RESEARCH ARTICLE

Esophageal/Gastric Cancer Screening in High-risk Populations in Henan Province, China

Yu-Fei Lu^{1,2}, Zhi-Cai Liu³, Zhong-Hong Li⁴, Wen-Hao Ma⁵, Fu-Rang Wang⁶, Ya-Bing Zhang⁷, Jian-Bang Lu^{6*}

Abstract

<u>Objective</u>: To summarize the endoscopic screening findings in high-risk population of esophageal and gastric carcinoma and analyze influential factors related to screening. <u>Methods:</u> In seven selected cities and counties with high incidences of esophageal carcinoma, people at age of 40-69 were set as the target population. Those with gastroscopy contradictions were excluded, and all who were voluntary and willing to comply with the medical requirements were subjected to endoscopic screening and histological examination for esophageal, gastric cardia and gastric carcinoma in accordance with national technical manual for early detection and treatment of cancer. <u>Results</u>: In three years, 36,154 people were screened, and 16,847 (46.60%) cases were found to have precancerous lesions. A total of 875 cases were found to have cancers (2.42%), and among them 739 cases had early stage with an early diagnosis rate is 84.5%. Some 715 patients underwent prompt treatment and the success rate was 81.8%. <u>Conclusions</u>: In a high-risk population of esophageal and gastric carcinoma, it is feasible to implement early detection and treatment by endoscopic screening. Screening can identify potential invasive carcinoma, early stage carcinoma and precancerous lesions, improving efficacy through early detection and treatment. The exploratory analysis of related influential factors will help broad implementation of early detection and treatment for esophageal and gastric carcinoma.

Keywords: Esophageal carcinoma - gastric carcinoma - high-risk populations - endoscopy screening - histology

Asian Pac J Cancer Prev, 15 (3), 1419-1422

Introduction

With the approach into the twenty-first century, esophageal carcinoma and gastric carcinoma remain the most common malignant tumors in China, even in the whole world (National institute of cancer prevention, 2008; Ministry of health, bureau of disease control and prevention, 2011; Ferlay et al., 2010; Zhao et al., 2012; Henan research division of cancer prevention, 2012). In the early of the 20 century, the cancer mortality in Japan was 6.8/100, 000, and major cancer such as the stomach, liver and esophagus, the proportion of 67.8% for deaths and 56.7% for cases, respectively (Aoki, 2006). According to 2010 annual cancer registration report by international agency for research on cancer (IARC, WHO), there are 12, 700,000 new cases of cancer and 7,600,000 people died of cancer. Among them, there are 481,000 new cases of esophageal carcinoma and 460,000 patients died, and eighty-three percent occurs in the developing countries.

In China, there are 258,000 new cases and 210,000 deaths, which account for over fifty percent of total

morbidity and mortality in the whole world. Globally, there are 9,880,000 new cases of gastric carcinoma and 736,000 deaths, and seventy percent occurs in developing country. In China, there are 463,000 new cases of gastric carcinoma and 352,000 deaths, which accounts for forty-eight percent of total cases (Ferlay et al., 2010). From 2009 to 2011, seven counties and cities in Henan province participated in the national early detection and treatment project for esophageal and gastric carcinoma, and completed endoscopic screening and histological examination in 36, 154 cases (at age of 40-69). In this study, we reported the endoscopic and histological findings in high-risk population of esophageal and gastric carcinoma and analyzed the related factors which may affect the screening results.

Materials and Methods

Background of the participating cities and counties

The seven participating cities and counties are: Linzhou, Jiyuan, Huixian, Yanshi, Neixiang, Hebi, and

¹Department of Oncology, Shandong University, Departments of Radiation Oncology, Shandong Cancer Hospital and Institute, Jinan, ²Department of Radiation Oncology, the Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, ³Linzhou Institute of Esophageal Cancer, Linzhou, ⁴Jiyuan cancer hospital, Jiyuan, ⁵Huixian People' Hospital, Huixian, ⁶Department of Tumor Hospital Cancer Prevention Research Office, the Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, ⁷Medical Science Research Institute of Henan Province, Zhengzhou, China *For correspondence: hncjbl@Sohu.com

Table 1. Endoscopic Examination of EsophagealLesions and their Distribution in 36154 Cases

Lesions	Number	%
Invasive carcinoma	72	0.20
Submucosal carcinoma	45	0.12
Mucosal carcinoma	98	0.27
Servere hypoplasia/in situ	353	0.97
Moderate hypoplasia	826	2.28
Mild hypoplasia	2556	7.07
Gastritis	5018	13.89
Normal	27200	75.23

Table 2. Endoscopic Examination of Gastric Cardiaand Gastric Lesions and their Distribution in 36154Cases

