

Changes of Z-line at gastroesophageal junction in symptom-free subjects from high-incidence area for esophageal cancer in Henan[☆]

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Abstract

Z-Line is the boundary at esophageal and gastric cardia junction. Upgrowth of Z-line has been regarded as a manifestation of reflux esophagitis, which may induce Barrett's esophagus in western countries. The present study was undertaken to characterize the appearance changes of Z-line and its correlation with esophageal and gastric cardia precancerous lesions on symptom-free subjects from the high-incidence area for esophageal cancer in Henan. Endoscopy and mucosal biopsy histopathological examination were performed on 1, 217 symptom-free subjects (≥ 30 years old) from the high-incidence area for esophageal cancer in Linzhou, Henan. Z-line appearance was recorded as upgrowth, irregular, and indistinct. All the biopsies were fixed with 85% alcohol and processed for routine HE staining and histopathology. The endoscopic observation was correlated with histopathological results. The detection rates for the upgrowth (≥ 3 cm), irregular and indistinct Z-line were 12%, 10% and 1%, respectively. The incidence for Z-line upgrowth and irregular in male at different age groups was apparently higher than that in female ($P < 0.05$). The incidence for irregular Z-line in young female was higher than in other age groups ($P < 0.05$). With the age increasing, a decreasing tendency for Z-line upgrowth was observed both in male and female. The subjects with Z-line upgrowth had a higher incidence for esophageal basal cell hyperplasia and dysplasia in lower esophageal segment than in those without Z-line upgrowth ($P < 0.05$). The incidence for chronic superficial gastritis, atrophic gastritis with intestinal metaplasia was higher in the subjects with Z-line upgrowth than in those without Z-line upgrowth. The present results demonstrate that there is an apparent change of Z-line upgrowth in symptom-free subjects from the high-incidence area for esophageal cancer in Henan. Z-line upgrowth is related with both esophageal and gastric cardia lesions, suggesting that Z-line upgrowth may be one of the early indicators for esophageal and gastric cardia carcinogenesis. The present observations provide new insight for understanding of esophageal and gastric cardia carcinogenesis. [Life Science Journal. 2007;4(1):21-23] (ISSN: 1097-8135).

Keywords: esophageal neoplasm; high-incidence area; precancerous lesion; Z-line; esophagus; gastric cardia

1 Introduction

The boundary of the transitional zone from esophageal squamous epithelium to gastric cardia columnar epithelium, which is collapsed by mucosa of the junction between esophagus and cardia, has been nomi-

nated as "Z-line". The description of normal conformation of Z-line is not unanimous. Abnormal appearance of Z-line, especially upgrowth, has been known as one of manifestation of reflux esophagitis, which may induce Barrett's esophagus in western countries^[1,2]. Barrett's esophagus has been regarded as one of precancerous lesions for esophageal adenocarcinoma^[3]. However, both reflux esophagitis and Barrett's esophagus are uncommon in Chinese population at high risk for esophageal cancer^[4]. In China, squamous cell carcinoma (SCC) is the predominant histological type of esophageal cancer (95%)^[5]. In contrast, in western countries, more than

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half of the esophageal cancer is adenocarcinoma^[6]. We have found the different abnormal appearance changes of Z-line under endoscopic examination on the symptom-free subjects from the high-incidence area for esophageal cancer in Henan, China. These changes become clear after esophageal mucosa stained with iodine, including upgrowth, irregular, and indistinct. Biological significance of the conformation changes is not clear. We hypothesized that Z-line upgrowth, resulted in prolongation of gastric columnar epithelium into the lower esophagus, might be one of the important early indicators in carcinogenesis of adenocarcinoma at the gastroesophageal junction. The present study was thus undertaken to characterize the appearance changes of Z-line in symptom-free subjects from the high incidence area for esophageal cancer in Linzhou, northern China and to correlate these changes with occurrence of esophageal and gastric cardia precancerous lesions.

2 Materials and Methods

2.1 Subjects

1,217 symptom-free subjects (26 – 65 years old) from Linzhou, the high-incidence area for esophageal cancer in Henan Province were enrolled for the screening of early esophageal and gastric cardia cancers. All the subjects were examined by endoscopy, mucosal biopsy and histopathological examinations, and the appearance changes of Z-line were recorded under endoscopy.

