



The impact of age on first-line systemic therapy in patients with metachronous metastases from colorectal cancer



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ABSTRACT

Objectives: The paucity of evidence for the optimal use of systemic therapy in elderly patients with metastatic colorectal cancer (mCRC) poses significant challenges to cancer specialists. The present population-based study provides insight into the impact of age on palliative systemic therapy in patients with metachronous metastases from CRC, in order to optimize the decision-making process.

Methods: Data on the development and treatment of metachronous metastases were collected for patients with primary resected CRC diagnosed between 2003 and 2008 in the Eindhoven area of the Netherlands Cancer Registry. Patients undergoing surgery for metastases were excluded, resulting in a study population treated with palliative intent, with or without systemic therapy (n = 746).

Results: 385 patients received palliative systemic therapy (52%). Patients aged ≥ 75 years were less likely to receive systemic therapy (31% ≥ 75 years vs 73% < 60 years) and more likely to receive single-agent chemotherapy than combination-chemotherapy. Elderly patients (≥ 75 years) treated with capecitabine-oxaliplatin (CAPOX) received fewer cycles (51% ≤ 3 oxaliplatin cycles, 43% ≤ 3 capecitabine cycles) and lower cumulative dosages compared to patients aged < 75 years, although initial dosages were similar. If capecitabine monotherapy (CapMono) was administered, starting dosages were 2414 mg/m²/d < 75 years and 1992 mg/m²/d ≥ 75 years (p < 0.05), but no differences in number of received cycles or cumulative dosages were observed.

Conclusion: Age beginning at 75 years significantly influenced palliative systemic therapy. Even in selected elderly patients, first-line treatment with CAPOX was associated with less cycles and lower cumulative dosages compared to younger patients. With single-agent fluoropyrimidine therapy, however, no such results were observed.

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1. Introduction

Colorectal cancer (CRC) is one of the most common cancers worldwide and currently the third most common malignancy in the Netherlands [1]. The occurrence of CRC increases with age, with 54% being 70 years or older and over one third being 75 years or older [1].

Most cancer deaths result from progressive growth of metastases. Metastases are present at the time of diagnosis in approximately one fifth of the patients with CRC [2,3] and another relatively large

proportion (14–34%) develops metachronous metastases during the course of disease [4–6].

Over the past decades, treatment modalities for metastatic CRC (mCRC) have made a substantial leap. Although nowadays an increasing proportion of patients with mCRC receive surgical treatment with curative intent, the majority of patients are still ineligible for curative treatment modalities and remain dependent on palliative treatment. Also, treatment has evolved for these patients. Various systemic regimens, combining cytotoxic agents and targeted agents, have become available.

Guidelines on mCRC are based on trials in which the elderly are generally underrepresented [7]. Because ageing is an individual process, treatment recommendations for fit, younger patients cannot automatically be extrapolated to older patients. Due to the paucity of evidence for the feasibility and optimal use of these systemic regimens in elderly patients with mCRC, decisions on optimal management for the growing

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number of elderly patients with mCRC poses significant challenges to cancer specialists. High quality population-based data, reflecting daily based practice, are needed to further optimize the decision-making process. Such data are currently lacking in the subset of patients with metachronous metastases from CRC, in which data collection is very time consuming and costly. Therefore, the aim of the present population-based study was to provide insight into the impact of age on the palliative treatment of metachronous metastases from CRC in daily practice.

2. Methods

2.1. Data Collection

Data from the population-based Netherlands Cancer Registry (NCR), more specifically from the Eindhoven area, were used. This registry collects data of all patients with newly diagnosed cancer in a large part of the Southern Netherlands and comprises approximately 2.4 million inhabitants (~15% of the Dutch population), six pathology departments, ten hospitals and two radiotherapy institutions. Information on patient and tumor characteristics are collected from medical records by specially trained registry staff after notification by pathologists and medical registration offices. In this registry, the tumor-node-metastasis (TNM) classification is used for stage notification of the primary tumor [8]. Anatomical site of the tumor is registered according to the International Classification of Diseases for Oncology (ICD-O) [9]. Comorbidity at cancer diagnosis was obtained from the medical records and was registered according to a slightly modified version of the Charlson Comorbidity index [10]. Data on socioeconomic status were based on individual fiscal data on the economic value of home and household income, which was provided at an aggregated level for each postal code [11]. Due to thorough training of the registration personnel and computerized consistency checks at regional and national levels, the quality of the data is high. Completeness of the data is estimated to be at least 95% [12].