Lesions	Number	%
Invasive carcinoma	64	0.18
Submucosal carcinoma	32	0.09
Mucosal carcinoma	50	0.14
High-grade mucosal carcinoma	161	0.45
Low-grade mucosal carcinoma	979	2.77
Atrophic gastritis	704	1.94
Non-atrophic gastritis	6764	18.71
Normal	27879	77.11

Xunxian. According to Henan province tumor registry in 2011, Linzhou has the highest esophageal carcinoma incidence and mortality, which is 83.77/100,000 and 58.93/100,000, respectively. And gastric carcinoma incidence and mortality in Linzhou are 77.73/100,000 and 51.33/100,000, respectively. The tumor incidence and mortality in Yanshi is lowest. The incidence and mortality for esophageal carcinoma are 39.35/100, 000 and 27.72/100,000, respectively, and the incidence and mortality for gastric carcinoma are 34.37/100,000 and 29.05/100,000, respectively. The incidence and mortality for tumor in other counties are in between. The geographical distribution is shown in (Figure 1).

Methods

In seven selected cities and counties with high incidence of esophageal carcinoma, local residents at age of 40-69 years old were defined as high-risk population. People with gastroscopy contradictions were excluded, and those who are voluntary and willing to comply with the medical requirements were subject to endoscopic screening. According to the national early detection and treatment manual (Ministry of health, bureau of disease control and prevention, 2011), endoscopic examination was performed in esophagus, cardia and non-cardia gastric regions. Through iodine staining and indicative biopsy, the diagnosis was determined by histopathology.

Results

Esophageal lesions: from 2009 to 2011, 36, 154 people were screened. People with normal esophageal mucosa accounted for 75.23%, people with precancerous lesions accounted for 23.23%, and people with various types of cancer accounted for 1.57%. Among the people with cancer, 87.32% have early stage cancer. The distribution

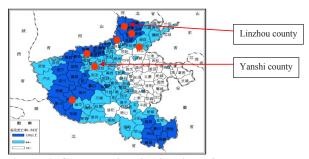


Figure 1. Geographic Distribution of the Esophageal Cancer Mortality in Henan, China

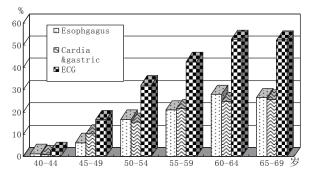


Figure 2. Relationship Between Target Population Age and Upper Digestiv Tract Cancer. *ECG=Upper digestiv carcinoma (esophagus/cardia/stomach)

is pyramid-shaped as shown in (Table 1).

Gastric cardia lesions: from 2009 to 2011, although we focused on esophagus and gastric cardia region, the rest gastric region was still required to be examined. Therefore, we combined the data for gastric cardia and the rest gastric region and did the statistical analysis. People with normal gastric mucosa account 77.11%, people with various precancerous lesions account for 23.36% and people with various cancer account for 0.85% in which 79.15% are early stage cancer. The distribution is pyramid-shaped as shown in (Table 2).

Esophageal, cardia gastric, non-cardia gastric lesions and their distribution: in order to further understand the esophagus, gastric cardia, non-cardia gastric lesions and their distribution, we analyzed 11035 cases from Linzhou in 2010-2011 and Hebi in 2011. In order to compare, the esophageal mucosal inflammation, mild hyperplasia and severe precancerous hyperplasia are categorized as stage 1, 2 and 3 precancerous lesions, respectively; the severe hyperplasia/carcinoma in situ and mucosal and submucosal carcinoma were categorized as interventional early stage cancer; gastric cardia superficial gastritis, atrophic gastritis and low-grade neoplasia are categorized as stage 1, 2 and 3 precancerous lesions, respectively; the mucosal high-grade tumors, mucosal and submucosal carcinoma are categorized as the interventional early stage cancer (Table 3).

The influential factors

Age: according to data from 9014 cases in 2011 from Linzhou, Jiyuan and Huixian, the distribution of esophageal, gastric cardia and upper gastrointestinal carcinoma (including esophageal and gastric cardia carcinoma) is as following: in the group of 40-44 years old,

Location	Normal		Precancerous lesions			Cancer		
		1	2	3	Total	Early	Late	Total
Esophagus	7038 (63.78)	2632 (23.85)	877 (7.85)	266 (2.41)	3775 (34.21)	203 (1.84)	19 (0.17)	222 (2.01)
Gastric cardia	9991 (90.54)	486 (4.40)	241 (2.18)	201 (1.82)	928 (8.41)	117 (1.06)	17 (0.15)	134 (1.21)
Gastric	10569 (95.78)	358 (3.24)	45 (0.41)	46 (0.42)	449 (4.07)	8 (0.07)	9 (0.08)	17 (0.15)

