RESEARCH COMMUNICATION

Esophageal Cancer Mortality Trends during the Last 30 Years in High Risk Areas in China: Comparison of Results from National Death Surveys Conducted in the 1970's, 1990's and 2004-2005

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Abstract

Background and Aims. China was one of the countries with the highest esophagus cancer (EC) mortality in the world during the 1970's. This report provides data on time trends of esophagus cancer mortality during the 1970's-21st century in high risk areas, considering the remarkable geographic variation of EC mortality in China. The aim was to explore changing trends of EC mortality during past 30 years, and provide basic information on prevention and control of EC in high risk areas in China. Methods: Among the high risk areas of EC defined in the 1970's, ten that have joined in all the three death causes sampling surveys were selected in this study. Subjects included all cases dying from esophageal cancer in these sites during 1973-1975, 1990-1992, and 2004-2005. The EC mortality data and relevant demographic data of ten areas covered by all the three surveys were extracted from the national death causes survey database. Results: Compared with the EC mortality of the ten high risk areas in the 1970's, the crude mortality rates (CMR) in the 1990's reduced by 0.04%~47.3%, and the CMRs in the early 21st century decreased by 9.25%~62.0% from the 1990's; the age specific mortality rate adjusted by China standard population (ASMRc) in the 1990's reduced by 8.22%~53.5%, and the ASWRc in the early 21st century decreased by 25.0%~78.0% from the 1990's; the age-specific mortality rates adjusted by world standard population (ASMRw) in the 1990's reduced by 7.54%~51.9%, and the ASMRw in the early 21st century decreased by 24.5%~79.2% from the 1990's; the proportional mortality ratios (PMR) in the 1990's reduced by 12.3%~41.3%, and the PMRs in the early 21st century decreased by 6.76%~52.6% from the 1990's. Conclusion: Our study indicated that the mortality of esophageal cancer in high risk areas of China had declined after three decades, but still remained high compared with the national level. Esophageal cancer is still a major cancer burden in high risk areas. It is necessary to further promote the prevention and control program of esophageal cancer in these areas of China.

Keywords: Esophageal cancer - mortality trends - 30 years - high risk area - China

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Introduction

Esophageal cancer (EC) is the world's eighth most common incident cancer, with 462,000 new cases and is the sixth most common cause of cancer death, with 386,000 deaths in 2002 (Parkin et al., 2005). The histological subtypes of esophageal cancer include esophageal squamous cell carcinoma (ESCC) and adenocarcinoma, with these two types accounting for more than 90% of esophageal cancers (Katrina et al., 2008). About 80% of the worldwide burden of esophageal cancers is ESCC. Although the incidence of esophageal adenocarcinoma in Western countries has been rapidly increasing over the past few decades (Bosetti et al., 2008), the incidence of ESCC seems to be relatively stable or slightly decreased (Devesa et al., 1998; Lepage et al., 2008). The greatest burden of EC occurs in the "Asian Esophageal Cancer Belt", extending from northern Iran, east to China, and north to Russia (Tammy, 2001). Approximately 50% of all esophageal cancer occurs in China.

It is found that there is a specific distribution characteristic of EC in China from the first national death causes sampling survey during 1973-1975, which is a remarkable geographic variation of EC mortality (National Control Office, 1979; Office for Cancer Prevention, Control, 1980; Li JY, 1982). The higher mortality rates concentrated on the Tai-hang mountains at the border of Henan province, Hebei and Shanxi province in North China; northern Sichuan province; the Da-bie mountains at the border of Anhui province and Hubei provinces; southern Fujian province and regions of north-eastern Guangdong province; northern Jiangsu province; and

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northern Xinjiang autonomous region (Armstrong, 1980). Such areas were defined as high risk areas of EC since 1970's. Thus, work on prevention and control of EC has concentrated on the high-risk areas and was initiated from epidemiology and etiology survey, then extended to screening, early detection and early treatment, and further to explore comprehensive prevention and control strategy.

