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Right colon cancer: Left behind

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Abstract

Introduction: Prognosis of colon cancer (CC) has steadily improved during the past three decades. This trend, however, may vary according to proximal (right) or distal (left) tumor location. We studied if improvement in survival was greater for left than for right CC.
Methods: We included all CC recorded at the Geneva population-based registry between 1980 and 2006. We compared patients, tumor and treatment characteristics between left and right CC by logistic regression and compared CC specific survival by Cox models taking into account putative confounders. We also compared changes in survival between CC location in early and late years of observation.
Results: Among the 3396 CC patients, 1334 (39%) had right-sided and 2062 (61%) left-sided tumors. In the early 1980s, 5-year specific survival was identical for right and left CCs (49% *vs*. 48%). During the study period, a dramatic improvement in survival was observed for patients with left-sided cancers (Hazard ratio [HR]: 0.42, 95% confidence interval [CI]: 0.29–0.62, $p < 0.001$) but not for right CC patients (HR: 0.76, 95% CI: 0.50–1.14, $p = 0.69$). As a consequence, patients with distal CC have a better outcome than patients with proximal CC (HR for left *vs*. right CC: 0.81, 95% CI: 0.72–0.90, $p < 0.001$).
Conclusion: Our data indicate that, contrary to left CC, survival of patients with right CC did not improve since 1980. Of all colon cancer patients, those with right-sided lesions have by far the worse prognosis. Change of strategic management in this subgroup is warranted.

Keywords: Colon cancer; Location; Survival; Cancer registry; Population-based study

Introduction

Clinical outcome of colon cancer (CC) is continuously improving in Europe,[1] North America,[2] and Asia.[3] Implementation of screening programmes,[4] facilitated access to colonoscopy,[5] and development of efficient chemotherapy regimen,[6] are factors which contributed to this process. In large descriptive data on cancer survival, the colon is considered as an organ *per se* and no distinction is made between CC sub-sites. Therefore, clinicians are likely to consider that improvement in survival encompasses all CC, irrespective of tumor location proximal or distal to the splenic flexure.

In fact, right- and left-sided CC may represent different embryological, epidemiological, physiological, pathological, genetic and clinical entities.[7] Relationship between CC location and survival has been recently investigated in several studies. In particular, two large population-based studies reported conflicting results, even though both queried the same (Surveillance, Epidemiology and End Results-SEER) database.[8,9] Most studies however, did not consider the evolution of prognosis over a long period of time. In addition, these studies are hampered by the fact that they do not report the cause of death and often fail to provide adequate information regarding adjuvant chemotherapy.[10,11] A recent meta-analysis concluded that the impact of tumor location on CC survival remains unclear.[12]

The objective of our study is to assess the differences of CC presentation and 5-year survival in Geneva between 1980 and 2006 according to tumor location. We postulated that better outcome was not homogenously distributed

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among all CC patients, and hypothesized that, during this time period, improvement in survival was superior for left than for right colon carcinomas.

Patients and methods

Geneva Cancer Registry

We used data from the Geneva Cancer Registry, which records since 1970 all incident cancers occurring in the population of the county (approximately 450,000 inhabitants in 2010). All hospitals, pathology laboratories and practitioners are requested to report cancer cases. Recorded data include socio-demographic variables, tumor characteristics (coded according to the International Classification of Diseases for Oncology [ICD-O]), stage at diagnosis (coded according to the Tumor Node Metastasis [TNM] classification of malignant tumors), and treatment received within 6 months after diagnosis.

The Registry regularly assesses survival. The index date refers to the date of confirmation of diagnosis (usually from the pathology report of the biopsy/operative specimen) or the date of hospitalization if it precedes the diagnosis. In addition to passive follow-up (routine examination of death certificates and hospital records), active follow-up is carried out yearly by linking the files of the Cantonal Population Office in charge of the registration of the resident population with the Registry database, using a personal identity number. The cause of death is established by consulting clinical records and/or by inquiring the patient's physician, and coded according to the international statistical classification of diseases and health-related problems established by the World Health Organization.

Patients

For the purpose of this study, we considered all invasive primary cancers of the colon occurring in the resident population diagnosed between 1980 and 2006. We excluded patients with previous malignant tumors other than basal cell skin carcinoma (n = 513), colonic tumors other than adenocarcinomas (lymphomas, sarcomas, n = 41), familial adenomatous polyposis, tumors of the appendix (ICD-O code 18.1, n = 58), and CC with undetermined location (ICD-O code 18.9, n = 37). We also excluded patients with cancer discovered at death or with less than 1 day of survival (n = 225). Finally, the study included a total of 3396 patients with sporadic adenocarcinomas of the colon. The Geneva Tumor Registry keeping all data strictly anonymous, and since the study did not require additional clinical information, approval of the Ethics Committee was not required.

We divided patients in 2 groups according to colonic tumor location. We considered that the frontier between right-sided and left-sided tumors was the splenic flexure: thus, right colon cancers included tumors occurring in the cecum, ascending colon, hepatic flexure, and transverse colon (ICD-O codes: C18.0, C18.2–18.4). Left-sided tumors included tumors located at the splenic flexure, descending colon, sigmoid, and recto-sigmoid junction (ICD-O codes: C18.5–18.7, 19.9). All patients were followed up for survival until 31 December 2011.

Variables

Variables of interest were: age at diagnosis (<65, 65–74, 75 years and more), year of diagnosis (3 years periods), social class based on patients' last occupation and for unemployed women, that of the spouse (high, medium, low, unknown), country of birth (Switzerland, other) and healthcare sector (public, private). The origin of diagnosis was considered in 4 groups: symptoms (tumor diagnosed following symptoms, fortuitous (tumor discovered during investigation of symptoms related to other pathology), screening (including test for fecal occult blood, sigmoidoscopy, or colonoscopy), and unknown. Tumor stage was coded according to TNM classification: we considered pathological classification and when missing clinical classification) and regrouped stage in 4 groups: I (T1, T2, N0, M0), II (T3, T4, N0, M0), III (Any T, N1, N2, M0), and IV (any T, any N, M1). We also considered pathological tumor size in mm, and tumor differentiation (well, moderate, poor, unknown). Treatment was considered in 5 groups: surgery alone, surgery with adjuvant chemotherapy, chemotherapy alone, other methods (radiation therapy, palliative measures), and no treatment.

Statistical analysis

We compared patients and tumor characteristics between left and right CC patients by chi-square test of heterogeneity. We calculated the effect of tumor location on 5-year specific survival (i.e. considering only death linked to CC) by Cox models. CC-specific survival time was measured from the date of confirmation of diagnosis to the date of death due to CC with times censored at last contact for patients who were lost to follow-up or who remained alive in December 2011, or at the date of death for those who died of causes other than CC. All other variables linked to 5-year CC mortality in monovariate Cox-model were considered as confounding variables and adjusted for when we estimated the independent effect of CC location on specific survival. Finally, 2 distinct adjusted models for right-sided and left-sided tumors were performed to study time trends in survival for each CC sub-sites. We considered differences to be statistically significant at p (two-sided test) value <0.05. We performed all analyses using SPSS software (Version 15; SPSS Inc., Chicago, IL, USA).

Results

Among the 3396 patients of the study, 1334 (39%) had right CC and 2062 (61%) left CC. Patients' and tumors