Table 4. Self-comparison of Biopsy Rate, DetectionRate and Early Diagnosis Rate

	0			
Location	Year	Biopsy		Early Diagnosis
		Rate (%)	Rate (%)	Rate (%)
Linzhou County	2009	111.82↑	4.64↑	96.84↑
	2010	50.40↓	3.41↓	88.30↓
	2011	57.68↓	2.97↓	87.24↓
Jiyuan County	2009	111.20↑	1.90↑	68.42↓
5	2010	77.20↓	1.05↓	71.43↓
	2011	103.05↑	2.45↑	89.80↑
Huixian County	2009	14.56↓	1.79↓	77.78↓
	2010	53.75↑	2.25↑	84.44↑
	2011	101.90↑	2.10↑	92.86↑
% 100 90 80 70 60 50 40 30			situ Int car Sub car ar ar sub car	ramucocosa cinoma mucosa cinoma asive- cinoma

Figure 3. Relationship Between Target Population Sex and Upper Digestiv Tract Carcinoma

the distribution is 1.4%, 1.03% and 2.43%, respectively; in the group of 45-49 years old, the distribution is 6.29%, 10.31% and 16.60%, respectively; in the group of 50-54 years old, the distribution is 16.78%, 15.46% and 32.24%, respectively; in the group of 55-59 years old, the distribution is 20.98% 21.65% and 42.63%, respectively; in the group of 60-64 years old, the distribution is 27.97%, 24.74% and 52.71%, respectively; in the group of 65-69years old, the distribution is 26.57%, 25.77% and 52.34%, respectively (Figure 2).

Gender: In this study, 59.44% are males and 40.56% are females. In the combination of males and females, the incidence of in situ/high-grade neoplasia, mocusal carcinoma, submucosal carcinoma and invasive carcinoma is 68.53%, 11.89%, 10.49% and 9.09%, respectively (Figure 3).

The correlation of biopsy and detection rate with early diagnosis rate: To exclude the influence of geography, technology, equipment and other factors, we selected 22085 cases from Linzhou, Jiyuan and Huixian and did self-comparison. The changes of biopsy rate, detection rate and early diagnosis rate were shown in (Table 4).

Discussion

In 1999, the National Cancer Screening Program (NCSP) was started, with free screening services for three types of cancer (stomach, breast, and cervix) in 2001, Since 2005, have expanded five types of cancer (liver,

colorectal). Organized cancer screening are performed by the government (Lee et al., 2011). In Korea, Cancer is associated with the largest disease burden and has bee 100.0 the most frequent cause of death. A total of 72,046 cancer death was reported in 2010, accounting for 28% of all death. The cancer incidence rate for all site combined 75.0 increased by 3.3% annually from 1999 to 2010 (Suh et al., 2013). Esophageal and gastric carcinoma remains the most common malignant tumor in China (Kamangar et al., 2006; Zheng et al., 2012), therefore, through iodine50.0 staining and endoscopic screening, the early detection and treatment (the treatment will be reported in another manuscript) of esophageal, gastric cardia and non-cardia25.0 gastric carcinoma in high-risk population (at age of 40 to 69 years old) will have practical significance in the prevention of upper gastrointestinal cancer (Lu et al., 0 2012).

Screening showed that in the esophageal high-risk population in Henan province, the gastric precancerous lesions occur in 23.23% of the population, gastric cardio precancerous lesions occur in 23.36% of the population and various esophageal, gastric cardia and gastric carcinoma occur in 2.42% of the population in which 84.46% of cases are early stage cancer. In all the male and female cancer patients, the incidence of in situ/high-grade neoplasia, mucosal carcinoma, submucosal carcinoma and invasive carcinoma is 1.42%, 0.41%, 0.21% and 0.38%, respectively.

Analysis of the target population by age showed that the detection rate of esophageal and gastric carcinoma in the group of 40-44 years old is 2.34% but this group accounts for 9.41% of the total population screened. If the age was extended to 70-74, the population increased only 1.75% but the incidence of cancer increased 14.65%. Obviously, if we set the high-risk population at the age of 45-74, the incidence will be higher. Furthermore, based on the national cancer registry in thirty rural regions, 2011 China annual report of cancer registration (National Cancer Center, 2012) indicates that the age group of 70-74 accounts for 2.82% of the population while the incidence of cancer in this group accounts for 15.26% of the total incidence. This data suggests that setting the screening population at 45-74 would be more appropriate. Data from other counties also showed that 95% of esophageal carcinoma occurs in the population above 55 years of (Jaffer et al., 2011; Elliot, 2012).