According to the recent data from the Third National Causes of Death Sampling Survey (2004-2005), the mortality rate has declined by 33.6% and 41.6%, compared with the second survey in 1990-1992 and the first survey in 1973-1975, respectively. However, EC remains the fourth most common fatal cancer in both the urban and rural regions of China. Most EC cases still arise from the high risk area which has limited health resources and an under-developed economy (Wei et al., 2010). During 1990-1992, the national second death causes sampling survey showed that compared with the 1970's, the EC mortality had a tendency of decreasing in the 1990s (Office for Cancer Prevention, Control, 2007). The point need to be stressed is that cardiac cancer was classified as EC in the first survey, but was not included in EC in the second survey. Meanwhile, it is difficult to select cardia cancer from upper gastrointestinal cancer since the detail disease code information was not available in the 1970's survey. Therefore, the mortality decreasing in the 1990's could not reflect the real disease burden of EC in high risk areas objectively and completely.

It is note that 87.6%, 10.0% and 6.0% of total population in China were covered in the 1970's, 1990's and 2004-2005 in China respectively. The different cancer burdens between different areas were considered in sampling procedure and data from 263 samples area were selected in the 1990's survey [Office for Cancer Prevention, Control, 2007]. 158 sample areas were included for analysis due to the stratified sampling by region in the survey from 2004-2005 (Wei et al., 2010). Although the sample selected in different period can explain the national EC burden of that time, considering of remarkable geographic variations of EC mortality, it is necessary to compare the data of high risk areas from three surveys.

In this paper, we focus on high risk areas which were covered by all the three national surveys during 1973-1975, 1990-1992, and 2004-2005 respectively, systematically analyzed the differences of EC mortality among such three periods. The objective of this study is to explore changing trends of EC mortality during past 30 years, and providing basic information on prevention and control of EC in high risk areas in China.

Materials and Methods

High risk areas and subjects selected

Among the high risk areas of EC defined in the 1970's, ten that have joined in all the three death causes sampling surveys were selected in this study, including Zanhuang county, She county, and Ci county in Hebei province, Yangquan city urban district, and Yangcheng county in Shanxi province, Chuzhou district of Huai'an city in Jiangsu province, Dafeng city in Jiangsu province, Linzhou county and Jiyuan city in Henan province, Yanting county in Sichuan province.

Subjects included all cases dying from esophageal cancer in these sites during 1973-1975, 1990-1992, and 2004-2005. From the national death causes survey database, we extracted the EC mortality data and relevant demographic data of these 10 areas covered by all the three surveys.

Death information collection

Data were from four publications (National Control Office, 1979; Office for Cancer Prevention, Control,1980; Wei WQ et al., 2010; Office for Cancer Prevention, Control, 2007). In the first survey, the investigators needed to check the death cases during 1973-1975 through village group meeting and build up the list of deceased cases firstly, and then collected history of disease, medical consultation, death cause, and evidences of diagnosis of each case. For information that cannot be collected in the meeting, the investigator went to subjects' families, or the hospitals that had clinical treatment for further investigation.

In the second survey, the list of deceased cases was built up on the basis of the death information from Police Station, Department of Obstetrics in hospitals, and Department of Maternal and Child Health Care. According to the list, the village doctors collected relative information mentioned above and filled out the form of Identification of Death.

In the third survey, the method to get the lists of the deceased cases was the same with the second survey for the areas without disease registry system. While for the sites with disease registry system, the investigators could get the original lists of deceased cases from the registration department firstly, then check them with the relative data from the Police Station, Department of Civil Affairs & Public Health, Department of Family Planning, and finally set up the intact and exact list of the decedent. Based on the deceased cases list, the investigator filled out the questionnaire of death causes followed by checking the medical certificate of death, medical record, or inquiring the family members.

Quality of data

79.2%, 91.0%, 93.9% cancer cases were diagnosed by county hospital or above, and 92.5%, 97.4%, 98.5% cancer cases were diagnosed by commune hospital or above in the national surveys during 1973-1975, 1990-1992, and 2004-2005 respectively. Less than 3% cancer cases did not have clinical diagnosis materials, and over 93% death causes were confirmed by clinical diagnoses or other higher-level technologies in all three surveys.

