A Study and Enhancement in Controlling and Patient Management in Colorectal Cancer
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Abstract:
Colorectal cancer (CRC) has potential to spread within the peritoneal cavity, and this transcoelomic dissemination is termed “peritoneal metastases” (PM). The aim of this article was to summarise the current evidence regarding CRC patients at high risk of PM. Colorectal cancer is the second most common cause of cancer death in the UK. Prompt investigation of suspicious symptoms is important, but there is increasing evidence that screening for the disease can produce significant reductions in mortality. High quality surgery is of paramount importance in achieving good outcomes, particularly in rectal cancer, but adjuvant radiotherapy and chemotherapy have important parts to play. The treatment of advanced disease is still essentially palliative, although surgery for limited hepatic metastases may be curative in a small proportion of patients.

Keywords — Colorectal Cancer, Survivorship Care, Patients, Preferences, Symptoms

INTRODUCTION:
Colorectal cancer (CRC) is a formidable health problem worldwide. It is the third most common cancer in men (663000 cases, 10.0% of all cancer cases) and the second most common in women (571000 cases, 9.4% of all cancer cases). Almost 60% of cases are encountered in developed countries. The number of CRC-related deaths is estimated to be approximately 608000 worldwide, accounting for 8% of all cancer deaths and making CRC the fourth most common cause of death due to cancer. In India, the annual incidence rates (AARs) for colon cancer and rectal cancer in men are 4.4 and 4.1 per 100000, respectively. The AAR for colon cancer in women is 3.9 per 100000. Colon cancer ranks 8th and rectal cancer ranks 9th among men. For women, rectal cancer does not figure in the top 10 cancers, whereas colon cancer ranks 9th.

CRC survivors are patients living with a diagnosis of colorectal cancer after primary treatment and are checked regularly for possible recurrent or metastatic disease. Traditionally, in most countries across Europe, this survivorship care of CRC is organized in a secondary care setting and consists of periodic CEA blood testing, imaging and colonoscopy. Survivorship care, however, entails more than detection of recurrent disease and should include rehabilitation, management of physical and psychosocial consequences of the disease and its treatment, and management of common comorbidities. Primary care providers are used to deliver comprehensive generalist care, including psychosocial support. Therefore, health care providers and policy makers argue that primary care might be a better setting for CRC survivorship care.

In the Netherlands, each patient is registered with a general practitioner (GP) who is the caregiver of first contact, refers patients to secondary care if necessary, and provides continuity of care after conclusion of treatment in secondary care.

Patients with colon cancer are often asymptomatic. Some have symptoms of change in bowel habits, blood in their stool, anemia, or are found to be fecal occult blood positive. Less often, a patient may have pain or obstructive symptoms or symptoms of metastatic disease. A complete history, including family history and colon cancer-specific history can guide the surgeon to suspect hereditary cancer syndromes, look for associated pathology or metastatic disease, and initiate additional workup such as mutational analysis of the tumor. Patients...
meeting clinical criteria for or having a family history of an increased susceptibility to colorectal cancer should be referred for genetic counseling for formal evaluation.

**Patient-reported outcome measures in colorectal cancer**

Colorectal cancer-specific patient-reported outcome measures (PROMs) should be developed for use in disease management and to inform outcome measures in future clinical trials.

**Why this is important**

Quality of life and PROMs are now frequently being used as secondary endpoints in clinical trials of cancer management. However, some investigators continue to use non-disease-specific generic methodology for this purpose. The treatment of colorectal cancer leads to very specific side effects relating to bowel function and activities of daily living. The Guideline Development Group therefore believes that colorectal cancer-specific patient-reported outcome measures should be developed to standardize the interpretation of quality-of-life reporting as a secondary endpoint in future clinical trials in colorectal cancer.

**Key priorities for implementation**

The following recommendations have been identified as priorities for implementation.

