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Management of patients over 80 years of age treated with resection for localised colon cancer: Results from a French referral centre

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ABSTRACT

Background: Few data are available on management of very elderly colon cancer patients, especially concerning the parameters of therapeutic decisions and the role of geriatricians.
Methods: We retrospectively reviewed the charts of patients over 80 years of age who underwent surgery for a localised colon cancer in a French academic hospital.
Results: A total of 176 patients underwent surgery (postoperative morbidity and mortality rates: 25% and 6.7%). Adjuvant chemotherapy was discussed at a multidisciplinary team meeting for 91% of stage III patients, but only 13.5% of them were treated. Twenty-five patients relapsed: 19 were discussed at the multidisciplinary meeting and 16 were treated (5 had a metastasectomy). Despite their increase with time, geriatric assessments were infrequent, 17% (33% after 2006), and had no impact on post-operative morbi-mortality. Median overall survival and recurrence-free survival were 65.3 months and 65.1 months, respectively. Age, emergency surgery, and Charlson comorbidity index were independent prognostic factors.
Conclusion: Selected elderly colon cancer patients have significant access to surgery. However, postoperative morbi-mortality rates remain high and adjuvant chemotherapy rarely prescribed. Perioperative geriatric assessment, especially before surgery, should be routinely proposed to these patients to evaluate its impact on postoperative morbi-mortality and prescription of adjuvant treatment.

1. Introduction

The population of the United States and Western countries is ageing and, as a result of longer life expectancy, a growing number of older subjects will be diagnosed with a cancer. Colorectal cancer (CRC) is the most frequent type of cancer and the second most common cause of cancer-related death in Europe [1]. Fourty percent of patients are 75 years old or older at diagnosis [2] and many studies have shown that elderly patients were less likely to be offered «optimal treatment» for CRC [3]. Surgery is the cornerstone of curative treatment for patients with colon cancer. Even if the proportion of elderly undergoing curative resection remains lower than that of younger patients [4,5], it has significantly increased over time [3]. Despite this, the increase of CRC patients' survival reported in Europe is less pronounced in patients aged ≥75 years than in younger patients [2]. In addition, survival of those with stage I–III tumour did not change significantly between 1976–1987 and 1988–1999 in the French registry of «Côte d'Or» [3]. This may be due to more advanced tumours at diagnosis, a higher risk of post-operative mortality, a lower proportion of aged patients receiving

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chemotherapy, and the proportion of deaths unrelated to cancer in this population with increased number of comorbidities [4,6–11]. However, the reasons for therapeutic abstention or sub-standard treatment in elderly CRC patients remain often unclear. Elderly people are a heterogeneous group of patients, with individuals ranging from fit to very frail conditions; therefore, a comprehensive geriatric assessment (CGA) should help oncologists to better select patients who can benefit from an optimal treatment and identify those at high risk [12]. However, CGA is not systematically performed for several reasons that have not yet been fully explored.

The majority of published studies on elderly CRC patients have included patients older than 70 or 75 but fewer data are available on more aged patients. The aim of this retrospective study was to describe the management of patients ≥80 years old operated for a localised colon cancer in a French University Hospital during a 12-year period. It included an analysis of (i) the different treatments received during the course of the disease, (ii) geriatric assessments performed and their impact on postoperative morbimortality and treatment decisions, and (iii) patient outcomes and prognostic factors.

2. Patients and methods

2.1. Study design and patients

All consecutive patients over 80 years of age that referred to our institution (Ambroise Paré University Hospital, AP-HP, Boulogne-Billancourt) for resection of a localised colon cancer were retrospectively included between July 1999 and July 2011. Patients with colon cancer were identified with our medical, surgical, and pathological computerised databases. Those with a rectal cancer or with a metastatic disease at diagnosis were excluded from the study.

The following data were recorded and analysed retrospectively: medical history, Charlson comorbidity index (CCI) [13], age, gender, tumour localisation, clinical presentation, surgery, postoperative morbidity and mortality, pathological findings, TNM staging, adjuvant chemotherapy, tumour recurrence, therapeutic toxicity, and date and cause of death. Multidisciplinary team (MDT) meeting reports and geriatric assessments or consultations were also collected to analyse their respective impact on therapeutic decisions.

