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### Original Research

## Volume-outcome relation in palliative systemic treatment of metastatic oesophagogastric cancer



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#### **KEYWORDS**

Oesophageal cancer; Gastric cancer; High-volume hospitals; Survival; Chemotherapy; Palliative therapy **Abstract** *Introduction:* Palliative systemic therapy has been shown to improve survival in metastatic oesophagogastric cancer. Administration of palliative systemic therapy in metastatic oesophagogastric cancer varies between hospitals. We aimed to explore the association between the annual hospital volume of oesophagogastric cancer patients and survival.

Methods: Patients diagnosed in the Netherlands between 2005 and 2013 with metastatic oesophagogastric cancer were identified in the Netherlands Cancer Registry. Patients were attributed according to three definitions of high volume: (1) high-volume incidence centre, (2) high-volume treatment centre and (3) high-volume surgical centre. Independent predictors for administration of palliative chemotherapy were evaluated by means of multivariable logistic regression analysis, and multivariable Cox proportional hazard regression analysis was performed to assess the impact of high-volume centres on survival.

Results: Our data set comprised 4078 patients with metastatic oesophageal cancer, and 5425 patients with metastatic gastric cancer, with a median overall survival of 20 weeks (95% confidence interval [CI] 19–21 weeks) and 16 weeks (95% CI 15–17 weeks), respectively. Patients with oesophageal cancer treated in a high-volume surgical centre (adjusted hazard ratio [HR] 0.80, 95% CI 0.70–0.91) and a high-volume treatment centre (adjusted HR 0.88, 95% CI 0.78–0.99) exhibited a decreased risk of death. For gastric cancer, patients treated in a high-volume surgical centre (adjusted HR 0.83, 95% CI 0.74–0.92) had a superior outcome.

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**Conclusion:** Improved survival in patients undergoing palliative systemic therapy for oesophagogastric cancer was associated with treatment in high-volume treatment and surgical centres. Further research should be implemented to explore which specific factors of high-volume centres are associated with improved outcomes.

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#### 1. Introduction

Cancers of the oesophagus and stomach are amongst the most challenging to treat because the majority of patients present with locally advanced or metastatic disease and have a poor median survival [1,2]. Combination chemotherapy has been shown to improve survival compared with best supportive care [3]. There is no established optimal first-line treatment. Two recently published meta-analyses showed that triplet chemotherapy compared to doublet chemotherapy resulted in a marginal improvement in survival, but at the cost of higher toxicity [3,4].

The absence of an optimal first-line palliative treatment option may have resulted in physicians being reluctant in offering palliative chemotherapy. A substantial inter-hospital variation in the administration of chemotherapy (9–27%) in patients with metastatic gastric cancer was found in a previous population-based study, even after correction for case mix [5].

In general, the most frequent associates for receipt of palliative chemotherapy are younger age and higher socioeconomic status of the patient; conversely patients with multiple distant metastases and patients with comorbidity are less often treated with palliative chemotherapy [6,7]. Moreover, the preference of a physician to apply an intensive treatment with marginal benefit and high probability of side-effects has been associated with a higher number of patients treated per year [8].

For oesophageal surgery, the association between higher procedural volume providers and less postoperative mortality and better survival has been recognised [9]. Likewise, we hypothesise that for treatment of
patients with metastatic oesophagogastric cancer, the
experience of a hospital or an individual medical oncologists providing oesophagogastric cancer treatment, as
defined by the number of patients treated per year, may be
an important associate for patient outcome. Therefore,
the aim of this study was to assess (1) the predictors for
administration of palliative systemic therapy and (2)
whether hospital volume is associated with overall survival for patients treated with palliative systemic treatment in patients with metastatic oesophagogastric cancer.

#### 2. Patients and methods

#### 2.1. Data collection

Data were retrieved from the population-based Netherlands Cancer Registry (NCR). This prospective registry collects information on all patients newly diagnosed with a malignancy in the Netherlands and is notified by the national automated pathological archive (PALGA). The registry area comprises nearly 17 million inhabitants. Next to pathological notification, additional sources are the national registry of hospital discharge, oncology departments, radiotherapy institutions, and diagnosis therapy combinations (specific codes for reimbursement purposes). Specially trained data managers of the NCR routinely extracted information on diagnosis, tumour stage and treatment from the medical records.

By this PALGA notification, approximately 98% of the patients with oesophagogastric cancer are registered as most patients having a histological confirmation of the primary tumour by gastroscopy. On a periodical basis and with the introduction of new variables, extra trainings are provided to the registration clerks. Through thorough training of the registration team and computerised consistency checks at regional and national levels, the quality of the data is high [10].

Information on vital status was obtained through an annual linkage with the Municipal Administrative Database, in which all deceased and emigrated persons in the Netherlands are registered.

Cancer topography and morphology are classified according to the International Classification of Disease for Oncology (ICD-O) third edition based on information from the medical files, including the pathology report. Tumours were staged according to the recommendations of the International Union against Cancer tumour lymph node metastases (TNM) classification in the respective period. In 2010, TNM staging for oesophageal cancer changed from the 6th to the 7th edition. In the 7th edition, celiac lymph nodes regardless of the location of the primary tumour were not classified as distant metastases anymore.

Patients diagnosed with an adenocarcinoma (ICD-O morphology codes 8140-8142, 8144, 8145, 8210, 8211, 8255, 8260-63, 8401, 8480, 8481, 8490, 8560, 8570, 8572, 8574 and 8576) or squamous cell carcinoma (ICD-O morphology codes 8070-78) between January 2005 and December 2013 were selected. Tumours with other or unknown histology were excluded. The modality (radiography and/or pathological verification) to detect metastases is not uniform in the Netherlands and may vary between and even within centres. Patients diagnosed at autopsy were not included.

It is a standard procedure not to impute missing variables as it is unknown whether these missing

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