For the present study, additional data were retrospectively collected between 2010 and 2011 on metachronous metastases for patients diagnosed between 2003 and 2008 with non-metastatic CRC (stage I-III).

Hospitals were asked to participate in the study by giving permission to use their data from the NCR and by giving permission for the retrospective registration of additional data. All hospitals voluntarily participated. Metachronous metastases were defined as distant metastases of primary CRC in other organs, diagnosed at least 3 months after CRC diagnosis. Median time from primary diagnosis to data collection was 5.3 years (range 1.5–8.8 years). The additional data collection encompassed detailed information on first-line systemic therapy for metachronous metastases, both chemotherapy and targeted therapy; which regimen and agents, dosages, and number of cycles of each agent received. In the Netherlands, all hospitals have multidisciplinary tumor boards. Nowadays, more than 90% of the patients are discussed in these boards [13]. Even though geriatricians are present in every hospital, it is unknown whether they were available for oncologic consultation.

All consecutive patients with metachronous metastases from primary resected stage I-III CRC (C18.0–C18.9, C190, C209) were selected. Patients undergoing surgery for metastases were excluded, resulting in a study population treated with palliative intent, with or without systemic therapy. Patients were divided into categories according to their age at time of metachronous metastases diagnosis and the usage of first-line systemic therapy was assessed.

2.2. Statistical Analyses

Descriptive statistics were used to provide an overview on patient and tumor characteristics of the total study population ($n = 746$). Variation in the receipt of palliative systemic therapy between age categories and hospital of diagnosis was assessed using a χ^2 test. Multivariable logistic regression analysis was used to assess the independent influence of age on the receipt of palliative systemic therapy. Adjustments were made for relevant patient and tumor characteristics: gender, comorbidity and socioeconomic status at time of CRC diagnosis, primary tumor localization, adjuvant chemotherapy, time to metastases, period of metastases diagnosis, the number of affected organs, and hospital of diagnosis. Differences in the received chemotherapeutic backbones between age categories were assessed and tested using a χ^2 test. Initial

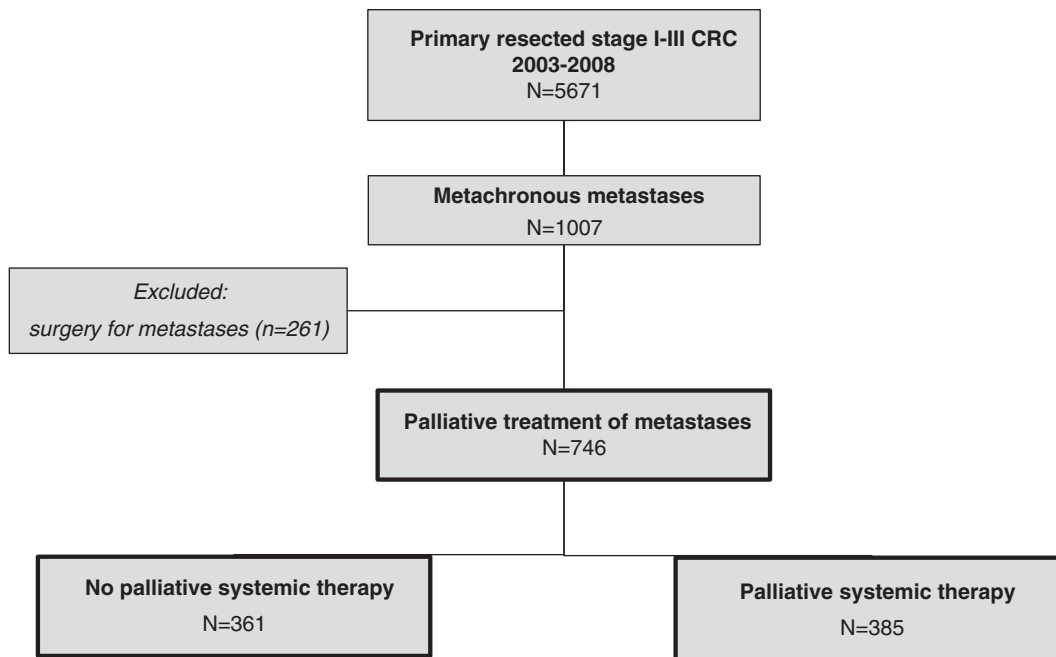


Fig. 1. Overview of patients included in the study.

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