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An international, multidisciplinary approach to the management of advanced colorectal cancer

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The International Working Group in Colorectal Cancer conducted a survey (the Colorectal Cancer Care Pathway Review) in the summer of 1995 to examine medical, surgical and oncology nursing perceptions of patient management throughout Europe and the United States. The sample included 319 oncologists (surgical, medical and radiation) and 103 oncology nurses from a variety of centres in France, Germany, Italy, the United Kingdom and the United States. In response to issues identified in the Colorectal Cancer Care Pathway Review, a model for the optimal management of patients has been developed by the Working Group. The objectives of the Patient Management Model are: to define current best practice in advanced colorectal cancer; and to identify areas for ongoing research and clinical trials. Due to the multicultural nature of the Working Group, the model incorporates the differences in treatment that occur between countries. The Patient Management Model gives recommendations on treatment issues such as diagnosis, staging of disease, management strategy and therapy considerations including surgery, radiotherapy, chemotherapy, palliative supportive care, therapy management, auxiliary management and patient support. A multidisciplinary team approach to patient management is recommended to ensure optimal treatment and care. The multidisciplinary team should include all those involved in the treatment of the patient including specialists such as the oncology nurse. A summary of the recommendations of the Patient Management Model is presented here.

Keywords: Advanced colorectal cancer, best practice, management

Introduction

The initial objectives of the International Working Group in Colorectal Cancer were to investigate current treatment patterns of patients with advanced colorectal cancer, to identify problems and issues in advanced disease and to make recommendations on improvements to the management of advanced disease.

In order to best fulfil the objective of identifying problems and issues in advanced colorectal cancer, the Working Group completed an international survey of the pathway of care for patients with advanced colorectal cancer in France, Germany, Italy, the United Kingdom and the United States. The survey sample was made up of 159 surgeons, 160 medical specialists including oncologists, radiation oncologists, gastrointestinal specialists, internists and nurse practitioners, and 103 oncology nurses.

This Care Pathway Review was completed and preliminary results analysed by the Working Group during the first quarter of 1996, with final results analysed in June 1996 (data on file, Zeneca Pharmaceuticals).

The survey identified variability in treatment practices between countries in the management of advanced colorectal cancer. Erratic referral was cited as common by 50% of the surgical and medical specialists surveyed. They also felt that 40% of patients who could have been referred for treatment were probably not referred. Of all those surveyed, 87% of total respondents believed that a review of the management strategy for advanced disease was 'imperative' or 'useful'.

It was apparent from these findings that a set of recommendations for best practice in the diagnosis, staging and treatment of advanced colorectal cancer would be helpful, and that such recommendations should not: (1) be a set of fixed rules designed to tell specialists how they should be treating their patients with advanced colorectal cancer; (2) supersede regional or institutional guidelines on how patients with advanced colorectal cancer should be treated; or (3) supersede the individual judgement of the specialists on the disease management team.

The consensus recommendations of the International Working Group in Colorectal Cancer will be published shortly [1], and it is hoped that these will help facilitate and improve the understanding and quality of treatment for patients with advanced disease. Although there are numerous sources of information on elements of managing advanced colorectal cancer, the objective of these recommendations was to provide a single, user-friendly and consistent reference. It is hoped that this reference will both address the needs of readers, for example general practitioners (GPs), and aid communication between specialists.

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1. *An International Multidisciplinary Approach to the Management of Advanced Colorectal Cancer.* London: Interscience Pan-Europa Group Ltd; 1997.

The recommendations discuss diagnosis, staging, management strategy, therapy considerations including surgery, radiotherapy, chemotherapy and combined modality therapy, palliative care, therapy monitoring, auxiliary management, and patient support.

An international, multidisciplinary approach to the management of advanced colorectal cancer: overview of specific recommendations

Definition of advanced colorectal cancer

Before beginning to develop the recommendations, it was clear that members of the International Working Group in Colorectal Cancer had different views on how to define advanced colorectal cancer, and that a unanimous definition had to be agreed before recommendations could be made. After careful consideration, the Group agreed that advanced colorectal cancer is defined as cancer which, at presentation or recurrence, is either metastatic or so locally advanced that surgical resection is unlikely to be carried out with curative intent.

Diagnosis

Diagnostic recommendations are directed at previously undiagnosed advanced colorectal cancer, specific investigative procedures and new diagnostic techniques.

At initial presentation, approximately 30% of patients with colorectal cancer have an advanced stage of the disease. More frequently, advanced colorectal cancer develops during follow-up and is detected using specific diagnostic techniques.

Symptoms of this cancer at initial presentation are either caused by the primary tumour or, less commonly, by metastases, and specific symptoms depend on the location of the cancer within the colon or rectum.

The principal differential diagnoses for previously undiagnosed colorectal cancer in both early and advanced stages are irritable bowel syndrome, haemorrhoids, diverticulitis, inflammatory bowel disease, benign polyps, colitis (e.g. ulcerative, infectious and vascular), ovarian cancer and arteriovenous malformation.

Upon identification of advanced disease through metastases, the differential diagnosis will also involve the determination of the site of the primary tumour.

The basic diagnostic procedure for colorectal carcinoma is independent of the disease stage and consists of a physical examination (palpation of the abdomen, digital rectal examination for rectal cancer), endoscopy (sigmoidoscopy/proctoscopy 15 cm into rectum, then colonoscopy through the remainder of the colon), biopsy (conducted during endoscopy for colorectal samples) and radiology (X-ray following double-contrast barium enema to identify irregular filling 'apple core' lesions). Total colonoscopy is preferred to other endoscopic procedures, and to contrast enema, especially in cases involving blockage. Computed tomography (CT) scans of the abdomen and pelvis, abdominal ultrasound scans and chest X-rays (CT scan of the thorax, if indicated) are used to determine local and distant tumour spread. Various blood tests (liver function, complete blood count and serum carcinoembryonic antigen) should be carried out.

The serum carcinoembryonic antigen test is primarily used in follow-up rather than diagnosis and should be used in preference to the serum tumour markers CA 19-9, CA 50 and CA 195, which have been reported to have slightly lower diagnostic power [2].

A biopsy is normally necessary, but may not be required in cases of metastatic disease in which the diagnosis is unambiguous and proven (multiple lesions, increasing with time, with elevated and increasing levels of serum carcinoembryonic antigen).

An unambiguous diagnosis of metastatic disease can be made on the basis of either: (1) radiographic evidence of two or more lung lesions preceded by histological evidence of colorectal cancer within the last 5 years; (2) two or more hepatic lesions on ultrasound or CT scan and elevated serum carcinoembryonic antigen levels in patients with a history of recent (<5 years) colorectal cancer; or (3) radiographic evidence of an expanding lesion that is clinically regarded as indicating a possible relapse (painful expanding lesions in patients previously operated on for rectal cancer).

Staging

The Dukes' system of staging for colorectal cancer is currently the most widely used, but its simple hierarchy lacks the versatility to describe different levels of primary, nodal and metastatic progression. The tumour, node, metastases (TNM) system [3], more commonly used by surgeons, is much more specific because the primary tumour, lymph node involvement and distant metastases are staged separately and in parallel. However, the TNM system lacks sufficient detail in its description of metastases.

The International Working Group in Colorectal Cancer recommends that the TNM system be used in the staging of advanced colorectal cancer, with additional record being made of the location of metastases (hepatic versus extrahepatic), the number of metastases and the degree to which the liver is affected.

Management strategy

The most important consideration in the management of advanced colorectal cancer is the need, irrespective of guidelines, to consider every patient as an individual, and every case as separate. Members of the management team should all strive to understand the unique needs of each patient and take these into consideration when formulating treatment strategy. These recommendations

should be viewed as a starting point, with modifications made to suit the needs of each patient.

Ideally, the patient should be treated in a specialist centre, by a team of specialists, who meet regularly to review the case and plan an individual management strategy based upon consensual, audited guidelines. If a designated colorectal cancer management team is not possible due to local resource limitations, specialists should attempt to create an environment as close to it as possible through close collaboration, a planned schedule of case reviews and audited management plans customized to individual cases.

Ideally, members of the multidisciplinary management team should include a core of essential or fixed participants, plus an additional group of complementary members. The core members should include a surgical oncologist, a medical oncologist, a radiation oncologist, a gastroenterologist (in some countries) and an oncology nurse.

The core team members should plan individual treatment strategies for discussion with other team members and the patient before a final decision is made. In addition to the necessary treatment provided by core members of the team, auxiliary services such as psychosocial review are essential given the seriousness of the disease and its emotional, financial, and social impact on the patient. Frequency of team meetings should be driven by the needs of each case, with the entire team deciding on an appropriate schedule. However, the team should meet on a regular basis. Meetings may be needed as often as weekly or as infrequently as every 3 months, depending on the patient being treated.

Due to the investigational nature of treatment for advanced colorectal cancer, participation in clinical trials should be encouraged.

Since the majority of an advanced colorectal cancer patient's time is spent in the community, it is essential that effective communication between the multidisciplinary team and primary health-care service providers is established and maintained. This should include ongoing communication with the patient, the GP, community nurses, social and psychiatric services, hospice and palliative care services and community pharmacists, where applicable. Education should also be an important part of the communications process, both between the multidisciplinary team and community health-care providers, and between professional and patient.

Effective referral between primary and secondary health care requires effective colorectal cancer screening services, increased use of diagnostic algorithms by GPs (who encounter relatively few cases) and ready access for patients with suspected colorectal cancer to early diagnostic units. GPs also require information on the symptomatic treatment of advanced colorectal cancer, the management of side effects and guidelines on when to refer.

An audit should encompass a review of case management and clinical outcome, in addition to treatment costs.

Therapy considerations

Any recommendations for therapy must begin with an understanding of treatment objectives. The Working Group agrees that the objectives of treatment for advanced colorectal cancer should include a cure (for patients in whom the primary tumour is controlled and distant metastases resectable), palliation of symptoms, prolongation of median survival, delay of disease progression and associated symptoms, objective response and improved quality of life.

Treatment options for advanced colorectal cancer include surgery, radiotherapy, chemotherapy, combined modality therapy and palliative care.

There are many issues surrounding therapy considerations, including diagnosis/prognosis, toxicity and the risk : benefit ratio, previous treatments and patient wishes. All of these issues are addressed in detail in the recommendations document [1]. The present paper presents recommendations on specific therapeutic modalities.

Surgery

Surgeons should be consulted in all cases of advanced disease. The objectives of surgery in advanced colorectal cancer are a cure in cases of advanced disease characterized by isolated, resectable metastases and a primary tumour that has either been successfully resected or is recurrent but resectable, and palliation where surgery may improve bowel function or relieve discomfort.

Patients with an isolated, solitary tumour or localized metastases should be considered for resection. When metastases can be resected with curative intent, surgery should be performed as soon as possible. Deferring surgery due to anticipated patient relapse is not justified.

Unresectable, locally advanced colorectal cancer may be operable following down-sizing of the tumour by combined modality radiotherapy and chemotherapy.

Palliative surgery to avoid or treat intestinal obstruction can be a most important intervention. Primary tumours should be considered for palliative resection even if metastases are present, unless the prognosis is very poor.

Radiotherapy

Radiotherapy in advanced colorectal cancer may be either potentially curative, or palliative. Radiotherapy can be given with curative intent in two instances [4]: (1) to downstage T4 rectal or recurrent colon cancer in the pelvis before surgery; or (2) post-operatively following re-

section with close or positive margins, although results in patients with residual disease appear to be inconclusive. Intra-operative radiotherapy remains investigational but is a promising new approach.

Specific doses and techniques for curative radiotherapy in locally advanced colorectal cancer are discussed in the recommendations document [1].

Palliative radiotherapy may be used for both the palliation of unresectable disease in surgically inoperable patients and the symptomatic treatment of metastases.

Chemotherapy

The function of chemotherapy is palliative in the majority of cases of advanced colorectal cancer. The side effects of traditional mainstay therapies such as combined 5-fluorouracil and folinic acid (leucovorin), particularly on the gastrointestinal tract, emphasize the need for a careful risk : benefit assessment before choosing whether, and how, to treat [5]. Additionally, the impact of administration schedules on the patient's normal daily activity should be considered. Chemotherapy should usually be reserved for patients whose functional status would allow outpatient treatment (Karnofsky >50; World Health Organization performance status ≤2).

New agents should be considered, particularly those that offer improved tolerability and ease of administration compared to existing agents. One of these new agents, raltitrexed ('Tomudex', formerly ZD1694) is a direct and specific inhibitor of thymidylate synthase [6]. It is recommended for single-agent use in advanced colorectal cancer.

Specific regimens recommended for first-line chemotherapy for advanced colorectal cancer are discussed in detail in the main document [1].

Treatment should be continued for 3 months, unless progression or intolerable side effects have occurred, and thereafter until the patient ceases to respond.

Options for second-line chemotherapy are also discussed in the recommendations document [1].

Of primary importance in patients with advanced colorectal cancer is the need to encourage participation in clinical trials, due to the investigational nature of chemotherapy for advanced colorectal cancer and the ongoing investigation of new agents and different regimens for use in this area.

Combined modality therapy

Combined modality therapy involves the use of surgery, radiotherapy and chemotherapy in combination. The recommendation of the International Working Group in Colorectal Cancer is for close and careful collaboration between specialities, and the use of all approaches as parts of an integrated treatment package.

Palliative supportive care

Palliative supportive care is designed to treat symptoms, without the intention of affecting the course of disease.

Patient selection is critical; palliative care alone should be considered only if one of the following criteria is met: (1) poor performance status (World Health Organization > 2/Karnofsky < 50) or mental incapability; (2) patients in whom standard chemotherapy has failed and who do not wish to receive further active treatment; or (3) patients in whom end-organ dysfunction mitigates against further chemotherapy.

Symptoms requiring palliative supportive care include pain, loss of appetite, nausea and vomiting, shortness of breath, symptoms of anaemia, constipation and diarrhoea. Palliative care should be specifically managed by an appointed member of the multidisciplinary team.

Monitoring therapy

Considerations for monitoring therapy should include an assessment of efficacy, an evaluation of the response, routine surveillance for metastatic disease, measurement of toxicity and continuation or withdrawal of treatment. Techniques for evaluating the response, surveillance tools for metastatic disease and factors that should be used to determine continuation or withdrawal of treatment are discussed in detail within the recommendations [1].

Tumour response should be assessed by techniques such as a clinical examination (hepatomegaly, Virchow's nodes), chest X-ray, CT scan (trials), ultrasound scan and the serum carcinoembryonic antigen test. Toxicity should be assessed according to predefined criteria (usually the National Cancer Institute's Common Toxicity Criteria). The decision to continue or withdraw treatment should be based on the clinical response (tumour regression, tumour progression, reduction in symptoms and delay in symptoms), toxicity and other factors including the performance status of the patient, the quality of life of the patient, the patient's wishes and any complications.

Auxiliary management and patient support

In advanced colorectal cancer, patient support should include the consideration of areas such as nutrition, pain control, psychological support, patient education and quality-of-life assessment.

Education and the provision of information is critical in patient support. It is essential that information be provided to patients in carefully considered ways. There are national and cultural differences in attitudes towards the availability of information to patients.

The International Working Group in Colorectal Cancer recommends that information be available on request to all patients (verbally on a 'walk-in' basis if possible, and in the form of clearly written take-home information).

Information should be made available for release in a stepwise way. Patients should be given the opportunity to ask more questions if required, but unsolicited information should be given with care and with a sensitive understanding of the individual.

The responsibility for informing patients about the basic nature of their condition and the selection and progress of management strategy rests with the supervising physician or surgeon. It is strongly recommended that a supportive person be present when sensitive information is given to the patient about his or her condition and prognosis.

Multidisciplinary team members should be encouraged to make themselves available to respond to patient questions following the initial conversation between patient and specialist. It is advisable to have the oncology nurse present at key meetings between consultant and patient because the oncology nurse will have more regular contact with the patient and can therefore be more often available to follow-up queries for the patient. Patients should be made aware of other agencies able to help them, such as voluntary sector organizations and local and national support groups.

Availability

The recommendations [1] will be made available to all professionals involved in the treatment of patients with advanced colorectal cancer, as a service to help guide the development of an optimal treatment approach and, it is hoped, to facilitate greater use of multidisciplinary resources to improve the treatment available for advanced colorectal cancer

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