**Diagnostic investigations**

Offer colonoscopy to patients without major comorbidity, to confirm a diagnosis of colorectal cancer. If a lesion suspicious of cancer is detected, perform a biopsy to obtain histological proof of diagnosis, unless it is contraindicated (for example, patients with a blood clotting disorder).

**Staging of colorectal cancer:**

Offer contrast-enhanced computed tomography (CT) of the chest, abdomen and pelvis, to estimate the stage of disease, to all patients diagnosed with colorectal cancer unless it is contraindicated. No further routine imaging is needed for patients with colon cancer.

Offer magnetic resonance imaging (MRI) to assess the risk of local recurrence, as determined by anticipated resection margin, tumour and lymph node staging, to all patients with rectal cancer unless it is contraindicated.

**Preoperative management of the primary tumour**

Do not offer short-course preoperative radiotherapy (SCPRT) or chemoradiotherapy to patients with low-risk operable rectal cancer (see table 1 for risk groups), unless as part of a clinical trial.

**Colonic stents in acute large bowel obstruction**

If considering the use of a colonic stent in patients presenting with acute large bowel obstruction, offer CT of the chest, abdomen and pelvis to confirm the diagnosis of mechanical obstruction, and to determine whether the patient has metastatic disease or colonic perforation.

**Stage I colorectal cancer**

The colorectal multidisciplinary team (MDT) should consider further treatment for patients with locally excised, pathologically confirmed stage I cancer, taking into account pathological characteristics of the lesion, imaging results and previous treatments.

**Imaging hepatic metastases**

If the CT scan shows metastatic disease only in the liver and the patient has no contraindications to further treatment, a specialist hepatobiliary MDT should decide if further imaging to confirm surgery is suitable for the patient – or potentially suitable after further treatment – is needed.

**Chemotherapy for advanced and metastatic colorectal cancer**

When offering multiple chemotherapy drugs to patients with advanced and metastatic colorectal cancer, consider one of the following sequences of chemotherapy unless they are contraindicated:

- FOLFOX (folinic acid plus fluorouracil plus oxaliplatin) as first-line treatment then single agent irinotecan as second-line treatment or
- FOLFOX as first-line treatment then FOLFIRI (folinic acid plus fluorouracil plus irinotecan) as second-line treatment or
- XELOX (capecitabine plus oxaliplatin) as first-line treatment then FOLFIRI (folinic acid plus fluorouracil plus irinotecan) as second-line treatment.

**Follow-up after apparently curative resection**

Offer patients regular surveillance with a minimum of two CTs of the chest, abdomen, and pelvis in the first 3 years and regular serum carcinoembryonic
antigen tests (at least every 6 months in the first 3 years).

Information about bowel function
Before starting treatment, offer all patients information on all treatment options available to them (including no treatment) and the potential benefits and risks of these treatments, including the effect on bowel function.

Patients and methods

Patients
We performed a cross-sectional study in patients that had been treated with curative intent for colorectal cancer (stages 1–3) at different time points after treatment. Recruitment was done at the outpatient clinics of the departments of surgery, oncology and gastroenterology of six Dutch hospitals. Patients were also eligible if they had a (temporary) stoma or if they had received adjuvant chemotherapy or neoadjuvantchemoradiation. Patients were excluded in case of stage 4 disease, hereditary colorectal cancer, cancer in a patient with inflammatory bowel disease, (sub)total colectomy, history of other primary cancer, or any other condition where specialised survivorship care was needed. The inclusion period was November 2013 until November 2014.

Methods
A cross-sectional study of CRC survivors at different time points. For 14 different symptoms, patients reported if they would consult a caregiver, and who they would contact if so. Patient and disease characteristics were retrieved from hospital and general practice records. The symptoms that patients were asked about were (1) abdominal pain, (2) fatigue, (3) nausea, (4) diarrhoea, (5) constipation, (6) fever, (7) rectal blood loss, (8) weight loss, (9) pain, (10) reduced stamina, (11) trouble sleeping, (12) fear that cancer had recurred, (13) social issues, and (14) work-related issues.