Statistical indicators

EC crude mortality rate (CMR), age-specific mortality rate and proportional mortality ratio (PMR, referring to the proportion that EC death accounted for in the total cancer death) were counted respectively for three surveys. Moreover, age-standardized mortality rates were adjusted

by China standard population in 1982 (ASMRc), and world standard population in 1985(ASMRw), respectively.

Results

Overall trends of EC mortality in high risk area in China

The EC CMRs of the 10 high risk areas were 46.56/100 000~144.91/100 000 in the 1970's (the highest appeared in She county of Hebei province), 26.08/100 000~127.93/100 000 in the 1990's (the highest appeared in Yangcheng county of Shanxi province), and 9.92/100 000~83.94/100 000 in the early 21st century (the highest appeared in Ci county of Hebei province). For the past 30 years, the EC CMRs of Yangquan city urban district in Shanxi province remained the lowest among the 10 sites (see Table 1). Compared with the 1970's, the CMRs in the 1990's reduced by 0.04%~47.34% (median, 31.30%); while the CMRs in the early 21st century decreased by 9.25%~61.96% from the 1990's (median, 28.81%).

The range of the EC ASMRc in 10 areas were from 59.77/100 000 to 150.26/100 000 (the highest was in Linzhou county of Henan province), 31.82/100 000~115.66/100 000 (the highest was in Yangcheng county of Shanxi province), and 6.99/100 000~78.32/100 000 (the highest was in Ci county of Hebei province) in the 1970's, 1990's and early of 21st century respectively. For the past 30 years, the ASMRc of Yangquan city urban district in Shanxi province remained the lowest among the 10 sites. Compared with the 1970's, the ASMRc in the 1990's reduced by 8.22%~53.49% (median, 35.30%); while the ASMRc in the early 21st century decreased by 25.01%~78.03% from the 1990's (median, 45.18%).

In chronological order, the EC ASMRw of 10 areas in three surveys were 82.27/100 000~192.89/100 000, 44.91/100 000~155.25/100 000, and 9.33/100 000~107.98/100 000 respectively. Compared with the 1970's, the ASMRw in the 1990's reduced by 7.54%~51.90% (median, 33.56%); while the ASMRw in the early 21st century decreased by 24.51%~79.23% from the 1990's (median, 44.42%).

In chronological order, the EC PMRs of 10 areas in three surveys were 38.14%~67.35% (six areas over 50%, and no area less than 30%), 23.09%~53.46% (one area over 50%, four areas less than 30%, and no area less than20%), and 11.69 %~42.61% (no area over 50%, and 4 areas less than 20%). Compared with the 1970's, the PMRs in the 1990's reduced by 12.28%~41.34% (median, 32.02%); while the PMRs in the early 21st century decreased by 6.76%~52.58% from the 1990's (median, 33.02%).

CMR, ASMRc, ASMRw and PMR of all high risk areas declined more remarkably than the national level which were 9.21%, 41.64%, 40.82% and 50.42% respectively for the past 30 years (Wei WQ et al., 2010). The corresponding results of Yangquan city urban district were 78.69%, 89.78%, 90.01% and 74.58%, respectively, which were declined most dramatically than other nine areas.

In the 1970's, the CMRs and ASMRcs of nine high risk areas (except Yangquan city urban district in Shanxi province) were over three times than the national level (CMRs:2.78~8.65 folds; ASMRcs:3.50~8.79 folds). Compared with the 1970's, the ratios in the 1990's decreased (CMRs: 1.50~7.36 folds; ASMRcs: 2.12~7.70 folds). The CMRs and ASMRcs of Zanhuang county in Hebei province, Yangquan city urban district in Shanxi province, Dafeng city in Jiangsu province and Jiyuan city in Henan province had reduced to around two times than the national level. Compared with the 1990's, the ratios in the early 21st decreasing (CMRs: 0.65~5.52 folds; ASMRcs: 0.70~7.85 folds). The CMR and ASMRc of Yangquan city urban district had dropped to below the national level; while there were only four areas whose ratios remained over three (Ci county in Hebei province, Yangcheng county in Shanxi province, Linzhou county in Henan province, Yanting county in Sichuan province). (Table 1)