2.2 Endoscopic biopsy and classification of Z-line appearance changes

Biopsies were taken from each subject at middle esophagus (30 – 32 cm to Z-line), lower esophagus (3 cm above gastroesophageal junction) and gastric cardia. All the biopsies were immediately fixed with 85% alcohol. The appearance of Z-line changes were classified into four different types, i. e., normal: Z-line was regular and clear; upgrowth: Z-line presents finger or ligulate-like prolongation into lower esophagus (≥ 3 cm); irregular: Z-line presents clear, irregular boundary, without apparent prolongation; indistinct: the boundary of esophageal and gastric cardia transitional zone is not clear.

2.3 Histopathological examination

Histopathological diagnosis for esophageal epithelia was made based on the changes in cell morphology and tissue architecture using previously established criteria^[6]. In brief, the normal esophageal epithelium contained one to three proliferating basal cell layers; the papillae were confined to the lower half of the whole epithelium thickness. In basal cell hyperplasia(BCH), the proliferating basal cells surpassed 15% of the total epithelial thickness. Dysplasia was characterized by nuclear atypia (enlargement, pleomorphism, and hyperchromasia), loss of normal cell polarity, and abnormal tissue maturation. SCC was characterized by confluent and in-

vasive sheets of cohesive, polymorphous cells with hyperchromatic nuclei. The following histopathological classification was used for the gastric cardia epithelia: chronic superficial gastritis (CSG), inflammation manifested by mild lymphocyte and plasma cell infiltration; chronic atrophic gastritis (CAG), glandular morphology disappeared partially or completely absent in the mucosa and replaced by connective tissue, interglandular space infiltrated mainly by plasma cells and lymphocytes; gastric cardia dysplasia (GDYS), neoplastic features including nuclear atypia and /or architectural abnormalities confined to the gastric cardia epithelium, without invasion; gastric cardia adenocarcinoma (GCA), invasion of neoplastic gastric cells through the basement membrane^[6].

2.4 Statistical analysis

The χ^2 test was used for the percentage of lesions with different types of Z-line appearance changes. Spearman correlation test and linear tendency test were used for the correlation between different Z-line types and epithelial lesions ($P < 0.05$) was considered significant.

3 Results

Of the 1,217 symptom-free subjects examined the detection rates for the Z-line appearance of upgrowth, irregular, indistinct and normal types were 12% (141/1,217), 10% (122/1,217), 1% (14/1,217) and 77% (940/1,217), respectively.

The distribution of appearance changes of Z-line by age and gender was summarized in Table 1. The incidence for Z-line upgrowth and irregular in male at different age groups was apparently higher than that in female ($P < 0.05$). With the age increasing, a decreasing tendency for Z-line upgrowth was observed both in male and female. The incidence for irregular Z-line in young female (40 – 49) was higher than in other age groups ($P < 0.05$). The incidence for indistinct type of Z-line in male and female at different age groups was apparently lower than that for upgrowth and irregular types of Z-line.

Table 1. Distribution of Z-line appearance changes by age and gender

Cases examined (n)	Appearance changes of Z-line			
	Uppgrowth n (%)	Irregular n (%)	Indistinct n (%)	
Male				
30 –	53	31 (22.0)*	21 (15.0)*	1 (0.7)
40 –	57	28 (20.0)	26 (18.0)	3 (2.1)
50 –	56	23 (16.0)	32 (23.0)	1 (0.7)
60 –	22	12 (8.5)	9 (6.0)	1 (0.7)
Female				
30 –	19	14 (10.0)	5 (4.0)	0 (0.0)
40 –	36	18 (13.0)	15 (10.0)**	3 (2.0)
50 –	26	13 (11.0)	10 (7.0)	3 (2.0)
60 –	7	2 (1.0)	4 (3.0)	1 (0.7)

*Male vs. female, $P < 0.05$ (χ^2 test). ** 40-age group vs. other age group in female, $P < 0.05$ (χ^2 test).

Table 2 showed the correlation between Z-line appearance changes and gastric cardia pathological lesions on the symptom-free subjects. Cardia pathological changes progressed from normal appearance to upgrowth Z-line ($P < 0.05$). However, the cardia pathological lesions were similar in irregular and indistinct Z-line groups ($P > 0.05$).

