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Delay in the diagnosis of esophageal carcinoma: Experience of a single unit from a developing country

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» Abstract

Objectives : Main objective was to analyze the time delay between the onset of symptoms and the histological diagnosis of esophageal cancer. The subsidiary objective was to analyze the relationship between the time delay and stage of the disease at the time of definitive treatment. **Study Design , Setting , and Methods :** A prospective analysis of patients with esophageal cancer presenting to a single unit over a period of 24 months was performed. Interval from the onset of symptoms to the histological diagnosis and stage at presentation was analyzed. **Results :** There were 48 patients (male = 26) with a median age of 59.5 (range 43 - 84) years. First symptom was progressive dysphagia in all patients. Subsidiary symptoms were, weight loss in 83.3% (n = 40), abdominal / chest pain in 10 (20.8%), regurgitation in 14 (29.2%), odynophagia in three (6.2%), abdominal discomfort in two (3%), and dyspepsia in two (3%). The mean delay from the appearance of the first symptoms to the end point was 14.9 weeks (range 3 - 37 weeks). Total delay was due to patient delay in 82%, endoscopy delay in 7%, and delay in histological diagnosis in 11%. **Conclusions :** As the majority (82%) in our study showed patient delay, a community education program may help in their early presentation to the hospital. However, there is also a notable delay in endoscopy and histology (15%) services, mainly due to a shortage of endoscopy units and qualified histopathologists in the state sector.

Keywords: Delay in diagnosis, endoscopy, esophageal carcinoma

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» Introduction

Esophageal cancer is the eighth common malignancy worldwide and the third among gastrointestinal malignancies. [1],[2] It is the fourth common malignancy in the developing world, and recently, some of the Asian countries have also reported a rise in its incidence. [3]

It was responsible for 462 000 new cases (4.2% of the total) and 386 000 deaths (5.7% of the total) in 2002, [4] and it is the sixth leading cause of death from cancer worldwide. [5] It is also one of the most virulent tumors with poor prognosis and not more than 14% of the patients could survive longer than five years despite the recent advances in surgical techniques. [6],[7] The prognosis for patients with esophageal cancer is closely related to the stage of the disease at the time of diagnosis. The outcome of this cancer is closely related to the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system. [8] According to that, five-year survival rates for Stages I, II, III are 50-80%, 30-40%, and 10-15%, respectively. Stage IV disease treated with palliative therapy has a median survival of < 1 year. [9] Therefore, if the disease is diagnosed and treated early (stages I and II) the outcome may be considerably better than if diagnosed in the late stages (stages III and IV).

According to what the previous studies suggest, where the tumor growth is calculated based on mathematical models, it takes a considerable time period (> 10 years) from the appearance of the first cancer cell to the possibility of detecting a tumor by conventional investigations. [10],[11] On these grounds someone may suggest that once an esophageal cancer clinically manifests, there has been a long tumor history of a number of years, and therefore, it is unlikely that the prognosis is changed by the relative short delay time in diagnosis and treatment. However, it is important note that the median values of potential doubling time in esophageal tumors is 4 - 5 days with a range of 2 - 20 days among the fastest of all types of tumors. [10] Therefore, a few months of delay may allow the tumor to double several times. Hence, long delays are probably a negative factor for the patient's prognosis. [11] In Sri Lanka, we do not have a screening program to identify the early stages of esophageal cancer. In our experience, a majority of patients present with advanced disease leading to a poor outcome. Therefore a fast diagnostic workup after the first consultation is important, because, a diagnostic delay may lead to delay in treatment. This factor may therefore have an influence on the stage of the esophageal carcinoma and subsequently on the prognosis. Therefore, a fast diagnostic workup is important to detect the disease at an early stage and to improve the outcome, by offering the necessary treatment modalities. At present there are no published data regarding the delayed presentation of esophageal cancer and a possible association between symptom-to-treatment delay or the stage of the esophageal cancer at the time of treatment. Therefore, we performed this study to, identify the time of delay from the first symptom-to-treatment of esophageal cancer investigate the possible correlation between symptom-to-treatment delay and the stage of tumor at the time of presentation

» Materials and Methods

Forty-eight consecutive patients diagnosed as having oesophageal cancer at the National Hospital of Sri Lanka were studied. The patients with cancer arising from the gastroesophageal junction and other esophageal tumors such as leiomyosarcoma were excluded from the analysis. One of the authors interviewed each patient at their first visit to the hospital. Data were collected using a structured data sheet. Data were analyzed using SPSS statistical package version 16.0.