For each area, the EC mortality rates of males were almost higher than those of females in all three surveys. However, the gender-specific CMRs, ASMRcs, ASMRws

Table 1. Mortality Rates (/10^5) and Proportional Mortality Rates (%) of EC in High Risk Areas in Three National Death Causes Surveys in China

	1973-1975				1990-1992				2004-2005			
	CMR	ASMRc	ASMRw	PMR	CMR	ASMRc	ASMRw	PMR	CMR	ASMRc	ASMRw	PMR
China	16.8	17.1	23.2	22.6	17.4	15.0	20.4	16.1	15.2	10.0	13.7	11.2
Urban of China	15.1	15.5	21.1	18.4	9.6	7.6	10.5	8.6	11.0	6.5	9.0	7.3
Rural of China	17.3	17.7	24.0	24.4	20.1	18.0	24.4	18.8	17.4	12.0	16.5	13.5
Zanhuang county	67.1	59.8	82.3	39.4	40.7	43.8	62. 5	23.1	25.0	17.0	23.4	14.0
She county	144.9	140.8	192. 9	53.3	76.3	79.0	109. 9	36.1	43.7	32.5	45.1	23.0
Ci county	135.9	131.0	179.8	67.4	105.3	112.7	154.2	53.5	83.9	78.3	108.0	42.5
Yangquan city urban	46.6	68.4	93.4	46.0	26.1	31.8	44.9	24.7	9.9	7.0	9.3	11.7
Yangcheng county	131.9	126.0	167.9	65.8	127.9	115.7	155.3	42.7	69.4	60.2	81.2	36.3
Chuzhou/Huai'an city	93.4	105.6	141.5	52.1	91.8	91.8	122.4	45.7	71.7	50.5	69.9	42.6
Dafeng city	60.0	65.5	90. 8	41.4	46.1	36.2	49. 8	26.2	34.3	27.1	37.6	16.7
Linzhou county	133.1	150.3	204.1	65.4	72.2	73. 9	100.7	44.6	56.7	40.4	54.5	37.5
Jiyuan city	78.3	84.1	116.3	38.1	43.9	41. 6	57.1	28.0	29.8	24.5	34.4	18.6
Yanting county	76.8	83.0	112.8	61.2	76.7	64.0	86.9	44. 8	69.6	37.8	51.4	30.2

CMR, crude mortality rate; ASMRc, age-standardized mortality rates adjusted by the China standard population in 1982; ASMRw,age-standardized mortality rates adjusted by the world standard population in 1985; PMR, proportional mortality ratio, referring to the proportion that EC death accounted for in the total cancer death

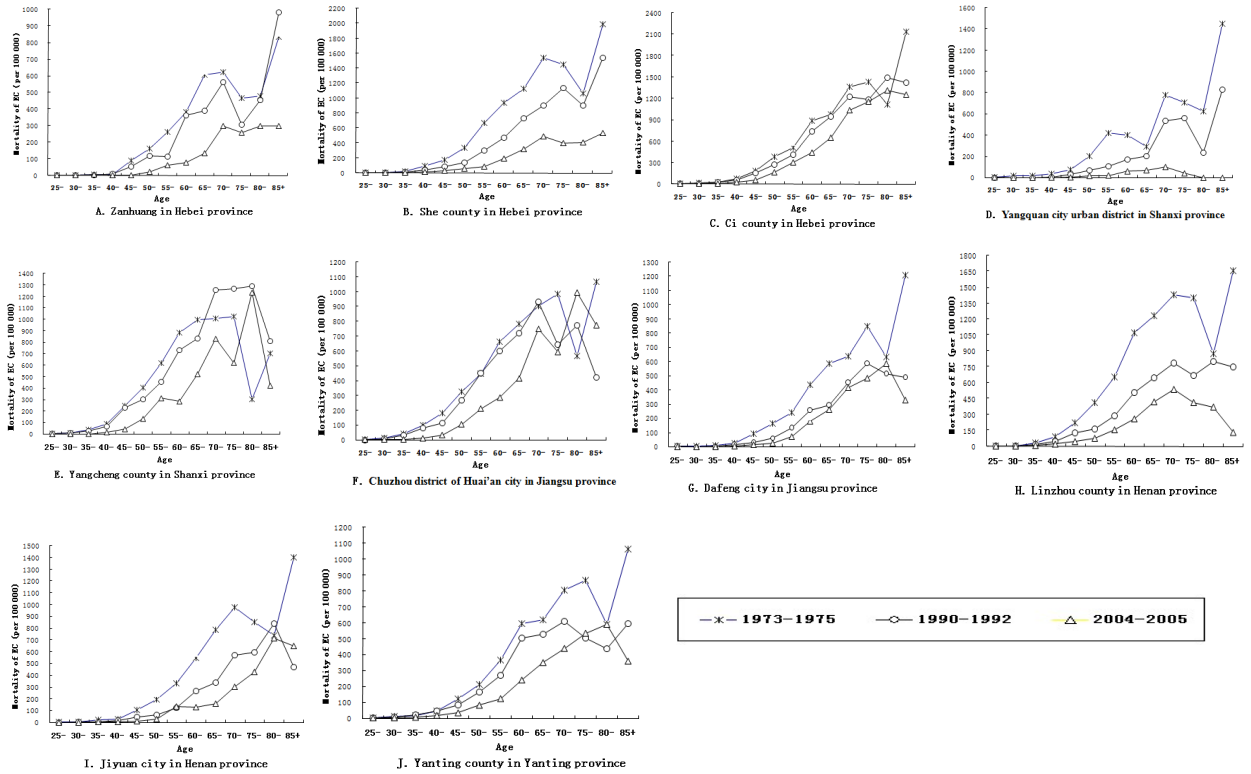

Figure 1. Age-specific Mortality of Esophageal Cancer in 10 High Risk Areas. Mortality of esophageal cancer before 25 years was close to zero, so the x-axis starts from 25 years old

and PMRs had a similar variation tendency as described above (data not shown).

Age-specific mortality of EC in high risk areas in China

For each area, the mortality rates of EC were close to zero before 25 years old, then increased with age, and reached the peak after 70 years old in all three surveys. In most of age-groups (except 75 plus age-group of some areas), the mortality of the first survey were the highest, and those of the third survey were the lowest. In Zanhuang county, She county, Ci county, Yangquan city urban district, Yangcheng county, Chuzhou district of Huai'an city, and Yanting county, the decline range of mortality in each age-group from the 1970's to the 1990's was much larger than those from the 1990's to the early 21st century. However, the conditions in Dafeng city, Linzhou county and Jiyuan city were the exact contrary. Generally, the age-specific mortality in Zanhuang county, She county, Yangquan city urban district, Linzhou county and Jiyuan city declined significantly, while slightly in Ci county and Yanting county (Figure 1).

Discussion

Esophageal squamous cell carcinoma is a common malignancy in China. The first survey showed the distribution of mortality of EC had remarkable geographic variations and thus identified many high risk areas. The mortality of EC had high levels in high risk areas, and the further from the high risk areas, the lower EC mortality (Armstrong, 1980; Li, 1982).

This study found the mortality of high risk areas decreased greatly for the past three decades. In the 1970's, the mortality rates of all ten areas were over three times of the national level. In the early 21st century, the mortality of Zanhuang county, She county, Yangquan city urban district, Dafeng city and Jiyuan city had reduced to less than two times of the national level, and the mortality of Yangquan city urban district was even less than the national average. For those areas with mortality remaining over three times of the national level, the mortality had reduced obviously for the past 30 years (CMRs down 9.29%~57.41%, and ASMRcs down 54.50%~73.14%).