Table 2. Correlation between Z-line appearance changes and gastric cardia epithelial lesions

Z-line's appearance changes	Cases examined (n)	Gastric cardia epithelial lesions			
		Normal n (%)	CSG n (%)	CAG+IM n (%)	GDYS n (%)
Upgrowth	106	45 (42)	39 (37)*	19 (18)*	3 (3)
Irregular	76	37 (49)	29 (38)	8 (11)	2 (3)
Indistinct	6	4 (67)	1 (17)	1 (17)	0 (0)
Normal	586	303 (52)	182 (31)	13 (12)	28 (5)

*Upgrowth vs. normal, $P < 0.05$ (χ^2 test).

Table 3 showed the correlation between Z-line appearance changes and lower esophageal lesions on the symptom-free subjects. The subjects with Z-line upgrowth had a higher incidence for esophageal basal cell hyperplasia and esophageal dysplasia (EDYS) in lower esophageal segment than in those without Z-line upgrowth ($P < 0.05$). However, the detection rate for lower esophageal lesions was similar in the irregular and indistinct types of Z-line appearance changes ($P > 0.05$).

Table 3. Correlation between Z-line appearance changes and esophageal epithelial lesions at lower esophagus

Z-line appearance changes	Cases examined (n)	Lower esophageal epithelial lesions		
		Normal n (%)	BCH n (%)	EDYS n (%)
Upgrowth	98	35 (36)	58 (59)*	5 (5)*
Irregular	85	56 (66)	29 (34)	0 (0)
Indistinct	7	6 (86)	1 (14)	0 (0)
Normal	707	425 (60)	263 (37)	19 (3)

*Upgrowth vs. normal, $P < 0.05$ (χ^2 test).

Table 4 showed the correlation between Z-line appearance changes and the middle esophageal lesions on the symptom-free subjects. The subjects with Z-line upgrowth had a higher incidence for esophageal basal cell hyperplasia and EDYS in middle esophageal segment than in those without Z-line upgrowth ($P < 0.05$). The similar results were observed in the middle esophageal lesions and the Z-line appearance changes of irregular and indistinct types as in the lower esophagus ($P > 0.05$).

4 Discussion

The present studies demonstrate that there is an apparent change (23%) of Z-line in symptom-free subjects from the high-incidence area for esophageal cancer in Henan, including upgrowth (12%), irregular (10%),

indistinct (1%). The incidence of esophageal and gastric cardia epithelial lesions, especially in the lower segment from the subjects with Z-line upgrowth was higher than in those without Z-line upgrowth. These results indicate that upgrowth of Z-line may be an early indicator for both esophageal and gastric cardia carcinogenesis in high-risk area. Z-line upgrowth might alternate both lower esophageal and gastric cardia epithelial environment and make these people prone to occurrence of pre-cancerous lesions. Our hypothesis is that the primary esophageal and gastric cardia adenocarcinoma, adenocarcinoma at the junction of esophagus and cardia and Barrett's esophagus related esophageal adenocarcinoma might be a group of related diseases.

Table 4. Correlation between Z-line appearance changes and esophageal epithelial lesions at middle esophagus

Z-line appearance changes	Cases examined (n)	Middle esophageal epithelial lesions		
		Normal n (%)	BCH n (%)	EDYS n (%)
Upgrowth	115	63 (55)	41 (36)*	11 (10)*
Irregular	84	61 (73)	21 (25)	2 (2)
Indistinct	7	5 (71)	2 (29)	0 (0)
Normal	749	444 (59)	267 (36)	38 (5)

*Upgrowth vs. normal, $P < 0.05$ (χ^2 test).

The mechanism of Z-line upgrowth is not clear. Reflux esophagitis may be one of the key factors in Z-line upgrowth development in western countries. Barrett's esophagus may develop after reflux esophagitis. However, the incidence of both reflux esophagitis and Barrett's esophagus in Chinese population, especially in high-risk area for esophageal and gastric cardia cancers, is much lower than in western countries. Z-line upgrowth in Chinese people may not be a result of reflux esophagitis. Further studies are needed to illustrate the mechanism and significance of Z-line upgrowth in Chinese people.

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