32 Gu HP, Shang PZ, Su H, Li ZG. Association of CD15 antigen expression with cathepsin D in esophageal carcinoma tissues. Shijie Hua ren Xiaohua Zazhi 2000; 8: 259-261

33 Huang ZZ, Wu XY, Liang YR, Li QS, Shen J. Immunohistochemical study of esophageal basaloid squamous cell carcinoma. Shijie Hua ren Xiaohua Zazhi 2000; 8: 1097-1100

34 Liu J, Chen SL, Zhang W, Su Q. P21WAF1 gene expression with P53 mutation in esophageal carcinoma. Shijie Hua ren Xiaohua Zazhi 2000; 8: 1350-1353

35 Corley DA, Levin TR, Habel LA, Weiss NS, Buffler PA. Surveillance and survival in Barrett's adenocarcinomas: a population-based study. Gastroenterology 2002; 122: 633-640

36 Anderson MR, Jankowski JA. The treatment, management and prevention of oesophageal cancer. Expert Opin Biol Ther 2001; 1: 1017-1028

37 Wilson KS, Wilson AG, Dewar GJ. Curative treatment for esophageal cancer: Vancouver Island Cancer Centre experience from 1993 to 1998. Can J Gastroenterol 2002; 16: 361-368

38 Zhang LJ, Chen KN, Xu GW, Xing HP, Shi XT. Congenital expression of mdr-1 gene in tissues of carcinoma and its relation with pathomorphology and prognosis. World J Gastroenterol 1999; 5: 53-56

Edited by Xia HHX