

## Brain Metastases from Esophageal Cancer: A Rare Entity – An Analysis of the Incidence Reported in Literature 1982-2010

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efforts are necessary to confirm the incidence and to demonstrate statistical interaction between the development of brain metastases and factors such as gender, staging, histology, treatment modality, etc. This information will be helpful for staging and planning treatment for esophageal cancer.

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**Key words:** Esophageal cancer; Brain metastases; Incidence analysis

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### ABSTRACT

**AIM:** To analyze the incidence of brain metastases in esophageal cancer based on published literature from 1982-2014.

**METHODS:** A literature search on PUBMED with key words “esophageal cancer” and “brain metastases” was performed. A total of 138 manuscripts matching the keywords were found. Eleven papers met the study requirements and were included.

**RESULTS:** A total of 11 studies were identified that retrospectively analyzed the incidence of brain metastases in esophageal cancer. Out of those 11, seven were conducted in the United States, three in Japan, and one in China. These studies looked at patients from 1982-2010. A total of 6,216 patients with esophageal cancer were identified and retrospectively analyzed in their respective study groups for the development of brain metastases. A total of 174 patients of the 6216 developed brain metastases; with an incidence of 2.8%. In the U.S population, 121 patients were affected, amounting to an incidence of 3.1%. The predominant histo-pathological cancers in all 11 studies were, as expected, either adenocarcinoma or squamous-cell carcinoma (SCC).

**CONCLUSION:** The incidence of brain metastases from esophageal cancer is low, ranging from 2.8% to 3%. Formal and large-scale

### AIMS AND OBJECTIVES

To analyze the incidence of brain metastases in esophageal cancer based on the retrospective analysis done from 1982-2010.

To analyze whether routine screening of brain metastases with head imaging would be beneficial in esophageal cancer.

### MATERIALS AND METHODS

#### Literature search

The authors separately performed a search on PUBMED with key words “esophageal cancer” and “brain metastases.” A total of 138 results were found. After careful review, only 32 results, including case reports, were selected. Of the 32, only 14 were retrospective analyses describing brain metastases in esophageal cancer. Eleven studies did a retrospective analysis at their institutions on incidence of brain metastases. Two studies described treatment with radiation and one was a clinical trial, which was then eliminated from our analysis. Finally, 11 studies were analyzed for incidence of brain metastases. Out of 11 studies, seven were conducted in the United States, three in

Japan, and one in China. These studies took place from 1982 through 2010.

**Data Analysis and Statistical Methods**

Total number of patients with esophageal cancer was calculated by addition of all the patients in the 11 selected studies. The development of brain metastases was followed in each study and all the patients that developed it were added together. A total of 6,216 patients with esophageal cancer from 1982-2010 were identified and 174 patients were found to develop brain metastases, amounting to an incidence of 2.8%. When we looked at the studies done in the United States alone, the incidence was found to be 3.1%. The majority of the patients in the United States had adenocarcinoma of the esophagus, unlike the studies in China and Japan, which had squamous-cell cancer of the esophagus as the primary cancer associated with brain metastases. Median survival was reported in six studies that ranged from 2.1 months to 17.7 months.

**RESULTS**

The results of the literature search have been presented in table 1. A total of 11 studies were identified that retrospectively analyzed incidence of brain metastases in esophageal cancer. The data has been presented with the name of the study, country, and institution where it was performed, the total number of retrospective years that were analyzed to find patients with esophageal cancer, number of patients in each study, number of patients that developed brain metastases in each study, and the histo-pathological type of esophageal cancer that was associated with brain metastases. The predominant histo-pathological cancers were either adenocarcinoma or squamous-cell carcinoma (SCC). A total of 6216 patients with esophageal cancer were identified and retrospectively analyzed in their respective study groups to develop brain metastases. A total of 174 patients of the 6216 developed brain metastases; with calculated incidence being 2.8%.

As most of the esophageal adenocarcinomas were associated with brain metastases in the United States, we decided to get an incidence in the United States alone. The total number of cases that were looked at was  $n=3876$ . The number of patients who developed brain metastases in the United States was 121 and with the incidence of brain metastases being 3.1%.

Median survival was reported in six studies in which a total of 125 patients developed brain metastases. The average median survival of these 125 patients was found to be three months.

