

## Case Series

Open Access, Volume 2

# Clinical complete response in esophageal adenocarcinoma, who do not undergo surgery

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Received: Mar 26, 2022

Accepted: Apr 22, 2022

Published: Apr 27, 2022

Archived: www.jjgastro.com

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**Keywords:** Adenocarcinoma; Esophageal cancer; Regrowth; Clinical complete response; Surgery.

## Introduction

Esophagectomy is currently the cornerstone of treatment for esophageal cancer [1-3]. Neoadjuvant therapy consisting of chemoradiotherapy, followed by surgery, [4] allows complete resections (R0) in up to 92% of patients ( $P < 0.001$ ); a median overall survival of up to 49.4 months ( $P = 0.003$ ) [5]. Currently, there are no standard protocols to assess the clinical complete response in patients with esophageal cancer after receiving chemoradiotherapy [6]. Furthermore, few articles describe the results of neoadjuvant chemoradiotherapy followed by active surveillance [7,8].

## Abstract

Few articles describe the results of neoadjuvant chemoradiotherapy, followed by active surveillance, raising the dilemma of whether all patients benefit from esophagectomy, since metastases will largely determine survival in these patients.

**Objective:** To describe the median overall survival and regrowth in patients with esophageal adenocarcinoma who present a clinical complete response after chemoradiotherapy who do not undergo surgery.

**Material and methods:** A descriptive and retrospective case series. All patients with a diagnosis of esophageal adenocarcinoma, treated with chemoradiotherapy, who did not undergo surgery, with a clinical complete response documented by imaging (contrast tomography, endoscopic ultrasound) and biopsy were identified. Results are presented using measures of central tendency. In the same way, the treatment schemes used (chemotherapy and radiotherapy) are described.

**Results:** Between 2010 and 2020, 3 cases were identified and included, 2 men (66%) and 1 woman (33%), median age of 71 years. 66% were in the middle third and 33% in the lower third. After treatment with chemoradiotherapy, all patients included refused the procedure. Median follow-up was 31 months (range 13 to 50 months). No regrowth was documented in any of the patients. Median overall survival was 31 months.

**Conclusion:** All patients remained alive and without regrowth. The small number of patients included in this study prompts us to do more research on this topic.

A 39% incidence of metastases has been reported during follow-up, after being treated with chemoradiotherapy followed by surgery. Thus, esophagectomy could be postponed or even avoided in patients with a complete response after neoadjuvant chemoradiotherapy, but also in patients who develop metastases during surveillance, since distant metastases will largely determine survival in these patients [5]. Our objective is to describe the median overall survival and regrowth in patients with esophageal adenocarcinoma, who present a clinical complete response after chemoradiotherapy who do not undergo surgery.

**Citation:** Gamboa-Hoil SI. Clinical complete response in esophageal adenocarcinoma, who do not undergo surgery. Japanese J Gastroenterol Res. 2022; 2(6): 1076.

## Materials and methods

A descriptive and retrospective case series. All patients at the Unidad Médica de Alta Especialidad, Yucatán, Mexico, between 2010 and 2020, with a diagnosis of esophageal adenocarcinoma, treated with chemoradiotherapy, who did not undergo surgery, with a clinical complete response documented by imaging (contrast tomography, endoscopic ultrasound) and biopsy were identified. We define clinical complete response as the absence of a tumor on the contrasted tomography, endoscopic ultrasound and biopsy. Patients decided on their own free will and without coercion the non-surgical treatment, after a detailed explanation of the standard treatment and all doubts were resolved. This paper complies with current regulations on bioethics research and the authorization of the institution's ethics committee (Ethics committee in health research 32038).

Based on the Declaration of Helsinki and the General Health Law in Research Matters, this study falls into the risk-free category; the information was kept confidentially.

## Results

We identified and included 3 cases, 2 men (66%) and 1 woman (33%), with a median age of 71 years. 66% in the middle third, and 33% in the lower third. All patients received chemoradiotherapy, 66% had positive lymph nodes at diagnosis, none of them had distant metastases. 1 patient (33%) had a history of comorbidities (diabetes mellitus and high blood pressure). Median follow-up was 31 months (range 13 to 50 months). Treatment schedules with chemotherapy and radiotherapy are shown in table 1. No regrowth was documented in any of the patients. Median overall survival was 31 months.

**Table 1:** Characteristics of the population with clinical complete response.

Gender	Age	Comorbidity	Location	Histology	Differentiation	T N M	Clinical response	Concomitance	Regrowth	Follow up
Male	84	Diabetes mellitus / high blood pressure	Distal	Adenocarcinoma	Moderate	T2 N0 M0	Complete	5 cycles of carboplatin / paclitaxel 45 Gys	No	Alive 50 months
Male	72	No	Middle	Adenocarcinoma	Moderate	T3 N+ M0	Complete	5 cycles of carboplatin / paclitaxel 45 Gys	No	Alive 13 months
Fem	57	No	Middle	Adenocarcinoma	Poorly	T3 N+ M0	Complete	5 cycles of carboplatin / paclitaxel 59.4 Gys	No	Alive 20 months

## Discussion

Currently, the standard treatment for esophageal cancer is chemoradiotherapy followed by surgery; however, it is important to emphasize metastases determine survival in these patients and clinical complete response has prevented loss of function in other oncologic conditions. In our study to measure the clinical complete response after treatment with chemotherapy and radiotherapy, we performed a contrasted tomography, endoscopic ultrasound and biopsy; according to Kim et al, endoscopic biopsy has a sensitivity to detect residual disease of 30.4% and specificity of 100% [6].

Taketa et al, reported 83% adenocarcinoma histology. In his experience, Taketa used induction chemoradiation consisting of fluoropyrimidine in 33% of cases plus platinum or taxane with a total radiation dose of 50.4 Gy. A mean follow-up of 51 months, Taketa, reported 72% recurrence of the disease; with a mean relapse-free survival of 18 months. 42% of the patients had locoregional recurrence, with median time to salvage surgery of 10.3 months; while 31% had distant recurrence. Overall survival was 57.9 months [7]. Our study differs from the previous one because 100% had adenocarcinoma histology, although with a very small number of patients, which could represent a difference in terms of regrowth and survival, in addition to a shorter follow-up in our study. Castoro et al, included patients with squamous cell histology, describing 63% with a location in the upper third of the thoracic esophagus. Chemotherapy regimen used consisted of 5-fluorouracil and platinum, as well as taxanes; total radiation therapy dose was 45–50 Gy. A mean follow-up of 33.7 months, he observed a recurrence of 58% ( $p=0.25$ ) and an overall survival of 57% ( $p=0.99$ ); Castoro, described

advanced lung disease as an independent factor for overall survival ( $HR=4.21$  (95 % CI:1.85–9.56);  $p<0.001$ ). Piessen et al, included 13.6% of the patients with adenocarcinoma cell histology; administration of fluorouracil plus cisplatin in combination with 50 Gys (range: 30–66) of concomitant radiation therapy, Piessen, reported a 5-year overall survival of 33.4% ( $P = 0.001$ ) and observed a recurrence of 50.8% ( $p = 0.021$ ), with a median recurrence at 7 months ( $P = 0.002$ ) [8,9]. Unlike these studies, we included 100% of our cases with adenocarcinoma histology, which made it impossible to compare the data. However, until the closure of our study, the overall survival of our patients with adenocarcinoma histology was 31%, without regrowth.

According to Wang J et al, in their meta-analysis included patients with clinical complete response after neoadjuvant chemoradiotherapy, they found that the addition of surgery to chemoradiotherapy does not provide any advantage for long-term survival [10]. That opens the question to new studies on the topic. It is noteworthy that in the literature there are few articles that describe the behavior of esophageal cancer with an emphasis on the histology of adenocarcinoma, as observed in the present paper.

## Conclusion

All patients remained alive and without regrowth. The small number of patients included in this study prompts us to do more research on this topic.

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