



Original Research

Potentially curable gastric adenocarcinoma treated without surgery



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Abstract Background: Surgery is the best option for cure of localised gastric adenocarcinoma (GAC). When surgery is not possible due to comorbidities or patient choice, definitive chemoradiation is an option. We report on one of the largest cohorts of localised GAC patients who did not have surgery.

Methods: We identified 71 patients with localised GAC who received chemo/chemoradiation therapy but did not have surgery. We assessed various end-points: overall survival (OS), relapse-free survival (RFS), and clinical complete response (cCR; negative post therapy biopsy and no evidence of cancer by imaging).

Results: The median follow-up time was 1.8 years (range; 0.4–10.6). Most of the patients were men (64.8%), and the median age was 73 years (range; 30–96). Reason for not having surgery included comorbidities in 34 (47.9%), poor performance status 14 (19.7%), and patient refusal 23 (32.4%). Of all 71 patients, a complete restaging evaluation with endoscopy and imaging

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could be performed for 50, and 32 (45.1%) achieved a cCR. For the entire cohort, the median OS was 2.1 years (95% confidence interval [CI] 1.78–2.55). The estimated OS rates at 2 and 5 years were 54% and 18%, respectively. Female gender (HR 0.39, 95% CI 0.16–0.98, $p = 0.045$) and chemoradiation (HR 0.25, 95% CI 0.06–1.01; $p = 0.05$) were independently associated with longer OS in the multivariate analysis.

Conclusion: Our data show that patients with localised GAC treated with chemotherapy and/or chemoradiation, who do not undergo surgery, have a 5-year OS rate of 18%.

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1. Introduction

Gastric adenocarcinoma (GAC) is a global health problem with an estimated 951,600 new cases and 723,100 deaths occurred in 2012 [1]. GAC is often diagnosed at an advanced stage when surgery is not a therapeutic option [2]. Although incurable at advanced stage, systemic chemotherapy can palliate symptoms, improve survival, and provide an improved quality of life. In 1969, Moertel *et al.* demonstrated that combined chemoradiation therapy may improve survival of locally unresectable GAC [3]. However, our patient population had potentially resectable cancer. We recently reported that combined chemoradiation therapy may improve survival in selected GAC patients with M1 disease [4].

A margin negative (R0) gastric resection with extended lymph node dissection is the most effective curative strategy for resectable GAC [2]. Adjunctive therapies as post-operative chemoradiation [5], adjuvant chemotherapy [6,7] or peri-operative chemotherapy [8,9] can increase 5-year overall survival rates approximately 10%. One of the most promising adjunctive therapeutic approaches is preoperative chemoradiation. Both ongoing phase III ‘Preoperative Therapy for Gastric and Esophagogastric Junction Adenocarcinoma’ (TOPGEAR) trial (NCT01924819) and CRITICS-II (NCT02931890) trial results are not available to determine the optimal adjunctive approach for resectable GAC.

Response to preoperative chemotherapy is one of the most important predictors of survival for resectable GAC [10]. For oesophageal adenocarcinoma, definitive chemoradiation is an alternative to surgery, and median OS time is significantly longer for patients that can achieve to a clinical complete remission (cCR) (negative post therapy biopsy and no evidence of cancer by imaging) [11]. In a previous study, we demonstrated that in patients with localised GAC who are unfit for surgery, decline surgery or have unresectable cancer, the 3-year OS rate was 22.6% with definitive chemoradiation [12]. However, in that study, 30.3% of patients had advanced stage disease at diagnosis, and another 33.3% were found to have advanced disease in the restaging that was done after definitive chemoradiation therapy. Only 22 patients (33.4%) in that previous study did not undergo surgery due to comorbid conditions or patient refusal.

It is uncommon not to pursue surgery for a technically operable GAC, and the reasons are usually either comorbidities or patient choice. Although these patients do not receive the best option for cure, combined modality chemoradiation or systemic chemotherapy remains as alternatives. The impact of non-surgical approaches on survival of technically operable GAC patients is not well documented.

In the present study, we aimed to evaluate whether combined chemoradiation or systemic chemotherapy can be an alternative treatment option for technically operable GAC patients who could not undergo surgery due to various reasons. We also evaluated the impact of other variables, especially achieving a cCR, on survival of resectable GAC patients treated with non-surgical modalities.

To the best of our knowledge, the present study is the largest cohort that includes technically operable patients that did not have surgery due to medical comorbidities, poor performance status, or patient choice.

2. Patients and methods

2.1. Patients

A total of 71 resectable GAC patients that did not have surgery and treated with either systemic chemotherapy or combined chemoradiation therapy were identified from our prospectively maintained and institutionally approved database in the Department of Gastrointestinal Medical Oncology at University of Texas MD Anderson Cancer Center. The patients treated between 1996 and 2016 were included in the study.

For this analysis, variables included age, gender, location of the primary tumour, baseline T and N stage, adenocarcinoma subtype, tumour grade, type of therapy (systemic chemotherapy or combined chemoradiation), status of cCR and reason for not having surgery.

2.2. Staging, treatment and follow-up

All patients had a baseline imaging study as computer tomography (CT) or positron emission tomography (PET)/CT scan and an endoscopic ultrasonography (EUS). More than half of the patients (37/71) had

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