**DISCUSSION**

Brain metastases from esophageal cancer have been seldom reported in the form of retrospective analysis or case reports. We found that there was a discrepancy among the various published studies; therefore, we decided to perform analyses of the various retrospective studies done in the past. In our multi-study analyses, we found the overall incidence of brain metastases in the published literature to be 2.8%. Routine screening for brain metastases in esophageal cancer, similar to patients with lung and breast cancers, has been a matter of debate. Multiple retrospective analyses done in the past have suggested that routine screening or surveillance is not necessary since the incidence of brain metastases has been low<sup>[1-3]</sup>. We report that the incidence of brain metastases to be approximately 3%. The prognosis after detection is very poor. Trimodality therapy with cisplatin, fluorouracil, and radiotherapy has shown to improve survival in patients with esophageal cancer<sup>[1,4]</sup>. Tepper *et al* report that the five-year survival of trimodality therapy was 39% compared to surgery (16%) alone<sup>[4]</sup>. The question has always been whether patients diagnosed with esophageal cancer be screened for cerebral metastases. Smith *et al* report a higher incidence in their paper than what has been previously reported<sup>[5]</sup>. When the incidences in all of the data is pooled together, we think the incidence of brain metastases from esophageal cancer is low and routine screening may not be needed, as has been previously advised<sup>[1,2]</sup>.

**Table 1** Results of literature search.

Study name	Country-Institution name	Years through which data collected	Number of patients with esophageal cancer retrospectively analyzed	Number of patients with brain metastases (BrM)	Type of esophageal cancer	Median Survival reported after diagnosis of BrM.
1. Wadhwa <i>et al</i> <sup>[1]</sup>	USA-MD Anderson Cancer Center	2000-2010	518	20 (3.9%)	All patients in the study had adenocarcinoma	10.5 months
2. Song <i>et al</i> <sup>[7]</sup>	China-Zhejiang Cancer Hospital	2000-2010	1,612	26 (1.61%)	22 patients with BrM had squamous-cell cancer (SCC) and 4 patients had adenocarcinoma	4.2 months
3. Hejleh <i>et al</i> <sup>[8]</sup>	USA-University of Iowa	2000-2010	142	9 (6.33%)		
4. Smith <i>et al</i> <sup>[5]</sup>	USA-Andreas Cancer Center, MN	1998-2007	53	7 (13%)	All patients with BrM had adenocarcinoma	
5. Kanemoto <i>et al</i> <sup>[9]</sup>	Japan-Shizuoka Cancer Center	2002-2008	391	12 (3.1%)	10 patients had SCC and 2 patients had others	2.1 months
6. Kawabata <i>et al</i> <sup>[10]</sup>	Japan-Osaka Medical Center	1984-2002	254	11 (4.3%)		17.7 months
7. Rice <i>et al</i> <sup>[11]</sup>	USA-Cleveland Clinic	1985-2002	403	29 (7.1%)		3.5 months
8. Weinberg <i>et al</i> <sup>[12]</sup>	USA-MD Anderson Cancer Center	1993-2001	1,588	27 (1.7%)	22 patients had adenocarcinoma, 3 patients had unclassified carcinoma, and 2 patients had SCC	3.8 months
9. Gabrielsen <i>et al</i> <sup>[2]</sup>	USA-University of Michigan	1984-1993	334	12 (3.6%)	10 patients had adenocarcinoma and 2 had SCC	
10. Quint <i>et al</i> <sup>[13]</sup>	USA-University of Michigan	1982-1993	838	17 (2%)		
11. Kaneko <i>et al</i> <sup>[14]</sup>	Japan	1991	83	4 (4.81%)		
<b>TOTAL</b>			<b>6,216</b>	<b>174 (2.8%)</b>		

Khunti *et al* report in their paper that patients who have brain metastases should be treated with aggressive therapy, such as stereotactic brain surgery, whole brain radiation, and surgery<sup>[3]</sup>. They report improvement of survival in these patients compared to patients with whole brain radiation therapy alone<sup>[3]</sup>. Da Silva *et al* report that gamma knife surgery may improve survival in patients with BrM of gastrointestinal origin. They demonstrated an increased median survival of about 6.7 months<sup>[6]</sup>.

The prognosis of metastatic esophageal cancer to the brain is very poor and patients who have such aggressive presentation should be treated with aggressive therapies. Patients with such disease should definitely be enrolled in clinical trials like in the trimodality therapy<sup>[1,4]</sup>.

## CONCLUSION

The incidence of brain metastases from esophageal cancer is approximately 3%. We concur with the previous recommendations, to not routinely screen these patients for metastatic disease to the brain.

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