



Original Research

Synchronous peritoneal metastases of small bowel adenocarcinoma: Insights into an underexposed clinical phenomenon



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CRS+HIPEC

Abstract *Background:* The aim of this population-based study was to provide insight into the incidence, risk factors and treatment-related survival of patients with peritoneal metastases (PM) of small bowel adenocarcinoma (SBA).

Methods: Data from the Netherlands Cancer Registry were used. All patients diagnosed with SBA between 2005 and 2014 were included. The influence of patient and tumour characteristics on the odds of developing PM was analysed. Subsequently, for all further analyses, patients without synchronous PM of SBA were excluded. The log-rank test and Kaplan-Meier analyses were conducted to estimate survival, and the Cox proportional hazards model was used to evaluate the risk of death.

Results: Of the 1428 included patients diagnosed with SBA, 181 (13%) presented with synchronous PM. Synchronous PM was found in 9% of the duodenal tumours and in 17% of the more distal tumours. Median overall survival of all patients with PM was 5.9 months, whereas survival of both 11 months was observed in patients treated with primary tumour resection or palliative chemotherapy and 32 months after cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS+HIPEC). Poor prognostic factors for survival were age ≥ 70 years (hazard ratio [HR] 1.6, 95% confidence interval [CI] 1.1–2.2), systemic metastases other

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than PM (HR 2.0, 95% CI 1.4–2.9) and an advanced (HR 1.9, 95% CI 1.3–3.0) or unknown T-stage (HR 2.1, 95% CI 1.2–3.5).

Conclusions: Synchronous PM was frequently encountered in SBA. Without treatment, prognosis was extremely poor. Survival was higher after primary tumour resection, palliative chemotherapy and CRS+HIPEC, but selection bias probably played a significant role calling for further clinical research.

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1. Introduction

One of the most frequently affected metastatic sites in patients with small bowel adenocarcinoma (SBA) is the peritoneal cavity, especially in tumours arising from the jejunum and ileum [1–3]. Other common metastatic sites of SBA include the liver and extra-regional lymph nodes. The prognosis of metastatic SBA is poor with a median overall survival of 4–5 months and 5-year survival rates of 3–5% [1,2,4,5]. Data on survival according to metastatic site in patients with a primary SBA are absent, and as a result, specific information on survival of patients with peritoneal metastases (PM) is unknown.

In gastro-intestinal malignancies, PM is usually regarded as a virtually untreatable condition, mainly because of the poor response to conventional types of therapy, such as systemic therapy, surgical resection or radiation [3,6–10]. Since the introduction of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS+HIPEC) more than two decades ago, major improvements in overall survival have been achieved in patients with pseudomyxoma peritonei and PM of colorectal cancer (CRC) [6,11–13]. Owing to similarities between SBA and CRC, it is thought that CRS+HIPEC might also benefit patients with PM of SBA [4,14]. Some small studies already showed the potential beneficial effect of CRS+HIPEC in small groups of selected patients with PM of SBA, but prospective studies are lacking [6,7].

Currently, data about PM of SBA are virtually absent. Since these data are of importance to patients suffering from this condition and physicians treating it, we performed a population-based study to establish incidence, risk factors and overall survival of patients with synchronous PM of SBA in the Netherlands between 2005 and 2014.

2. Materials and methods

2.1. Data collection

Data were retrieved from the Netherlands Cancer Registry (NCR). The NCR covers nearly 17 million inhabitants of the Netherlands and comprises population-

based data on all newly diagnosed malignancies of all Dutch citizens. Primary source of notification of the NCR is the automated nationwide pathological archive (PALGA), supplemented with data from the national registry of hospital discharge diagnoses. The NCR comprises information on patient and tumour characteristics, diagnosis and treatment, which is routinely extracted from medical records by specially trained registrars operating on behalf of the NCR. In the databases of the NCR, the stage of the primary tumour is established according to the tumour-node-metastasis (TNM) classification. In case of missing pathological data, the clinical TNM stage is used. The anatomical site of the tumour and metastases are registered according to the third version of the International Classification of Disease for Oncology (ICD-O).

Patients diagnosed with SBA (ICD-O code C17) between 2005 and 2014 were included in this study and analysed for synchronous PM (C48). Synchronous metastases were defined as metastases diagnosed within 3 months after the initial SBA diagnosis. Tumours were classified as adenocarcinomas with the following morphology codes: 8140, 8144, 8145, 8210, 8255, 8260, 8261, 8263, 8480, 8481, 8490, 8560, 8570 and 8574. Patients were excluded if they were diagnosed with neuro-endocrine tumours, including carcinoids, gastro-intestinal stromal tumours or undifferentiated tumours or if they were newly diagnosed during autopsy.

The following treatment modalities were included in the study: palliative chemotherapy, palliative primary tumour resection and CRS+HIPEC. Palliative chemotherapy was defined as the administration of cytotoxic drugs or targeted agents. CRS+HIPEC was performed according to a nationwide Dutch protocol.

Vital status of patients was assessed on 1 February 2016 through linkage of the NCR with civil municipal registries and the central bureau for genealogy, which collects data on all deceased inhabitants of the Netherlands. Survival was computed on all-cause mortality.

2.2. Statistical analysis

Age-standardised incidence rates were calculated per 100,000 person-years using the European standardised

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