



Surgery in oesophago-gastric cancer with metastatic disease: Treatment, prognosis and preoperative patient selection[☆]

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Abstract

Background: The role of surgical resection in metastatic oesophago-gastric adenocarcinomas (EGA) is not defined and regularly discussed in interdisciplinary tumour boards. Primary objective of this retrospective study was the outcome of patients after surgery. We additionally evaluated our preoperative prognostic score (PPS) based on tumour grading, clinical response to chemotherapy and presumed R-status.

Methods: 123 of 811 EGA patients were evaluated as cM1, either confirmed intraoperatively or by imaging. Response evaluation after chemotherapy was performed by endoscopy, CT-scan and histopathologically. The prospectively documented patient and outcome data were analysed retrospectively.

Results: 70 patients with adenocarcinoma of the oesophago-gastric junction and 53 patients with gastric cancer were included. The majority had one M1 site (n = 102). 72 received preoperative chemotherapy (CTx) and 51 underwent primary resection. 11 were explored without resection. 49/112 (40%) had multivisceral resections and 63/112 (56%) were completely resected (R0). 26/72 (36%) were clinical responders and 30 patients had a favourable PPS.

Median survival was 20.0 months. Survival was significantly prolonged by resection, especially complete resection, and by preoperative CTx (all p = 0.001). Multivisceral resection, type or number of metastases, or primary tumour localization had no impact on survival. In patients undergoing preoperative CTx, clinical response and the PPS influenced survival significantly. In R0 resected patients, preoperative CTx, clinical response and the PPS remained prognostic.

Conclusion: Primary resection without preoperative CTx is not appropriate for metastatic EGA. Subgroups of patients with a favourable PPS with response to CTx may be good candidates for surgical resection in metastatic oesophago-gastric cancer.

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Keywords: Metastasis; Surgery; Gastric cancer; Oesophageal cancer; Prognosis

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KeyMessage

Our data strengthen the role of surgery in Oesophago-gastric adenocarcinoma with resectable metastatic disease with encouraging survival data in favourable subgroups. Induction chemotherapy improves survival significantly compared to surgery alone. Clinical response or a favourable preoperative prognostic score are independent prognostic factors. Therefore patients of these subgroups are the best candidates for surgery.

Introduction

The therapeutic approach in metastatic Oesophago-gastric cancer has changed significantly. Whereas formerly any M1-category was excluded from surgery, nowadays surgery for patients with metastatic disease are often discussed in multidisciplinary tumour boards.^{1–3} Individually for each patient, expectations have to be weighted against surgical feasibility, risk and overall benefits since so far results of randomized studies are not available.^{4,5} The treatment goals in an M1 situation theoretically range from relief of symptoms and prevention of complications caused by the primary tumour to improvement of quality of life up to a significant survival benefit or cure in some patients. Surgical strategies vary from a mere resection of the primary tumour to a complete resection of the primary tumour and all metastatic sites. The problem of the literature on this topic is its extreme heterogeneity. The inclusion criteria for surgical treatment in published series are wide and often not clearly disclosed, making comparison of studies difficult. Studies include patients with syn- or metachronous metastases, with and without preoperative therapy and with different sites and number of metastases.^{1,2,6–8} Preliminary results of the FLOT-3 study suggest a benefit for resected patients with limited metastatic disease compared to patients with chemotherapy alone.⁹ Mariette et al. also demonstrated a survival benefit for surgically treated patients compared to non-surgical treatment in gastric cancer.¹⁰ Median survival for resected patients with metastatic disease ranges from 8 months to 20 months,^{6,8,10,11} which is in line with the 18.6 months reported for limited metastatic patients treated with surgery or other local therapies in the FLOT trial.⁹ We have to be aware that results might be influenced by a selection bias of the included patients in the surgical treatment arms. Several factors have been suggested as indicators for potential benefits from resection, i.e. response to induction therapy,^{1,12} number and pattern of metastasis,^{1,6,12–15} performance status,^{6,13} and extent of the primary tumour.^{2,14} Previously published prognostic factors include the delivery of chemotherapy, resection, length of the primary tumour, number of metastatic sites and histopathological response.^{1,2,7} The primary objective of this retrospective study was to assess the outcome of patients with limited metastatic Oesophago-

gastric adenocarcinoma with special emphasis on preoperative chemotherapy and response evaluation. Additionally, our preoperative prognostic score (PPS)¹⁶ was now assessed in a larger patient series.

Patients and methods

Between 2002 and 2012 811 patients with histopathologically proven adenocarcinoma of the Oesophago-gastric junction (AEG) or stomach were treated and continuously documented in a patient database at the department of surgery of the university hospital Heidelberg. 123 patients (15.3%) were confirmed as M1, either intraoperatively as pM1 or as cM1 by imaging (Figure S1). 32 of the M1 patients were already included in the paper of Blank et al.¹⁶ with shorter follow-up. The institutional review board approved the conduct of a retrospective study.

Table 1
Pre-treatment clinicopathologic patient characteristics (n = 123).

	n and (%)
Gender	
Male	87 (70.7)
Female	36 (29.3)
Localization (UICC 7th)	
Oesophagus	70 (56.9)
AEG I	25 (20.3)
AEG II	35 (28.5)
AEG III	10 (8.1)
Gastric	53 (43.1)
Gastric body	21 (11.1)
Gastric antrum	25 (11.1)
Total gastric carcinoma	7 (6.1)
Grading	
G1/2	37 (30.1)
G3/4	75 (61.0)
Not classified	11 (8.9)
Lauren classification	
Intestinal type	64 (52.0)
Non-intestinal type	44 (35.8)
Not classified	15 (12.2)
cT category	
cT2	10 (8.1)
cT3	83 (67.5)
cT4	24 (19.5)
Missing	6 (4.9)
cN category	
cN0	9 (7.3)
cN1	111 (90.2)
Missing	3 (2.49)
M category	
M0	0 (0)
M1	123 (100)
Hepatic	27 (22.0)
Lymphatic	43 (35.0)
Peritoneal	16 (13.0)
Pulmonary	10 (8.1)
Multiple	21 (17.1)
Other	6 (4.9)

AEG = adenocarcinomas of the Oesophago-gastric junction.

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