The delay in diagnosis and treatment was measured from the date when the patient first experienced the symptom/s that led to diagnosis. The end point was taken as the date when the patient had definitive histological diagnosis following upper GI endoscopy (UGIE). The overall delay in months was recorded from the appearance of the first symptom/s to the end point, for each patient, and was divided into three periods:

- time from appearance of the first symptoms to first contacting the healthcare system, that is, patient del
- time from first contacting the healthcare system to endoscopic delay in the diagnosis, that is, endosc delay
- histology report delay, that is, histology delay

Endoscopic lesions were classified according to their location, that is, upper, middle, or lower

esophagus. [12] Upper-third lesions extended from the cricopharyngeal sphincter (15 cm) to the tracheal bifurcation (23 cm). Middle-third lesions extended from 23 cm to 32 cm. Lower-third lesions extended from 32 cm to the gastroesophageal junction (40 cm). If the lesion involved more than one site, both locations were recorded. The American Joint Committee on Cancer (AJCC) staging system was used. Tumor infiltration was staged by Computer Tomography (CT) and /or Endoscopic Ultrasound (EUS).

» Results

Forty-eight patients (26 men and 22 women) were included in this study. The median age when they first developed symptoms was 59.5 (range 43 - 84) years. The first symptom was progressive dysphagia in all the patients (100%). In addition, 40 patients (83.3%) had loss of weight at presentation to the endoscopic examination. Apart from dysphagia, other presenting symptoms were, abdominal or chest pain in 10 (20.8%), regurgitation in 14 (29.2%), odynophagia in three (6.2%), abdominal discomfort in two (3%), and dyspepsia in two (3%) patients, respectively. All patients complained of progressive dysphagia and 46 (95.8%) experienced more than one symptom.

All patients underwent UGIE, barium swallow and staging investigations (i.e., chest X-ray film, abdominal ultrasonography, computed tomography, and/or endoscopic ultrasound).

Tumor location/histology

The tumor was located in the upper (cervical) esophagus in one patient, middle esophagus in 18 (37.5%) patients, and lower esophagus in 24 (50%) patients. In five patients the tumor was seen in both the middle and lower esophagus. Morphology of the tumor during UGIE was, ulcerative, obliterative, proliferative, and ulceroproliferative in 22 (45.8%), 18 (37.5%), 4 (8%), and 4 (8%) patients, respectively. Thirty-four (70.8%) patients had squamous cell carcinoma and 14 (29.2%) had adenocarcinoma. The histopathological differentiations of squamous cell carcinoma were well-differentiated carcinoma in six patients, moderate in 16 patients, and poor in 13 patients. The differentiations of adenocarcinoma were poor in eight patients and moderate in six patients [Table 1]. Two (4.1%) patients had stage I disease, eight (16.7%) had stage II disease, 24 (50%) had stage III disease, and 14 (29.2%) had stage IV disease.

According to the preoperative CT scan, 1, 20, 9 and 16 patients had stage I, II, III, and IV tumors, respectively. Two tumors (4.2%) were not detected by CT due to early disease (but confirmed on upper GI endoscopy and histology as moderately differentiated squamous cell carcinoma).

The symptom-to-treatment delay and its impact on the stage of the disease

The median delay concerning the interval from the appearance of the first symptom to the end point was 14.9 weeks. Twenty-seven (56.25%) patients had a delay of three months or more, 19 (39.58%) had four months or more, and six (12.5%) patients had a delay of six months or more [Figure 1] prior to presentation to the hospital.

Delay from the appearance of the first symptom to first contacting the healthcare system accounted for 82.2% of the total, endoscopy delay accounted for 7.1%, and the delay in the histological diagnosis accounted for 10.7%. Forty (83.3%) patients had a delay of more than one month from the appearance of the first symptom to contacting the healthcare system, 25 (52%) patients had more than a two-month delay, and seven (14.6%) patients more than four months. Only seven (14.6%) patients underwent primary esophagectomy and the majority of patients (41, 85.4%) received neoadjuvent therapy, chemoradiotherapy followed by surgery or palliation, as they presented with a more advanced stage of cancer [Table 2].