SURGERY
There is no doubt that surgery remains the definitive treatment for localised colorectal cancer and it is important that the patient undergoes appropriate preoperative preparation. Mechanical bowel preparation is widely employed but evidence from randomised trials fails to show that it has a significant effect. However, for aesthetic reasons if for no other, the vast majority of surgeons employ bowel preparation certainly for left sided lesions, though less commonly for right sided tumours. Prophylaxis against deep vein thrombosis is important and the most commonly used method is low dose subcutaneous heparin. Likewise, prophylactic antibiotics to reduce the incidence of wound infection are well established and current best practice is to give a single dose of intravenous antibiotics providing both aerobic and anaerobic cover within 30 minutes of induction of anaesthesia. The surgery itself can be subdivided into surgery for colonic cancer and for rectal cancer.

RESULTS:
Of 318 treated for CRC, 37 patients had a history of first-degree relative with CRC. After excluding patients with non-verified histopathological report (4 patients) and Lynch syndrome (based on Amsterdam II criteria; 2 patients), thirty-one patients remained included in the study. None of the patients with positive family history was diagnosed as part of a symptomfree screening due to family history of CRC. Patients with positive family history had a lower T (tumour) stage (p=0.008) and were more able to develop second primary cancer, such as kidney, prostate, urinary bladder, skin, lung and breast cancer (p<0.001) than patients with no family history. In those patients with a positive family history and colon cancer, there was improved overall survival (p=0.012) (Figure 1), but this was not the case for patients with rectal cancer (p=0.416). No recurrences were observed in patients curatively treated for colon cancer and positive family history of CRC (p=0.035) (Figure 2). In the multivariate analysis, there was an increased risk for shorter overall survival among patients with no family history for CRC.
DISCUSSION:
In this study, the relationship between CRC patients with a family history of CRC in first-degree relatives and survival was analysed. We demonstrated that patients with colon cancer and positive family history had better overall and cancer-specific survival and prolonged time to recurrence compared to patients with negative family history. The basis of survival benefits associated with familial CRC is though unclear. However in recent years increased attention has gained towards tumour biology. MSI tumours are associated with hereditary CRC, rightsided colon cancer and improved survival, and one explaining factor in the discrepancy of why colon cancer patients have improved survival might be due to MSI. As CRC is a common disease in the general population, the proportion of patients with positive family history of CRC has been reported between 16-19%. In the present cohort, only 10% of patients with first-degree relative with CRC were identified. The proportion of patients with positive family history was low which is due to only including patients with verified histopathological reports of their relatives with CRC. In contrast to previous studies, the median age of patients with positive family history in this cohort was 75 years; and therefore, it was considered population based.

CONCLUSION
Significant advances in the treatment of colorectal cancer have been made in recent years and in terms of improved survival the most important areas appear to be early detection and high quality surgery, particularly in the pelvis. The role of adjuvant therapy has been partially clarified but the treatment of advanced disease remains inadequate; as our understanding of the genetic and biochemical basis of cancer improves it is hoped that new biological modifiers and gene therapy may have a part to play in the future. Family history of CRC in first-degree relative in patients with CRC was an individual prognostic factor in patients with colon cancer. This improvement in survival could not be explained by known clinico-pathological factors. For many symptoms that may occur, however, patients would contact their GP. Men, older patients and patients with chronic comorbid conditions more likely prefer to consult their GP, while women patients with stage 3 disease, and patients that have been treated with adjuvant chemotherapy more likely prefer to consult a
secondary care provider. Symptoms that alarm patients to possible recurrent disease, such as rectal blood loss, weight loss or the fear that cancer has recurred would prompt patients to consult either both primary and secondary care providers simultaneously or a secondary care provider directly.

REFERENCES:


