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Forum

Keeping abreast of the evidence in management of colorectal cancer

Finlay Macrae

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Primary prevention of colorectal cancer

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Abstract

Colorectal cancer is the third most common type of cancer worldwide, with the highest incidences in Australia, New Zealand, Europe and North America, and the lowest in Africa and South-Central Asia. Rates are substantially higher in males than in females. Bowel cancer is the most preventable cancer type in Australia, with an estimated 44% preventability achievable through improvements in diet and physical activity. In 2005, the National Health and Medical Research Council published *Guidelines for the Prevention, Early Detection and Management of Colorectal Cancer*. This chapter builds on the conclusions from these guidelines, drawing on the comprehensive review undertaken by the World Cancer Research Fund/American Institute for Cancer Research (Second Expert Report) published in 2007, and Continuous Update Project review published in 2011. The evidence is convincing that physical activity and foods containing dietary fibre protect from colon and colorectal cancer respectively, and that red and processed meat, ethanol from alcoholic drinks and body and abdominal fatness increase risk of colorectal cancer. Strategies to support these lifestyle and dietary changes in practice should be strongly recommended. The smoking of tobacco probably causes colorectal cancer and foods containing garlic, milk and calcium probably protect against colorectal cancer. The use of anti-inflammatory drugs as prophylaxis against further adenoma development in individuals with familial adenomatous polyposis should be considered, especially where surgery is inappropriate; low dose aspirin in those at high familial or personal risk is recommended. Based on the current evidence, the level of protection offered by physical activity and dietary fibre, and the level of risk resulting from the consumption of red and processed meat and high body and abdominal fatness, is stronger and more conclusive than the evidence documented in previous reviews.

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Screening for colorectal cancer – new evidence in the last 10 years

Graeme P Young

Abstract

The evidence base for screening for colorectal cancer has expanded at a rapid pace in the last 10 years. Faecal immunochemical tests for haemoglobin have been proven to be superior to guaiac-based faecal occult blood tests in terms of acceptability to screenees and analytic and clinical sensitivities for cancer and advanced adenomas. In addition, flexible sigmoidoscopy has been proven to reduce incidence and mortality from colorectal cancer, demonstrating that structural detection of preinvasive lesions will reduce its incidence. Both methods are now proven screening tool options and should be considered for implementation in screening programs. The requirements of screening programs are also much clearer. The monitoring and reporting outcomes of screening programs have been subject to consensus processes and have been clearly enunciated. They include quality, population acceptance, costs, adverse effects and measures of disease burden. The data needed to measure these should be an obligatory aspect of organised screening programs. The evidence base supporting communication strategies has expanded. These, combined with strategies proven to increase participation, should be part of all screening programs. Australian society is clearly benefitting from colorectal cancer screening and guidelines need revision to reflect the new evidence.

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Risk profiling: familial colorectal cancer

Aung Ko Win, Driss Ait Ouakrim, Mark A Jenkins

Abstract

Family history of colorectal cancer is a well-established and consistently strong risk factor for this disease. However, simply counting the number of affected relatives is an imprecise measure of colorectal cancer risk. We have reviewed current colorectal cancer screening guidelines from Australia, New Zealand, Canada, the US and UK, and found that all, including the Australian National Health and Medical Research Council 2005 guidelines, assign people to risk categories largely based on age and rudimentary metrics of family history and recommend screening regimens. We claim that these guidelines are not sufficiently precise for a large proportion of people within these categories, as there is a substantial variation in colorectal cancer risk, even for people with the same family history, and even for people with a predisposing mutation in the same gene, or set of genes. If there was a tool to estimate individual colorectal cancer risk based on all known risk factors for the disease - personal and family history of cancer (including ages, ages at diagnoses, and genetic relationships across multiple generations), all known genetic factors (rare high-risk genetic mutations as well as common genetic variants), environmental factors and personal characteristics - then accurate prediction of future risk of colorectal cancer (personalised risk) may be possible. The development and utility of such a comprehensive risk prediction tool is important for appropriate personalised clinical management, including targeted colorectal cancer screening.

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Familial colorectal cancer clinics

Nicholas Pachter

Abstract

Familial cancer clinics strive to identify at-risk individuals with an inherited predisposition to cancer. Familial predisposition to colorectal cancer includes Familial Adenomatous Polyposis and Lynch Syndrome. The latter condition has no clear phenotype, leading to difficulties in its recognition. While family history remains an important tool in diagnosing inherited predisposition to cancer, many cases of Lynch Syndrome are diagnosed in the absence of a clear-cut family history. Therefore identification of Lynch Syndrome cases has moved in the direction of tumour-based testing, initially on cases selected for family history, young age of onset and tumour histological features, but now it has been suggested that Lynch Syndrome be screened for more widely via tissue testing of all newly diagnosed colorectal cancers under a certain age (e.g. <60 years).

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Risk profiling and surveillance: previous adenomas and colorectal cancer

Finlay Macrae and Karen Barclay

Abstract

The brief of this issue of *Cancer Forum* is to review information available since the 2005 publication of the National Health and Medical Research Council relating to risk management of individuals with previous adenomas or colorectal cancer. However, this can be abbreviated to the last three years, as Cancer Council Australia commissioned a review of colonoscopy in surveillance for colorectal cancer, which included adenoma and cancer follow-up. This has subsequently been endorsed by the National Health and Medical Research Council. Since then, there have been advances in some areas, although many questions remain and clinical judgement comes into play. In the current era of accountability, economic hardship and increasing demand, surveillance strategies should be proven effective and individualised, based on issues such as fitness, quality of life and personal preferences. International guidelines have aligned, although the simpler strategies specified in European guidelines are noted with interest. Despite clear recommendations, the lack of guideline use in routine practice is concerning and widespread promulgation of simple ‘aid-memoirs’ could help, along with incentives. Information supports risk related to multiplicity, size and histopathology of adenoma and cancer findings at the index colonoscopy. Quality issues relating to colonoscopy and pathology reporting are being driven through professional fora and training. The paradox of multiplicity and quality colonoscopy needs addressing in a patient-centred response. Risk-stratification and adjustment over time is likely to gain increasing importance. The serrated pathway, its biology and epidemiology, have attracted attention for the rapid progression and association with interval cancers. Practice points for the management of malignant polyps continue to be topical. The effectiveness of intensive follow up strategies following curative treatment for colorectal cancer remains unproven, although colonoscopic surveillance is still of value.

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Targeting treatment for colorectal cancer: the EGFR antibody story

Melvin Chin and Robyn L Ward

Abstract

Frequent overexpression of the epidermal growth factor receptor in colorectal cancer was the rationale for the development of anti-epidermal growth factor receptor antibodies. The development of the drug cetuximab, led to considerable expectations in terms of clinical and commercial success. The registration of the anti- epidermal growth factor receptor antibodies, cetuximab and panitumumab, was granted on the basis of improvement in progression free survival. Other drugs targeting the epidermal growth factor receptor, such as the oral tyrosine kinase inhibitors, have minimal efficacy in colorectal cancer when used alone, and are too toxic when combined with chemotherapy. Cetuximab and panitumumab have activity only in patients with metastatic disease who have a reasonable performance status. Retrospective analyses of tumour samples collected from trial enrolees showed the presence of KRAS mutations in exon 2 were a negative predictor of response to the anti-EGFR antibodies. Recent data suggests that patient selection should be based on a more extensive analysis of KRAS, NRAS, BRAF and potentially other genes. The anti-EGFR antibodies have been used alone or in combination with other chemotherapies, however use with oxaliplatin appears to compromise patient outcomes. When used as monotherapy, toxicities include rash and fatigue, however more severe adverse effects are observed when used with chemotherapy. Anti-epidermal growth factor receptor treatments for colorectal cancer, demonstrate the complexity of using targeted treatments. They remain a useful treatment in colorectal cancer but have not fulfilled their initial expectation of being highly effective and non-toxic treatments.

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Adjuvant therapy for colorectal cancer

Michael Michael and John R Zalcberg

Abstract

Patients with resected colon cancer (stage III [T1 to T4, N1-N2] or high-risk stage II [T3 or T4, N0]) or stage II/III rectal cancers (T3 or T4, N0-2) are at significant risk of local and distant failure, with reduced survival due to microscopic residual disease. To reduce this risk, adjuvant therapy has been the standard of care for both cancer populations, as stated in the 2005 *Guidelines for the Prevention, Early Detection and Management of Colorectal Cancer* developed through Cancer Council Australia's Clinical Guidelines Network. This review provides an update to the guidelines. Patients, with resected stage III colon cancer should, where possible, be offered six months of adjuvant chemotherapy. The optimal regimen is oxaliplatin-5FU or -capecitabine, based on relevant clinical factors. For patients with resected stage II colon cancer, adjuvant 5FU-based chemotherapy should be considered for those at particularly high risk of relapse. For patients with stage II/III rectal cancer, treatment approaches include: (i) short course radiotherapy and immediate total mesorectal excision; or (ii) neoadjuvant chemoradiotherapy (with 5FU infusion or capecitabine) followed by TME. Post-operative adjuvant chemotherapy should be offered to all medically fit patients. At present, there are no markers to identify patients who may not require neoadjuvant chemoradiotherapy or who can avoid surgery.

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Surgery for colorectal cancer

Cherry E Koh and Michael J Solomon

Abstract

Surgery is the mainstay in the treatment of colorectal cancer. Considerable progress has been made in the past eight years since the publication of the most recent clinical practice guidelines for colorectal cancer by the National Health and Medical Research Council. The most notable changes in surgery are the result of trials in minimally invasive approaches, including laparoscopic cancer resection, new advances yet to be tested such as robotic assisted cancer resection and the use of self-expanding metallic stents in patients with curable malignant obstruction. This paper provides an overview of these minimally invasive techniques and summarises the recommendations that could be considered for inclusion or update in the next edition of the guidelines.

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Colonoscopy and colorectal cancer

Natalie Kiel and Mark Appleyard

Abstract

Colonoscopy has a central role in the detection and prevention of colorectal cancer. This is based on the fact that most colorectal cancer develops from premalignant adenomatous or serrated polyps, which can be removed at colonoscopy and hence prevent the development of colorectal cancer. The success of colonoscopy in preventing bowel cancer is dependent on the quality of the colonoscopy performed. This review highlights the key performance indicators measuring quality of colonoscopy, including consent, indication, preparation, caecal intubation rates, polyp detection and removal, withdrawal time and complication rates,

and sets minimum target recommendations for each of the key performance indicators.

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Surviving bowel cancer

Mark Dunstan

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Palliative care and colorectal cancer

Penelope Cotton, Peter Eastman, Brian H Le

Abstract

Recent advances in anti-cancer treatment have seen improvements in survival for patients with metastatic colorectal cancer. Increasingly, patients with advanced disease are living longer, sometimes with significant morbidity related to the disease or its treatment. Integration of palliative care in the management of patients with advanced malignancy improves symptom control and quality of life for patients and their families. This article reviews the role of palliative care and provides an overview of current management for commonly experienced symptoms in patients with colorectal cancer.

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