The follow-up was performed until October 2012. For patients lost during follow-up, patients, their family, or the general practitioner were asked for information by phone. If no follow-up information was available, a request was sent to the town hall of the city of birth to obtain the death date.

2.2. Microsatellite instability

Microsatellite instability (MSI) had been prospectively determined by immunohistochemistry.

Since January 2007, immunohistochemical expression of the 4 MMR proteins (MLH1, MSH2, MSH6, and PMS2) was prospectively investigated in all tumours. Before this date, expression was investigated non-systematically on the request of the clinician, and with the investigation of MLH1 and MSH2 expression only. Non-neoplastic colonic mucosa was used as control. Negative protein expression was defined as complete absence of nuclear staining within tumour cells despite concurrent positive labelling in internal non-neoplastic tissues.

2.3. Statistical analysis

Quantitative data were expressed as mean ± SD and qualitative data as frequency and percentage. Comparisons between groups were analysed with the chi-squared or Fisher exact test. For studying the association with tumour stage, patients with stage I, II, and III were firstly compared. Then, patients were divided into a "high-risk tumour stage", including stage III and high-risk stage II (<12 lymph nodes examined, occlusion, perforation, poorly differentiated, pT4, perineural or lymphovascular invasion), and a "low-risk tumour stage" (stage I and low-risk stage II), which might be more relevant in clinical practice.

Overall survival (OS) was defined as the interval between the date of surgery and the date of either death or last follow-up, at which data point was censored. Recurrence-free survival (RFS) was defined as the interval between the date of surgery and tumour recurrence or death. Both RFS and OS were estimated by the Kaplan–Meier method and compared using the log-rank test. A multivariate Cox model stratified by gender was used to estimate the impact of different variables on survival after adjustment for age, CCI, emergency surgery, and tumour stage. As MSI status was known only in 123 tumours, it was not included in the multivariate analysis. Adjuvant chemotherapy was not included in this multivariate analysis due to the low number of patients treated. Statistical analyses were carried out using STATA (STATA Corp, College Station, TX). Statistical significance was set at $p < 0.05$.

3. Results

3.1. Patient and tumour characteristics

From July 1999 to July 2011, 1130 colon cancer patients were managed at our institution. Among them, 240 subjects (21.2%) were over 80 years old, including 176 (73.3%) with a localised resected tumour.

Patients and tumour characteristics are presented in Table 1. The median age was 84.9 years (range: 80–98 years). Charlson comorbidity index (CCI) was significantly associated with age (CCI >2 for the 80–84 years group: 13.6%; for 85–89 years: 21.6%; for 90–94 years: 30%; for ≥95 years: 50%; $p < 0.0001$). We found a trend towards a more advanced stage at diagnosis in aged patients ("high-risk tumour stage"; 80–84 years: 68.2%; 85–89 years: 51.6%; 90–94 years: 70%; ≥95 years: 87.5%; $p = 0.08$). The main symptoms leading to the diagnosis were anaemia (31%), haemorrhage (24%), intestinal transit modification (22%), asthenia and/or weight loss (11.7%), and occlusion (15%) or perforation (5%), for a total of 20% of emergency admissions. Only 4 patients were diagnosed at colonoscopy performed for follow-up of previously resected adenoma ($n = 3$) or following a positive faecal occult blood test ($n = 1$). Obstruction/perforation was more frequent in very aged patients (80–84 years: 14.7%; 85–89 years: 18.3%; 90–94 years: 30%; ≥95 years: 50%; $p = 0.058$).

Microsatellite instability (MSI) testing was performed in 126 patients, but MSI status of the tumour could not be determined in 3 of them. Among the 123 tumours with successful MSI testing, 43 (35%) were MSI tumours (Table 1). MSI status was significantly associated with female gender (women vs men: 42.1% vs 23.4%; $p = 0.026$), proximal colon tumour (proximal vs distal: 46.1% vs 22.4%; $p = 0.005$), high-grade tumour (high vs low grade: 80% vs 28.7%; $p < 0.001$), and early tumour stage (I vs II vs III: 60% vs 40.5% vs 22.7%; $p = 0.05$), but not with age ($p = 0.2$).

The indication of surgery was previously discussed at an MDT meeting for 23 patients (13%). A laparoscopic colectomy was performed in only 8 patients (4.5%), whereas the majority of the patients ($n = 168$) underwent conventional open surgery.