» Discussion

Esophageal cancer is a malignancy that is relatively common in Sri Lanka and we found that the median overall delay from the appearance of the first symptom to definitive treatment was 13 weeks. Nearly more than half (n = 25, 52.1%) of the patients had an overall delay of more than three months and 12.5% (n = 8) of the patients had a delay exceeding six months. Delay from the appearance of the first symptoms to first contacting the healthcare system (patient delay) accounted for 82.4% of the total, endoscopy delay and delay in histological diagnosis accounted for 7 and 10.7%, respectively.

The median overall delay in the diagnosis in esophageal cancer was 3.25 (3 - 37 weeks) months in which was nearly similar to the median overall delay (3 months) found by some of the previou Martin *et al*. [14] have found more than four months of median delay from the first sympto

diagnosis of the disease. Both studies were conducted in the UK. However, it is longer than that of the median overall delay (2.2 months) found by Wittzig *et al.*,[15] in Germany, and Wang *et al.*[16] in China. The reasons for these differences are many, some being, the difference in the healthcare systems and different referral patterns. As Sri Lanka is a developing country in South East Asia, in the state sector, we have limited facilities for diagnostic and staging investigations such as Upper GI endoscopy, CT, MRI, and endoscopic ultrasound. Even if available, the state health sector in Sri Lanka being a free health provider, there may be a considerable 'waiting list' for these investigations.

Many studies have indicated a negative relationship between delayed diagnosis and the stage of cancer for lung and colorectal cancer, but there seems to be a controversy regarding the final outcome between diagnostic delay and stage of the disease for esophageal carcinoma. Regarding esophageal carcinoma, some investigators have found that a shorter delay progressively decreases the degree of invasion and increases the survival rate, [17],[18] while others have proven that there is no relationship between delay and the stage of the tumor or mortality. [19],[20],[21] In addition, some have even indicated that shorter delay is associated with poor prognosis. [22] The reason for the contradiction of the studies is not clear. However, the results of the studies by Martin *et al*. and Wang *et al*.[14],[16] in China have suggested that a longer delay before final treatment of esophageal cancer increases the stage of the cancer and thereby worsens the patients' prognosis.

Most patients with esophageal cancer (74%) have dysphagia and some (17%) report odynophagia at the time of diagnosis. [23] Weight loss is also common (57%) and is an independent indicator of poor prognosis if there is a loss of more than 10% body mass. [24] However, in our setting, all the patients presented with dysphagia with or without other symptoms. In our study the majority of the patients (83.3%) had loss of weight when they presented for the endoscopic examination. In addition to the TNM stage, multivariate analyses suggest that a weight loss of more than 10% of body mass, dysphagia, and advanced age are independent predictors of a poor prognosis. [24],[25],[26],[27]

Although esophageal cancer is a common malignancy seen in Sri Lanka (incidence, male = 7.9, female = 9.4), [28] a considerable delay in the diagnosis of this disease still occurs. According to our results it shows that a delay in diagnosis is mainly due to a delay in seeking medical attention (82%). Due to this, the majority of our patients presented at an advanced stage of the disease, which resulted in neoadjuvant therapy prior to surgery or palliative treatment [Table 3] and [Table 4]. Another factor shown in our study is the notable delay in carrying out endoscopy and histology in 18% of the patients. At present Sri Lanka faces an acute shortage of qualified histopathologists in the state sector, and most of the district and provincial hospitals do not have qualified histopathologists. There is also a relative dearth of endoscopists. Therefore, the specimens have to be sent to a central unit in the capital, Colombo, for reporting, and this process may even take several weeks (if not months) to issue a report. In Sri Lanka, carcinoma esophagus is predominantly a disease of the lower socioeconomic strata, and due to financial constraints, 0 these patients are unable to go to the private sector for histopathology services.

The results of our study indicate that long delays in diagnosis and treatment of esophageal cancer still occur in Sri Lanka. This is mainly due to patient delay, although nonavailability of diagnostic facilities also appears to contribute in a notable way. Therefore, a community education program to increase the awareness regarding esophageal cancer may help in reducing patient delay. This will also potentially identify the high risk groups to be screened, and the disease can be identified at an early stage. Therefore a national patient education program with establishment of regional centers of excellence is recommended.

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Figures

[Figure 1]

Tables

[Table 1], [Table 2], [Table 3], [Table 4]

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