Adenocarcinoma of the Esophagogastric Junction in China 
According to Siewert’s Classification

Ji-Gang Bai¹, Yi Lv¹ and Cheng-Xue Dang²

¹The Department of General Surgery, The First Hospital of Xi’an Jiaotong University, Xi’an and ²The Department of Oncosurgery, The First Hospital of Xi’an Jiaotong University, Xi’an, China

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Background: There had never been a clear definition of the cancer of cardia before Siewert’s classification, which was proposed in 1996 and approved in 1997 at the second International Gastric Cancer Congress in Munich. On the basis of the classification, this study aims to research into the clinicopathological characteristics and surgical modes of adenocarcinoma of the esophagogastric junction in China.

Methods: The study reviewed the data of the distal esophageal cancer, the cancer of cardia and the proximal gastric cancer at the First Hospital of Xi’an Jiaotong University from January 1995 to December 1999. Surgical patients were defined and classified according to Siewert’s classification, and 203 patients were up to the classification. Then the study compared and analyzed the clinicopathological characteristics and the survival rates of the three types of the tumor.

Results: Among the 203 patients, there were 29 patients with adenocarcinoma of the distal esophagus (Type I); 80 patients with true carcinoma of cardia (Type II); and 94 patients with subcardial carcinoma (Type III). Obvious differences were found in the clinicopathological characteristics of the three types, but no significant difference of the 5-year survival rates was found among the three types of patients with curative resection.

Conclusion: On the data, the distribution of the three types of tumor was found to be different from that reported in Western countries and in Japan; and the three types of patients who had undergone curative resection were found to have similar 5-year survival rates.

Key words: adenocarcinoma of the esophagogastric junction – resection – adenocarcinoma of the distal esophagus – true carcinoma of cardia – subcardial carcinoma

INTRODUCTION

In Western countries, contrasting with a decrease of gastric cancer in recent decades, the incidence of adenocarcinoma of the esophagogastric junction (AEG) is rising strikingly. Because of the lack of clear definition and classification, the cancer of cardia has sometimes been considered and treated as distal esophagus cancer, sometimes as proximal gastric cancer and sometimes as an entity separate from both esophagus cancer and gastric cancer. This confusing state has resulted in an ambiguous definition, classification and treatment of AEG and has impeded the academic exchange (1–7).

With the aim to clarify the definition of cancer of cardia, Siewert and Stein (7) published a classification of AEG in 1996. The classification was later approved at the second International Gastric Cancer Congress in Munich in April 1997. According to the classification, a tumor can be identified as AEG as it centers within 5 cm above and 5 cm below the anatomic EGJ, which is further classified into three types (Type I, Type II and Type III) according to the anatomic location of the tumor center.

In China, all the tumors on EGJ were vaguely called the cancer of cardia, which had been actually treated as the cancer of distal esophagus or the proximal gastric cancer instead of an independent entity. The study focuses on the clinicopathological characteristics of AEG in China according to Siewert’s classification.

PATIENTS AND METHODS

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The study reviewed the data of the distal esophageal cancer, the cancer of cardia and the proximal gastric cancer at the First Hospital of Xi’an Jiaotong University from January 1995 to December 1999. Surgical patients were defined and classified...
According to Siewert’s classification, AEG are subdivided into three types: Type I: adenocarcinoma of the distal esophagus with the center located within 1 cm above and 5 cm above the anatomic EGJ; Type II: true carcinoma of the cardia with the tumor center within 1 cm above and 2 cm below the junction; Type III: subcardial carcinoma with the tumor center between 2 and 5 cm below EGJ, which infiltrates the EGJ and distal esophagus from below. Among the surgical patients, 203 were up to the classification.

Through reviewing and analyzing the case records, pathological reports and operative records, the study mainly analyzed the clinicopathological characteristics of these three types of adenocarcinomas. Type I was staged according to the UICC/AJCC classification for esophageal cancer; Type II and Type III were staged according to the classification for gastric cancer (8,9).

Statistical Analysis
Data were shown as prevalence or mean (±standard deviation). Continuous data were compared by the Mann–Whitney test; ordinal data were compared by the Chi-square test. Survival was analyzed by using a Kaplan–Meier survival plot followed by a Log Rank Test to identify significant differences in survival between these curves. \( P < 0.05 \) was considered significant.

Results
Clinicopathological Characteristics
There were 153 males and 50 females among the 203 patients who had undergone operations. The ratio of male to female was 3.06 : 1 and the average age of the patients was 60.7. There were 29 patients of Type I, 80 of Type II and 94 of Type III. On comparison, obvious differences were found in the clinicopathological characteristics of the three types. The percentage of male patients was much higher than that of the female patients, but there were no obvious gender differences between the three types. The mean age of patients was similar in each type. Intestinal metaplasia in the distal esophagus was mainly found in Type I, but the positive rate was not as high as what had been reported in Western countries (7,10). Poorly differentiated and undifferentiated cancer was mainly found in Type II and Type III (Table 1).

