

A Single Center's 30 Years' Experience of Esophageal Adenocarcinoma

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Background : Adenocarcinoma of the esophagus has been reported to be increasing in incidence in a number of regions throughout the world, while the incidence of squamous cell carcinoma (SCCA) of the esophagus is mostly stable or decreasing. To evaluate the increasing tendency of adenocarcinoma of the esophagus.

Methods : we studied retrospectively the records of patients with histologically proven esophageal cancer between 1970 and 1999 at the Yonsei Medical Center.

Results : Total cases of esophageal cancer were 969 patients of which the cases of adenocarcinoma and SCCA were 27 patients and 918 patients, respectively. The ratio of esophageal adenocarcinoma to SCCA was 0.0375 in the 1970s, 0.0241 in the 1980s and 0.0292 in the 1990s. There was no statistical difference ($p=0.811$) in the ratios of adenocarcinoma of the esophagus between the three consecutive 10-year groups.

Conclusion : In conclusion, unlike the US and other western countries, it seems that the ratio of esophageal adenocarcinoma compared to SCCA has not increased among patients with esophageal carcinoma at the Yonsei Medical Center.

Key Words : esophageal adenocarcinoma, squamous cell carcinoma

INTRODUCTION

Adenocarcinoma of the esophagus is increasing in a number of countries, whereas the incidence of gastric carcinoma is decreasing^{1,7)}. Except for an association with Barrett's esophagus, little is known about the etiology of these cancers. Barrett's esophagus is a complication of gastroesophageal reflux disease (GERD) and is regarded as an important risk factor of esophageal adenocarcinoma in western countries⁸⁾. The incidence of esophageal squamous cell carcinoma has decreased or remains stable in the USA and European countries, whereas the incidence of adenocarcinoma is rapidly increasing^{1,2,9)}. But, the prevalence of esophageal adenocarcinoma has

not been surveyed or reported in Korea, as far as we know. Therefore, we reviewed the medical records of 969 patients with histologically proven esophageal cancer during the last three decades (1970-1999) to assess indirectly the ratio of esophageal adenocarcinoma to SCCA.

MATERIALS AND METHODS

Patients with histologically proven esophageal cancer between 1970 and 1999 were retrospectively studied. The pathologic diagnosis of esophageal cancer was obtained by the evaluation of the specimen from surgical resection or endoscopic biopsy. The data were taken from the Yonsei Medical Center. The patients were divided into three consecutive 10-year groups (group 1, 1970-1979; group 2, 1980-1989; group 3, 1990-1999). Patients with SCCA or adenocarcinoma that secondarily invaded the

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esophagus from a nonesophageal primary tumor and patients in whom the esophagus was involved with metastatic disease were excluded. Esophageal cancers were divided according to the International Classification of Diseases of Oncology (ICD-O) morphologic criteria into adenocarcinoma and non-adenocarcinoma. Three cell types were defined as follows : adenocarcinoma group, SCCA group and other cell types, including neuroendocrine carcinoma, small cell carcinoma and adenosquamous cell carcinoma. Patients' age at diagnosis, tumor stage, tumor location, histological type and body mass index (BMI) were recorded and analyzed.

Statistical analysis

The Statistical Analysis System (SAS Inc., Cary, NC, USA) was used for all analysis. Trends from the three groups were compared using chi-square test. The influence of BMI on two cell types was evaluated with *t*-test. The *p* value less than 0.05 was considered statistically significant.

RESULTS

Between 1970 and 1999, a total of 969 cases of SCCA, adenocarcinoma, or other cell type cancers in the esophagus were retrieved in the pathology records at the Yonsei Medical Center. There were 918 patients with SCCA and 27 patients with esophageal adenocarcinoma. Overall, SCCA was the most common cell type. Other cell types of esophageal cancer consisted of adenosquamous carcinoma (n=4), small cell carcinoma (n=2), neuroendocrine carcinoma (n=1) and undifferentiated type (n=17). The distribution of the cell types of esophageal carcinomas is shown in Table 1.

Table 1. The distribution of the cell types of esophageal carcinomas

Cell type of esophageal cancer	Patient numbers	Percent	Sex (M/F)
Squamous cell carcinoma	918	94.7%	862/56
Adenocarcinoma	27	2.8%	25/2
Undifferentiated	17	1.8%	17/0
Adenosquamous cell carcinoma	4	0.4%	4/0
Small cell carcinoma	2	0.2%	2/0
Neuroendocrine carcinoma	1	0.1%	1/0

The mean age of patients with esophageal cancer was 61.1±8.8 years (mean age of adenocarcinoma group and SCCA group, 62.2±10.6 and 61.1±8.7 years, respectively) and the mean height and body weight were 166.0±6.7 cm and 53.0±15.9 kg, respectively.

We discovered 541 cases (56.6%) of esophageal cancer in the mid-esophagus, 207 cases (21.7%) in the upper esophagus and 207 cases (21.7%) in the lower esophagus (Table 2). A total of 27 cases of esophageal adenocarcinoma were identified in this study. The lesion site of 21 cases was located in the lower esophagus and that of the remaining 6 cases was located in the mid-esophagus. The ratios of adenocarcinoma to SCCA were 10.4% (2/201) in the lower esophagus, 1.1% (6/529) in the mid-esophagus and 0.0% (0/201) in the upper esophagus. Thus, adenocarcinoma was located in the lower esophagus more frequently than in the mid or upper esophagus with a statistical significance (*p*=0.001).