We believe that the purpose of screening in high-risk population is to detect more early lesions. It is impossible to detect by visual examination without biopsy. Therefore, it is necessary to optimize esophageal mucosa iodine staining (Wang et al., 2004) and improve overall biopsy detection rate. 1.2% to 1.5% Lugol iodine was used and the comparison of before- and after-staining appearance was 56

recorded, and suspicious specimen was send for further histological examination. The use of iodine staining in esophageal endoscopy can significantly improve the detection rate of superficial esophageal carcinoma and dysplasia. Normal esophageal squamous epithelium is rich in glycogen, and after contact with iodine it turns into brown color. The abnormal squamous cells fail turning color or show lighter color after iodine staining due to decreased or absent glycogen content. Therefore, we can detect the presence of cancer according to the size of lesion, the clearance of lesion edge or the appearance of lesions, and characterize it by histopathological examination. Thus, the use of iodine staining in endoscopy to detect esophageal precancerous lesions and early has a very important practical value (Wang et al., 2003). According to trial edition of 2009 China cancer screening and early detection and treatment manual (Dong, 2009), the requirement of gastric cardia biopsy is: if gastric cardia mucosa is normal, biopsy specimen can be collected at the root of gastric cardia. Therefore, the biopsy rate at gastric cardia root in Jiyuan and Linzhou is as high as 70% and total biopsy rate of esophagus and gastric cardia is 111%. In 2010, the 2011 edition was implemented and its requirement for gastric cardia biopsy is that biopsy is only performed if there are supspicious lesions. Therefore, the biopsy rate decreased, which led to decreased cancer detection rate and early diagnosis rate. In 2009, the biopsy rate in Huixian was low and it increased in 2010-2011, at the meantime, cancer detection rate and early diagnosis rate increased accordingly. In other four counties, the biopsy rate is also related to the cancer detection rate and early diagnosis rate.

Screening can detect potential invasive cancer and early stage cancer and increase treatment efficacy. Screening and early detect and treatment open up a new direction in the cancer prevention, indicating that our national cancer prevention strategy improves. The incidence of cancer is various in different regions. Therefore we need to modify our strategy based on scientific proof and our circumstance in order to promote national early detection and treatment program for esophageal and gastric cancer.

References

- Aoki K (2006). Early history of cancer epidemiology and prevention in Japan. *Asian Pac J Cancer Prev*, **7**, 170-6.
- Dong ZW (2009). Cancer screening and early diagnosis and treatment manual in China (Trial). People's Health Publishing House, 1st Edition.
- Elliot M. Livstone. Esophageal cancer tumors of the GI tract. Merck Manual, 2012.
- Ferlay J, Shin HR, Bray F, et al (2010). Estimates of worldwide burden of cancer in 2008: Globocan 2008. Int J Cancer, 127, 2893-917.
- Henan research division of cancer prevention (2012). 2011 Annual report of cancer registration. Henan Hospital of Tumor Press, 33-41, Henan, China.
- Jaffer A. Ajani, James S, et al (2011). Esophageal and esophagogastric junction cancers. *J Natl Compr Canc Netw*, 9, 830-87.
- Kamangar F, Dores GM, Anderson WF (2006). Patterns of cancer incidence, mortality, and prevalence across five continents:

defining priorities to reduce cancer disparities in different geographic regions of the world. *J Clin Oncol*, **24**, 2137-50.

- Lee YY, Oh DK, Choi KS, et al (2011). The current status of gastric cancer screening in Korea: report on the National Cancer Screening Programme, 2009. Asian Pac J Cancer Prev, 12, 3495-500.
- Lu JB, Liu ZC, Ma WH, et al (2012). Practice and exploration of early diagnosis and treatment in Henan, which is of high incidence of esophageal carcinoma/cardia carcinoma. *Chin J Tumor*, 21, 828-30.
- Ministry of Health Bureau of Disease Control and Prevention (2011). Technical proposals for early detection and treatment of cancer (2011 edition), People's Health Publishing House, Beijing, China.
- National Cancer Center (2012). China Cancer Registry Annual Report in 2011. Beijing Military Medical Science Press, 194.
- National institute of cancer prevention (2008). 2004 Annual Report of cancer registration, Peking Union Medical College Press, Beijing, China.
- Suh M, Choi KS, Lee YY, et al (2013). Cancer screening in Korea, 2012: results from the Korean national cancer screening survey. Asian Pac J Cancer Prev, 14, 6459-63.
- Wang GQ, Hao CQ, Lai SQ, et al (2003). The application and effect of iodine staining in endoscopic screening in region of high incidence of esophageal carcinoma. *Chin J Gastroenterology*, **20**, 377.
- Wang GQ, Liu YY, Hao CQ, et al (2004). The relationship of esophageal mucosa iodine staining and histological changes of superficial esophageal carcinoma and precancerous lesions. *Chin J Cancer*, 26, 342-4.
- Zhao P, Chen WG, Kong LZ (2012). 2003-2007 cancer incidence and mortality in China. Military Medical Science Press, Beijing, China.
- Zheng RS, Zhang SW, Wu LY, et al (2012). China cancer registry 2008: analysis of incidence and mortality of malignant tumors. ???PLEASE SUPPLY 21, 1-2.