ORIGINAL RESEARCH

International Journal of Surgery 12 (2014) 621–625

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

# Complete pathological response after neoadjuvant treatment in locally advanced esophageal cancer predicts long term survival: A retrospective cohort study☆

Farrukh Hassan Rizvi*, Aamir Ali Syed, Shahid Khattak, Syed Shahrukh Hassan Rizvi, Syed Ather Kazmi, Muhammad Qayum Khan

*Department of Surgical Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, 164-J3 Wapda Town Phase 1, Lahore, Pakistan*

ARTICLE INFO

*Article history:*
Received 12 April 2014
Received in revised form
16 April 2014
Accepted 30 April 2014
Available online 5 May 2014

*Keywords:*
Esophageal cancer
Complete pathological response
Neoadjuvant treatment

ABSTRACT

*Background and objectives:* Esophageal cancer incidence is gradually increasing worldwide. Studies have looked at the pathological stage rather than clinical stage as predictor of survival. We looked at patients with complete pathological response to compare their survival outcomes to those who had residual disease after neoadjuvant treatment.
*Materials and methods:* All patients with esophageal cancer who underwent neoadjuvant treatment followed by resection at our institute were retrospectively reviewed. Overall survival and disease free survival were calculated for patients with complete pathological response and compared to those with residual disease using log rank test.
*Results:* Mean age of our patients was 51.08 years with standard deviation of 10.17 years. 39% belong to stage IIa while 5% belong to Stage IIb. 56% were Stage III. Final histopathological stage was recorded and both disease free and overall survival were calculated. 45% of our patients had complete pathological response. Patients with complete pathological response had mean survival of 62.73 months ± 17.02 compared to 41.42 months for patients who had residual disease. 5 year disease free survival was 58%.
*Conclusion:* Complete Pathological response significantly improves overall and disease free survival. It is also the predictor of long term survival.


## 1. Introduction

Esophageal cancer incidence is gradually increasing worldwide [1]. It is an aggressive disease with 5 year survivals of less than 25% for all stages [2]. There is great interest in neoadjuvant treatment for esophageal cancer, but there is no clear survival advantage and majority of studies have been criticized for flawed designs [3,4]. With the availability of endoscopic ultrasound, better CAT scanners and PET/CT; there is improvement in reliability of clinical staging but still there is difference between clinical and pathological stage of disease making it difficult to predict survival on the basis of clinical stage. Studies have looked at the pathological stage rather than clinical stage as predictor of survival. However only 20–30% patients who show complete pathological response indicate better long term and disease free survival [5–8].

So far there are no tools to tell us with surety that there is no residual disease after chemoradiotherapy. So patients require esophagectomy as part of standard treatment. Randomized control trials with long term follow up are lacking for patients who do show response and do not undergo esophagectomy [6,9].

We are the only tertiary care cancer hospital in Pakistan. We generally encounter esophageal cancer at locally advanced stage and offer neoadjuvant treatment. We looked at our data to assess the response of patients to neoadjuvant treatment and specifically looked at patients with complete pathological response to compare their survival outcomes to those who had residual disease.

## 2. Objective

To determine if complete pathological response in locally advanced esophageal cancer, predicts long term survival after neoadjuvant treatment.

☆ There are no financial or other affiliations of any author.

* Corresponding author.
*E-mail addresses:* farrukhrizwi@gmail.com, farrukhrizwi@live.com (F.H. Rizvi).

http://dx.doi.org/10.1016/j.ijsu.2014.04.014
1743-9191/

## 3. Materials and methods

All patients with esophageal cancer who underwent neoadjuvant treatment followed by resection at our institute from January 2005 to December 2011 were retrospectively reviewed. Patients were staged according to AJCC staging system using EUS and CAT scan as primary staging modalities. All patients were discussed in multidisciplinary team meeting and treatment plan was decided. Patients assigned for neoadjuvant treatment followed by surgery were selected for review. Patients with irresectable disease and planned for palliative treatment were excluded. A total of 109 patients were identified, out of which 4 required emergency surgery while 5 had missing data for analysis. We were left with 100 patients who completed neoadjuvant treatment and were therefore selected for final analysis (see Table 1).

Patient medical records were analyzed, and information was collected into an esophageal database. Variables recorded include epidemiological factors (age, comorbidities and symptoms) treatment factors (type of chemotherapy and dose of radiation), tumor factors (histology, clinical stage, pathologic stage, and completeness of resection—R0, R1, or R2), operative and hospital course factors (operation performed, duration of procedure, blood loss, type of anastomosis, and complications), and tumor recurrence and long-term survival.

Patients received external beam radiation between 45 and 55 Gy with concurrent cisplatin and 5FU. Patients were restaged with CAT scan after 4 weeks of completing neoadjuvant treatment and were then planned for surgery depending on the resectability status. Patients with metastasis or T4b disease were not offered surgery.