Table 2. The location of esophageal cancers

Tumor location in the esophagus	Total	SCCA*	Adeno [†]	Other cell type
Upper	207 (21.7%)	201	0	6
Mid	541 (56.6%)	523	6	12
Lower	207 (21.7%)	180	21	6
Total	955(100.0%)	914	27	24

(missing data=14)

SCCA*, squamous cell carcinoma; Adeno[†], adenocarcinoma

The ratios of the adenocarcinoma group to the SCCA group among the three groups were 0.0375, 0.0241 and 0.0292 for group 1, 2 and 3, respectively (*p*=0.811). The ratios of the adenocarcinoma group to the SCCA group have not risen in the three groups (Table 3).

Table 3. The distribution of the esophageal cancers according to the cell types in each group

	Adenocarcinoma	SCCA*
Group 1 (1970- 1979)	3 (3.75%)	77 (96.25%)
Group 2 (1980- 1999)	6 (2.41%)	243 (97.59%)
Group 3 (1990- 1999)	18 (2.92%)	598 (97.08%)
Total	27	918

(*p*=0.811)

SCCA*, squamous cell carcinoma

In the adenocarcinoma group, the mean BMI was 19.6±6.3 and that of the SCCA group was 19.4±5.6 (*p*=0.3445).

DISCUSSION

Our study of esophageal adenocarcinoma has several limitations in methodology. At first, it is a single center's experience of 30 years about esophageal cancer and so the results of this study cannot represent the overall prevalence of esophageal adenocarcinomas in Korea. At least several multi-center studies are needed for the purpose of defining the prevalence of esophageal adenocarcinoma in Korea. But our study tried to find indirect evidence of an increasing tendency of esophageal adenocarcinoma and the result seems to be that the ratio of adenocarcinoma to SCCA has not increased in patients with esophageal carcinoma in the past three decades in single medical center in Korea.

From the late 1970s, a significant increase in the incidence of adenocarcinoma of the esophagus and gastric cardia has been reported from many countries, including the US¹⁻³⁾, the United Kingdom⁴⁾, France⁵⁾ and Sweden⁶⁾. In the US, adenocarcinoma of the esophagus has continued to increase in frequency in the early 1990s and an estimated 25,000 people die every year of this cancer⁷⁾. Lord *et al* reported from a large scale prevalence study done in 1998¹⁰⁾ that the incidence of esophageal adenocarcinoma in men has increased evidently in Australia. The incidence of SCCA of the esophagus is mostly stable or decreasing whilst that of adenocarcinoma of the esophagus has been reported to be increasing in incidence in a number of regions^{1, 2, 9)}. These two types of esophageal cancer have distinctly different demographic patterns (i.e., the incidence of squamous cell tumors is more than 5 times higher among black men than among white men, whereas the incidence for adenocarcinoma is more than three times higher in white men compared with black men).

Although adenocarcinoma of the esophagus has been increasing rapidly in many regions of the world, the risk factors of the cancer are largely unknown. The proposed candidates as risk factors for adenocarcinoma of the esophagus are Barrett's esophagus, high BMI, alcohol and tobacco use, H₂ receptor antagonist use, *Helicobacter pylori* (*H. pylori*) infection, etc.

Adenocarcinomas of the esophagus can possibly arise from mucosal glands, submucosal glands, ectopic gastric mucosa and Barrett's esophagus. Rare cases of esophageal adenocarcinomas in the upper esophagus have been described in the literature¹¹⁾.

The recently reported increasing incidence of adenocarcinomas in the lower esophagus is related to malignant

transformation of Barrett's esophagus. In Barrett's esophagus, the normal squamous epithelial lining of the lower esophagus, damaged by gastroesophageal reflux, is replaced by columnar epithelium. Barrett's esophagus is a precursor lesion for adenocarcinoma of the esophagus and gastric cardia and is more common in men¹²⁾. Patients with Barrett's esophagus have a 30-125 times increased risk of developing esophageal carcinoma¹³⁻¹⁵⁾. Barrett's esophagus is thought to arise in conditions with prolonged reflux of duodenal contents into the esophagus¹⁶⁻¹⁸⁾.

It is believed that GERD is more common in obese patients, especially those with abdominal obesity. Brown *et al* reported that obesity (upper quartile of BMI) was associated with a three times higher risk of adenocarcinoma than the lowest quartile¹⁹⁾. The mechanism by which obesity might affect the risk of esophageal adenocarcinoma is unclear, although it may be linked to the predisposition of obese individuals to GERD and to the commonly associated hiatal hernia²⁰⁾. Reflux esophagitis is a major risk factor for Barrett's esophagus²¹⁾, which in turn is a precursor lesion for esophageal adenocarcinoma. As for BMI, our observation showed no statistically significant difference between adenocarcinoma and SCCA groups (BMI of the adenocarcinoma group=19.6, BMI of the SCCA group=19.4, $p=0.833$).

There is no report on the prevalence and incidence of reflux esophagitis in the general Korean population. In Korea, it is generally accepted that the prevalence and incidence of reflux esophagitis are lower than those in the western countries. Yi *et al* found that the estimated age-adjusted prevalence of endoscopically-proven reflux esophagitis in a general health screening population was 2.7%, which was very low prevalence compared to those from western countries²²⁾. The study of Yeom *et al* also showed that the prevalence of reflux esophagitis in patients with symptoms of gastrointestinal tract was 5.4%, which means that the prevalence of reflux esophagitis in the Korean population would be much lower than that of western countries²³⁾. But it is expected that GERD in Korea may increase in incidence because of the increase in the obese population due to westernized diet and life style.

In conclusion, unlike the western countries including US, our retrospective study found that the ratio of adenocarcinoma to SCCA has not increased in patients with esophageal carcinoma in the past three decades at a single medical center in Korea. However, further epidemiologic studies are needed to evaluate the possibility of an increasing tendency to develop esophageal adenocarcinoma in Korea in the near future.

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