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### Correlation between duration of Dysphagia and Stage of Esophageal Cancer at the time of presentation - An observational study from a tertiary care centre of Eastern India

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#### Introduction

Upper gastrointestinal (UGI) cancers (of the oesophagus and stomach) characteristically present at a late stage in the world. This contributes to the poor overall 5-year survival rates of patients with UGI cancer, which are 13% for those with oesophageal cancer <sup>1</sup>. BB

The management of esophageal cancer remains clinically challenging, not only in terms of identifying patients at high risk, but also because of the overall poor prognosis of the disease. Most esophageal cancers are diagnosed after symptoms develop and tumors are locally advanced.<sup>2</sup>

In contrast, in countries like India, there is a higher incidence of esophageal squamous cell carcinoma (SCC) in comparison to developed countries. Currently, SCC is the most common type of esophageal cancer in the Indian subcontinent.<sup>[3]</sup>

The National Cancer Registry Programme (NCRP) instituted by the Indian Council of Medical Research (ICMR) has information on cancer incidence and mortality in the community covering 10% of the country's population. Although the coverage is still low, it gives a fair idea of the pattern of cancer incidence emerging in various regions or parts of the country. The Northeast registry tops the chart in relation to carcinoma of the esophagus, for both men and women.<sup>[4]</sup>

Population-based data suggest that esophageal cancer incidence peaks in the sixth decade in most parts of the world.<sup>[5]</sup>

Typical symptoms of esophageal carcinoma are dysphagia<sup>[6]</sup>, vomiting, loss of body weight, and gastrointestinal bleeding, Most esophageal cancers are diagnosed after symptoms like dysphagia develop and tumors are locally advanced.<sup>[7]. [8].</sup>

In the earliest stages, when it's easiest to treat, esophageal cancer has very few symptoms, so unfortunately it's rarely caught early. As esophageal cancer begins to progress and advance to the later stages, symptoms become more apparent, and the cancer becomes more difficult to treat.<sup>[9]</sup>

Survival rates depend on several factors, including the stage of the cancer when it is first diagnosed. As the stage advances, the overall survival decreases. The 5-year survival rate of people with cancer located only in the esophagus is 43%. The 5-year survival rate for those with disease that has spread to surrounding tissues or organs and/or the regional lymph nodes is 23%. If it has spread to distant parts of the body, the survival rate is 5%.<sup>[10]</sup>

In this study we assessed the average duration of dysphagia at the time of presentation and the stage at the time of presentation at Medical College & Hospital, Kolkata, to state the necessity of earliest investigative work up to detect esophageal cancer at early stage to improve treatment outcome and overall survival in this cancer.

### Background

In the esophagus, two different kinds of primary neoplasias may arise: squamous cell carcinomas (SCC) and adenocarcinomas (AC). While the development of SCC is associated with tobacco and alcohol abuse, n-nitrosamines, alkali burn, and achalasia, the major risk factors for EAC are reflux disease and body mass index (BMI). Although SCC is in general more common than EAC, the incidence of EAC is rising very fast in Western countries <sup>[11,12,13,14].</sup>

In 2012, there was an estimated 455800 new cases of esophageal carcinoma and 400200 deaths worldwide<sup>[15]</sup>.Esophageal carcinoma is the eighth most common cancer and sixth leading cause of cancer related deaths<sup>[7].</sup> While other types of cancer are expected to decrease in incidence over the next 10 years, the prevalence of esophageal cancer is expected to increase by 140% by the year 2025<sup>[16]</sup>. The predominant esophageal cancer in North America and Europe is esophageal adenocarcinoma (EA), while esophageal squamous-cell carcinoma (ESCC) is the predominant type in Asia, Africa, and South America<sup>[17]</sup>.