Table 1. Incidence and clinicopathological characteristics

<table>
<thead>
<tr>
<th>Classification</th>
<th>Total (n = 203)</th>
<th>Type I (n = 29)</th>
<th>Type II (n = 80)</th>
<th>Type III (n = 94)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, years)</td>
<td>60.7</td>
<td>59.7</td>
<td>60.1</td>
<td>61.3</td>
<td>NS</td>
</tr>
<tr>
<td>Male : female</td>
<td>3.06 : 1</td>
<td>3.5 : 1</td>
<td>3.1 : 1</td>
<td>2.9 : 1</td>
<td>NS</td>
</tr>
<tr>
<td>Intestinal metaplasia in the distal</td>
<td>22 (11%)</td>
<td>11 (39.1%)</td>
<td>5 (6.6%)</td>
<td>2 (1.6%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>esophagus (Barrett esophagus)</td>
<td></td>
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<tr>
<td>Tumors with pathological grade 3 and 4</td>
<td>97 (47.9%)</td>
<td>6 (19.5%)</td>
<td>34 (42.8%)</td>
<td>62 (65.9%)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Although the majority of patients of Type I (72.4%) or Type II (58.8%) had a UICC tumor stage I or stage II, only 32.9% patients of Type III had this tumor stage at the time of operation (Table 2). The percentages of metastatic nodes of the three types were 66.7, 65.1 and 79.9%, respectively. The metastatic rate of Type III was higher than the other two types; distant metastasis was found in 39 patients, with 4 from Type I (12.6%), 14 from Type II (16.9%) and 21 from Type III (24.9%).

Operative Procedures and Extent of Lymphadenectomy
The operative procedures of the three types of patients is shown in Table 3. Left thoracotomy approach was employed in subtotal esophagectomy with proximal gastrectomy, while laparotomy approach was employed in other operations for the AEG patients. Of the 203 AEG patients, curative resection was performed on 136 (67%). Of the 136 curative resection patients, 24 patients had Type I (83%), 55 had Type II (69%) and 57 had Type III (61%). (Table 4).

Extent of lymphadenectomy includes mediastinal lymph nodes, distal paraesophageal lymph nodes and upper abdominal lymph nodes (11,12). In Type I patients, the lymph nodes resected in subtotal esophagectomy and distal esophagectomy were (21 ± 10) and (17 ± 8), respectively. In Type II patients, the lymph nodes resected in those who underwent subtotal esophagectomy were (25 ± 12) and the lymph nodes resected in those who underwent distal esophagectomy were (23 ± 11). The lymph nodes resected in total gastrectomy (31 ± 15) were more than the lymph nodes resected in proximal gastrectomy (23 ± 11) in Type II and Type III patients.

Morbidity and Mortality
In hospital, the average morbidity was 17%. Anastomotic leakage occurred in 23 patients, of whom 4 died. Severe cardiopulmonary complications were observed in 15 patients, of whom 4 died. One patient died of peritoneal abscess and one died of postoperative hemorrhage. Other complications such as intestinal obstruction, anastomotic stenosis, and so forth were also observed, but were improved eventually without resulting in death. The mortality in hospital was 4.9% (Table 4).
Total survivals of the three types of cancer were 34, 27.5 and 24.5%, respectively. A further analysis of the 136 R0-resection patients did not suggest significant difference in the prognosis, with 37.5% for Type I, 34.5% for Type II and 33.3% for Type III (Fig. 1).

DISCUSSION

Siewert’s classification of AEG has been increasingly accepted all over the world (1–3,6). It was found that the distribution of the three types of AEG in this study was not the same as that reported in Western countries (13) and in Japan (1). Compared with Type I and Type III, Type II was found a bit less in reports from Western countries (13), while according to an institute in Japan, there was no Type I in AEG patients (1). In this study, it was found that Type II and Type III formed the majority of AEG and there was no significant difference between the distribution of the two types. Type I tumors were much less. The reason probably is that Asian people have less esophageal reflux, and hence there is less intestinal metaplasia in the distal esophagus. However, it still needs further study to confirm whether the distribution is the typical distribution of Chinese.

There are various modes of operation for AEG, such as subtotal esophagectomy with total gastrectomy, subtotal esophagectomy with proximal gastrectomy, total gastrectomy with distal esophagectomy, esophagogastrectomy, and so forth (7). For Type I tumor, a subtotal esophagectomy with proximal gastrectomy is often preferred (14). In this study, a major portion of Type I patients underwent subtotal esophagectomy, while a small portion underwent distal esophagectomy. For Type II tumor, there are controversial opinions on the approaches and the extent of operation. A majority of people prefer total gastrectomy with distal esophagectomy (15), while some people believe proximal gastrectomy with distal esophagectomy would have a satisfactory result. In the study, most of Type II patients underwent total gastrectomy or proximal gastrectomy, while a small portion underwent subtotal esophagectomy with proximal gastrectomy. For Type III tumor, total gastrectomy with distal esophagectomy is recommended (16). For the Type III patients in this study, the number of those who underwent proximal gastrectomy and of those who underwent total gastrectomy was roughly the same.

At present, though the therapy of AEG mainly depends on surgical treatment, there is still not a standard with regard to the operative procedure and resection extent. Advocates of extended AEG resection believe that extended resection would remove more lymph nodes (1,7). However, an extended AEG resection might result in higher postoperative morbidity and mortality. Moreover, the extended resection is not necessary as it was found that the incidence of lymph node metastasis was low in the early tumor at the position (1,17). In recent years, limited resection for early AEG has been performed by many surgeons and has been found satisfactory. In this study, it was found that the 5-year survival rates of Type I was higher than that of Type II and Type III, but no obvious differences were found in the 5-year survival rates of the three types of patients who underwent curative resection. One of the reasons probably rests with the fact that Type I could be found earlier than the other two types. The extended resection could not prolong the lives of patients, but increased the morbidity and mortality instead.

According to Siewert’s classification, AEG is classified into Type I, Type II and Type III. It is still not very clear whether
the classification can properly reflect the pathogenesis and their relations. Although there are similarities in epidemiology, morphology and other aspects, there are still great differences in the pathogenesis of the three types of the cancer (18–21). Obvious differences were also found in the clinicopathological characteristics of the three types in this study. That is to say that the three types differ from one another. Between Type I and Type II, differences are dominating, while between Type II and Type III tumors, similarities are more prominent. Further study is still necessary to clear the relations between them thoroughly.

References