Clinical studies over the past decade, which focused on a variety of areas, ranging from refinements in diagnostic techniques to the development of new chemotherapy drugs, have led to considerable improvement in the outcomes of patients with colorectal cancer.

Diagnosis and Prevention

The increased use of flexible sigmoidoscopy and colonoscopy in average-risk patients older than 50 years of age is likely to reduce considerably the risk of late-stage cancers. Identification of patients at higher risk, based on family history of colorectal cancer or polyps, has provided improved screening and monitoring strategies. The National Polyp Study, for instance, has devised a strategy for the endoscopic surveillance of patients after removal of an adenoma.

Perhaps even more exciting, albeit somewhat futuristic, are new opportunities for effective chemoprevention with aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), or the new cyclo-oxygenase (COX) 2-specific NSAIDs.

Rectal Cancers

Although this issue of CA is more specifically focused on colon cancer, treatment of rectal cancer patients continues to involve the appropriate use of neoadjuvant and postoperative adjuvant chemoradiation therapy. Patient selection for neoadjuvant therapy through the use of computed tomography and endorectal ultrasound, for example, is rapidly becoming widespread.

Surgical technique utilizing sharp mesorectal excision and autonomic nerve preservation appears to maximize the oncologic outcome and preserve sexual and sphincter function in the majority of patients.

The papers in this issue address three important areas in the clinical care of patients with colorectal cancer: The use of minimal-access surgical techniques; the increasingly effective use of adjuvant therapy in colon cancer; and the delineation of potentially curative surgical therapy of patients with isolated hepatic metastases.

Laparoscopic Techniques

It would seem overwhelmingly obvious that minimal-access surgery using laparoscopic techniques would result in more rapid recovery after operation. Laparoscopic cholecystectomy, for example, indeed represented a revolution in abdominal surgery. However, a randomized trial demonstrated that surgery using the minimal-access technique provided only a
slight advantage, with increased complications.\(^8\)

Driven by patient preferences, the use of laparoscopic-assisted surgery was applied initially to benign colon disease, and more recently to the treatment of malignant disease.\(^9\) The approach utilizes laparoscopic techniques for mobilization of the bowel. For experienced surgeons, such resections are technically feasible, and laparoscopic surgery is being used increasingly for palliative colostomy, palliative right colectomy, and right colectomy in the patient with a large sessile adenoma in the cecum.\(^9\) Intracorporeal anastomoses, however, are rarely done.

Dr. Greene discusses salient concerns about the application of this surgical technique for the treatment of cancer patients in this issue of CA.\(^10\) With early cancers, for example, which are not visible from the outside, the lesion site should be “tattooed” with India ink. This avoids removing the wrong segment of bowel.

Whether the putative improvement in recovery will be demonstrated, and whether oncological outcomes will be comparable to those achieved with open procedures, are questions that await the results of randomized clinical trials underway in the United States and the United Kingdom.

As Dr. Greene points out, pending these results, such surgical approaches should be considered investigational rather than the standard of care.

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**Adjuvant Therapy**

**NODE-POSITIVE DISEASE**

After three decades of negative or equivocal clinical trials, the data are quite compelling that fluorouracil-based chemotherapy regimens increase long-term survival and cure in patients with node-positive colon (and rectosigmoid) cancer.

Dr. Macdonald’s paper presents efficacy data and toxicity profiles for several common regimens, as well as an excellent review of ongoing and future multicenter trials.\(^11\) As no current trials in node-positive cancer patients have a “surgery-only” control arm, it is likely that large numbers of patients will feel comfortable about continuing to enter these trials.

As with all adjuvant programs, careful assessment of overall survival and disease-free survival should be balanced against acute and late toxicity, cost, and overall quality of life under treatment. Future studies in node-positive patients will evaluate the use of new agents, such as irinotecan, oxaliplatin, and various immunological strategies, such as cytotoxic antibodies (17-1A) and vaccines (anti-CEA) as potential complementary maneuvers with chemotherapy.

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**NODE-NEGATIVE DISEASE**

Appropriate use of adjuvant therapy in the node-negative colon cancer patient remains problematic. Patients with clinical obstruction or perforation through the tumor, or those with transmural penetration to the free mesothelial surface (T4), generally have worse prognoses.

Clinical, pathological, and biological measures are being used to identify a subset of node-negative colon cancer patients likely to benefit from adjuvant therapy. DNA ploidy and percent S-phase, for example, have been studied for a decade, with conflicting results. The Mayo clinic ploidy data, however, are quite compelling. Molecular markers, such as allelic deletion, p53 mutation, and
metastasis-associated molecular changes, are promising but not yet suitable for routine use.

Unfortunately, “high-risk” patients often receive treatment outside of clinical trials. Unlike trials involving patients with node-positive disease, immunotherapy trials in node-negative patients all have a “surgery-alone” control, and are appropriate for many patients.

Surgery for Hepatic Metastases

Despite a lack of randomized clinical trial data, the report by Dr. Fong provides compelling evidence from multiple centers that hepatic resection, even in patients with multiple liver metastases, can result in long-term survival and cure. In addition, using current surgical technique, major liver resection in the hands of experienced teams can be done with a mortality of approximately 3%. Improved patient selection by high-quality magnetic resonance imaging, $^{18}\text{FDG}$ positron emission tomography, and laparoscopy should further improve results. Systemic adjuvant therapy following hepatic resection should be offered to patients, particularly if they have not had adjuvant therapy or such was completed at least a year before surgery.

In view of the advances in colorectal cancer prevention, screening, and therapy that have already been made, as well as those sure to be achieved in the near future, family physicians, internists, gynecologists, surgeons, and oncologists should encourage appropriately selected patients to enter clinical trials and thereby accelerate this process.

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