In developing countries like India, there is a higher incidence of esophageal squamous cell

carcinoma (SCC). Currently, SCC is the most common type of esophageal cancer in the Indian subcontinent and the most common location is the distal third of the esophagus.<sup>[3]</sup> Approximately, 47,000 new cases are reported each year and the reported deaths reach up to 42,000 each year in India.<sup>[18]</sup> <sup>EE</sup> Data shows the projected increase in number of cancers in India for selected sites between 2015 and 2020 for both sexes.<sup>[4]</sup>

Population-based data suggest that esophageal cancer incidence peaks in the sixth decade in most parts of the world.<sup>[5]</sup>

The same trend has been reported in India, with the mean age in women slightly earlier than in men. SCCs are twice as common in men compared to women.

More recent data from Christian Medical College Hospital, Vellore comprising of the 138 patients who underwent resectional surgery for esophageal cancer over the 7-year time period from 2010 to 2016, revealed the following. SCC was the most common histology (105 patients), as compared to AC (33 patients). The mean age was 52 years, mean body mass index was 21.5, and the male: female ratio was about 3:1. Most common geographical region in this cohort was the East and Northeast India (92 patients), followed by the South (36 patients) and the North (10 patients)<sup>[3]</sup>.

Malignancies of the esophagus are diagnosed by upper Gastrointestinal endoscopy with mucosal biopsies. The sensitivity for mucosal biopsies to detect esophageal carcinoma reaches 96% when multiple samples are obtained<sup>.[19,20,21].</sup>

Esophageal Cancer usually diagnosed when there is symptoms like dysphagia, vomiting, upper G.I. bleeding, haemoptysis, anaemia, weight loss. Most esophageal cancers are diagnosed after symptoms like long term unresolved dysphagia noticed and tumors are locally advanced. Therefore, only one out of eight esophageal cancers is identified at an early stage (T1)<sup>[22].</sup>

Accurate staging information is crucial to establishing appropriate treatment choices for esophageal cancer, whether it is determining the depth of tumor to determine the feasibility of

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endoscopic management or to establish tumor margins and/or lymph node involvement before possible surgical resection or chemoradiation. Complete staging of esophageal cancer has traditionally involved in EUS and FNA conjunction with cross-sectional imaging. Overall, fluorodeoxy glucose positron emission tomography/CT appears to have better accuracy than EUS or CT to detect response to neoadjuvant chemoradiation.<sup>[23]</sup>

In the earliest stages, when it's easiest to treat, esophageal cancer has very few symptoms, so unfortunately it's rarely caught early. As esophageal cancer begins to progress and advance to the later stages, symptoms become more apparent, and the cancer becomes more difficult to treat. At stage-I & II, the gold standard of therapy of Esophageal cancer is Surgery, more the advanced stage, the cancer becomes inoperable. Moreover, squamous cell cancer is more sensitive to chemotherapy and radiation therapy treatment than adenocarcinoma.[24]

Esophageal cancer staging is defined by the American Joint Committee on Cancer (AJCC) Staging System that establishes tumor-nodemetastasis (TNM) based staging system and is classified into four stages, I through IV. In Stage I of esophageal cancer, the five-year survival rate is 34 percent and usu all the patient is asymptmatic. By the Stage II, the five-year rate of survival is 17 percent, when most frequently patients seek medical help for the first time with the complaint of dysphagia. In stage III, patients present with prominent dysphagia of Grade II to IV. Twenty to 30 percent of patients in stage III who receive treatment, are likely to survive between three and years. In stage IV, five the cancer has metastasized, the five-year rate of survival drops to 2.8  $percent^{[25]}$ 

### Material & Method

The study was done from the hospital record of Esophageal Cancer patients reported from January 2016 to April 2018 at Medical College Hospital, Kolkata. Total 48 patients were taken for the analysis of data. The tabulation of data done in Microsoft Office Excel 2007 noting the age, sex, duration of dysphagia and the stage and analysis was done in SPSS version 20.

The inclusion criteria were as follows:-

1. Age-more than/equal to 18 years

2. Patients given consent to be a part of this study

3. Patients who submitted all medical reports during first visit

4. Patients who could recall the onset of dysphagia with certainty and relatives also supported the data Patients who were very ill at the time of admission were excluded from the study.