In all the three surveys, the EC mortality of ten areas increased with age, and reached the peak after 70 years old. On the basis of the China standard population in 1982, the EC deaths in the over 70 year-old group accounted for 19.98%~31.25% of total population in the 1970's, whereas in the early 21st century, they increased to 25.38%~47.02%. This result indicated that along with the average life increase in high risk areas, the elder population is the major group attacked by EC since lacking the primary prevention plan and population based screening program.

Compared with the 1970's, the EC mortality had a decrease tendency in high risk areas in the 1990's. It could not be ignored that gastric cardiac cancer used to be classified with esophagus cancer mainly to avoid classification biases since the International Classification of Disease (ICD) was not used in the first survey, so the mortality reported for EC in the 1970's was for esophagus and gastric cardiac cancer combined. However,, the gastric cardiac cancer was a separate category and not included in EC in the survey of 1990's, since ICD-9 was used, therefore, it is difficult to distinguish this decrease trendy was from the change of disease classification or the real mortality decrease. In the survey during 2004-2005, ICD-10 was also used, compared with the 1990's, the third

survey showed that the EC mortality kept decreasing in the early 21st century. Moreover, the ASMRc dropped more significantly in the latter 10 years than in the former 20 years. Decreasing trends of age-specific mortality were same with that of ASMRc. So, the decrease trends of EC mortality in high risk areas really existed and were not from the difference of disease classification. The same decrease trends were also observed in high risk areas in Linxian (Ke, 2002) and Ci county (He et al., 2005).

The potential reasons for the decreasing mortality from EC in high risk areas are not well understood. Changes in specific dietary factors are likely to be involved, high consumption of fruits and vegetables has been associated with a reduced risk of both esophagus and gastric cancers in many epidemiology investigations. A nutrition intervention trial of multiple vitamins and minerals was carried out in Linxian during 1985–1991 and the findings indicated that a combination of beta-carotene, vitamin E and selenium may result in a reduction in esophagus, and gastric cardia cancer risk in this population, and benefit was consistently greater in participants who were younger at the beginning of the intervention. (Qiao et al., 2009). Recent study in Linxian also showed that over the last 20 years, the consumption of fresh fruit, vegetables, and animal protein increased, especially in the younger age group. The dietary change is developing in Linzhou which are associated with incidence and mortality decreased of esophageal cancer in the past ten years. The findings have raised the possibility that dietay changes of residents in Linxian may be responsible for esophageal cancer reduction (Lu et al., 2001).

Change in other environmental factors also may play important roles. To improve the quality of the drinking water by decreasing the pollution of nitrosamine, to administer the storage of agricultural products and advocate the people to expose grain and drinking water to the sunshine, not to eat the food with mold may also be involved. Recent study showed that the exposure concentration of Nitrosamine compounds and mold toxin in Linxian residents have a significant decreasing in the last 20 years (Yang et al., 2008)

In this analysis, in order to further explore the exact influence of disease classification differences on the EC mortality, we try to integrate the data of gastric cardiac cancer with EC in the second and third surveys, and then compare the integrated-mortality of EC and gastric cardiac cancer with mortality of EC in the 1970's. However, it was difficult to extract gastric cardiac cancer from original database since although all gastric cardiac cancer were coded as C16.0 in the second and third national surveys, the quality of data of gastric cardiac cancer was poor based on limited diagnostic techniques of rural medical units. So the effects of disease classification variations on the EC mortality changing trends cannot be estimated quantitatively. It was also a shortage of this study.

In conclusion, the EC mortality in high risk areas of China had declined after three decades, especially in Yangquan county. However, the mortality of Ci county, Yangcheng county, Chuzhou district of Huai'an city, Linzhou county and Yanting county presented decreasing trends, but still remained the high level compared with the national level. Therefore, EC is still a serious problem in high risk areas. It is necessary to further promote the prevention and control program of esophageal cancer in high risk areas in China

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