**Table 1**
Patient and tumor characteristics.

| | $N = 100$ | $N$ % |
|---|---|---|
| Age | 51.08 ± 10.17 | |
| Gender | | |
| Male | 52/100 | 52% |
| Female | 48/100 | 48% |
| Comorbidity | 18/100 | 18% |
| Site | | |
| Mid thoracic | 26/100 | 26% |
| Lower thoracic | 67/100 | 67% |
| GE junction | 7/100 | 7% |
| Histology | | |
| Squamous cell ca | 76/100 | 76% |
| Adenocarcinoma | 24/100 | 24% |
| Grade | | |
| Well differentiated | 15/100 | 15% |
| Moderately differentiated | 57/100 | 57% |
| Poorly differentiated | 28/100 | 28% |
| Clinical T stage | | |
| T1 | 0/100 | 0% |
| T2 | 8/100 | 8% |
| T3 | 76/100 | 76% |
| T4a | 16/100 | 16% |
| Clinical N stage | | |
| N0 | 43/100 | 43% |
| N1 | 57/100 | 57% |
| Clinical stage | | |
| I | 0/100 | 0% |
| IIA | 39/100 | 39% |
| IIB | 05/100 | 5% |
| III | 56/100 | 56% |
| IV | | |
| Pathological stage | | |
| Complete response | 45/100 | 45% |
| I | 03/100 | 3% |
| IIa | 25/100 | 25% |
| IIb | 18/100 | 18% |
| III | 09/100 | 9% |
| IV | 0/100 | 0% |

**Table 2**
Surgical intervention and treatment response.

| | $N$ | $N$ % |
|---|---|---|
| Surgical procedure | | |
| Transhiatal | 58/100 | 58% |
| Minimally invasive | 33/100 | 33% |
| Open three stage | 9/100 | 09% |
| Type of neoadjuvant | | |
| Chemoradiotherapy | 95/100 | 95% |
| Chemotherapy | 05/100 | 05% |
| Treatment response | | |
| No change | 14/100 | 14% |
| Decrease in disease stage | 33/100 | 33% |
| Progression of disease | 08/100 | 08% |
| Pathological complete response | 45/100 | 45% |
| Margin status | | |
| R0 | 97/100 | 97% |
| R1 | 03/100 | 03% |

Patients were followed quarterly for first 2 years and then semi-annually for 1 year and yearly thereafter till completion of 5 years. Patients required CAT scan every year to look for any radiological evidence of recurrence. Frequencies and percentages were calculated for categorical data while means with standard deviation were calculated for continuous variables. Chi square, Fischer's exact test and $t$ test were applied and $p$ value of less than 0.05 was considered statistically significant. Overall survival was calculated from the time of diagnosis till death while disease free survival was calculated from the time of surgery till documented recurrence (either radiological or histopathology proven) using Kaplan Meir survival curves. Patients with complete pathological response on histopathology specimen were compared to those having residual disease both for overall and disease free survival and log rank test applied to evaluate significance. All data was analyzed in SPSS version 19 (see Table 2).

## 4. Results

Mean age of our patients was 51.08 years with standard deviation of 10.17 years. Gender distribution was comparable. Preoperative staging of patients were performed using EUS and CAT scan of chest and abdomen. 39% belong to stage IIa while 5% belong to Stage IIb. 56% were Stage III. Major histopathological diagnosis was squamous cell carcinoma. All patients received neoadjuvant treatment, 95% received chemoradiotherapy while 5% received chemotherapy alone. Patients receiving chemotherapy alone were those having GEJ tumors. 85% of our patients received cisplatin and 5FU along with 45 Gy of radiotherapy. Patients were restaged 4 weeks post completion of neoadjuvant treatment to assess response. Patients then underwent surgical intervention, if resectable on post treatment scan. 58% of our patients underwent transhiatal esophagectomy while 34% underwent minimally invasive esophagectomy, rest had open three stage procedure. All patients had cervical anastomosis and gastric tube placed in posterior mediastinum. Anastomosis was made hand sewn, single layer using prolene 4/0. Final histopathological stage was recorded and both disease free and overall survival were calculated. 45% of our patients had complete pathological response. Overall mean survival for all stages was 51.86 months ± 9.87 months (median is 44 months), with 5 year survival of 38%. When analyzed according to histopathological response, patients with complete pathological response had mean survival of 62.73 months ± 17.02 (median is 68 months) compared to mean survival of 41.42 months (median is 29 months) for patients who had residual disease. Log rank test showed $p$ value of 0.007. There were 26 recurrences of which 5 were local, 14 were in regional nodes and 7 were distant. Overall