The dysphagia grade followed by the Inter-rated Agreement for Clinical Dysphagia scale.<sup>[26]</sup>

The staging system was followed as per the TNM staging of AJCC, 2010.<sup>[27]</sup>

The staging was based upon the UGI endoscopy report, Contrast Enhanced CT scan report and biopsy report along with PET CT scan report whenever the PET CT Scan report was available.

The statistical analysis was done by using Chi square test.

### Result

The Microsoft word excel sheet was used for tabulation of result .The result was as follows:

The total 87.5 % of patients were found Squamous cell CA histology which is both Chemotherapy and Radiotherapy sensitive.

## Esophageal CA according to histology Table1

| Histology               | Percent |
|-------------------------|---------|
| Squamous Cell Carcinoma | 87.50   |
| Adenocarcinoma          | 12.50   |
| Total                   | 100.00  |



### **Stages of Esophageal CA**

The most common stage of the Esophageal CA during first presentation at our Department were found of Stage II(28/48). The subsequent numbers of Stage II & IV were 8/48 & 4/48 respectively. **Table 2** 

| Stage   | Percent | Frequency |
|---------|---------|-----------|
| Stage 2 | 70.00   | 28        |
| Stage 3 | 20.00   | 8         |
| Stage 4 | 10.00   | 4         |
| Total   | 100.00  | 40        |



Pie chart of distribution of stage of Esophageal CA

# Duration of dysphagia and age mean, SD and range

Duration of dysphagia varied from 1month to 24 months as per the patients' version and cross examination by questionnaire. The most frequent duration of dysphagia was 2months.And one person recalled dysphagia of 24 months. But most of the patients stated dysphagia of 1 to 3 months during presentation at our Institute.

### Table 3

| Variables      | Duration of Dysphagia | Age   |
|----------------|-----------------------|-------|
| Mean           | 3.35                  | 56.28 |
| Std. Deviation | 3.7007                | 9.637 |
| Minimum        | 1                     | 26    |
| Maximum        | 24                    | 84    |



# Association between stage of esophageal Ca and duration of dysphagia

While analysing the data of duration of dysphagia and the stage of the disease at presentation at Medical College & Hospital, Kolkata, it was clearly seen that the locally advanced & advanced stages of esophageal Ca is 1.53 times (Range-.30-7.79) commonly present with more duration of dysphagia rather than early stages, though the results are not statistically significant as chi square value is .007 and p=0.45

#### Table 4

| Association between stage of esophageal Ca and duration of dysphagia (in months) n=40 |       |           |          |       |  |  |  |
|---|-------|-----------|----------|-------|--|--|--|
|   |       | Dysphagia |          |       |  |  |  |
|   |       | More      | Less     |       |  |  |  |
|   |       | duration  | duration | Total |  |  |  |
| Advanced & Locally<br>advanced stage(Stage-<br>III & IV)                              | Count | 3         | 9        | 12    |  |  |  |
| Early stage<br>(Stage-II)   | Count | 5         | 23       | 28    |  |  |  |
|   | Total | 8         | 32       | 40    |  |  |  |

Component bar diagram showing association between stage of esophageal Ca and duration of dysphagia (in months) n=40



### Discussion

Esophageal cancer is most often detected when the patient becomes symptomatic. Most common presentation is dysphagia. The stage of presentation of Esophageal CA is usually late. But our institutional data shows majority of cases presented at Stage –II, which may be the health consciousness and availability of medical service & diagnostic facilities. But the interesting change of presentation of less duration of dysphagia and lower stage of presentation, squamous cell CA histology is a trend towards better outcome of treatment in Esophageal cancer patients.

### Conclusion

Oesophageal cancer may be diagnosed at lower stage if investigative workup is done at an at the onset of symptom like dysphagia. More common histopathological type ie. Squamous cell cancer is good responder of Chemotherapy and Radiotherapy which may be utilized in inoperable cases to improve treatment outcome and overall survival of Esophageal cancer. More studies are required increasing number of cases of the study group to establish the observed result of proportional correlation between duration of dysphagia and stage of the disease in future which may be applicable while deciding the protocol of diagnostic workup for esophageal cancer targeting to find the disease at early stage.

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