Complete Summary

GUIDELINE TITLE

Practice parameters for the treatment of patients with dominantly inherited colorectal cancer (familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer).

BIBLIOGRAPHIC SOURCE(S)

Church J, Simmang C. Practice parameters for the treatment of patients with dominantly inherited colorectal cancer (familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer). Dis Colon Rectum 2003 Aug;46(8):1001-12. [108 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

* * REGULATORY ALERT * *

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released:

On April 7, 2005, after concluding that the overall risk versus benefit profile is unfavorable, the U.S. Food and Drug Administration (FDA) requested that Pfizer, Inc voluntarily withdraw Bextra (valdecoxib) from the market. The FDA also asked manufacturers of all marketed prescription nonsteroidal anti-inflammatory drugs (NSAIDs), including Celebrex (celecoxib), a COX-2 selective NSAID, to revise the labeling (package insert) for their products to include a boxed warning and a Medication Guide. Finally, FDA asked manufacturers of non-prescription (over the counter [OTC]) NSAIDs to revise their labeling to include more specific information about the potential gastrointestinal (GI) and cardiovascular (CV) risks, and information to assist consumers in the safe use of the drug. See the FDA Web site for more information.

Subsequently, on June 15, 2005, the FDA requested that sponsors of all non-steroidal anti-inflammatory drugs (NSAID) make labeling changes to their products. FDA recommended proposed labeling for both the prescription and over-the-counter (OTC) NSAIDs and a medication guide for the entire class of prescription products. All sponsors of marketed prescription NSAIDs, including Celebrex (celecoxib), a COX-2 selective NSAID, have been asked to revise the labeling (package insert) for their products to include a boxed warning, highlighting the potential for increased risk of cardiovascular (CV) events and the well described, serious, potential life-threatening gastrointestinal (GI) bleeding

associated with their use. FDA regulation 21CFR 208 requires a Medication Guide to be provided with each prescription that is dispensed for products that FDA determines pose a serious and significant public health concern. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Inherited colorectal cancer: familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer

GUIDELINE CATEGORY

Counseling
Management
Prevention
Treatment

CLINICAL SPECIALTY

Colon and Rectal Surgery
Gastroenterology
Internal Medicine
Oncology
Radiation Oncology

INTENDED USERS

Health Care Providers
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide appropriate recommendations for the treatment of patients with dominantly inherited colorectal cancer

TARGET POPULATION

Patients with or at-risk of dominantly inherited colorectal cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment/Management of Familial Adenomatous Polyposis

1. Patient counseling
2. Colectomy and ileorectal anastomosis
3. Proctocolectomy with ileostomy
4. Proctocolectomy with ileal pouch-anal anastomosis
5. Colectomy using laparoscopy or Pfannenstiel incision in children
6. Lifetime follow-up of the rectum, pouch, and ileostomy
7. Proctoscopy using video endoscopy
8. Random biopsies
9. Snare removal of adenomas
10. Chemoprevention with sulindac [Clinoril®), celecoxib, exisulind (not recommended as primary therapy)
11. Duodenectomy or pancreaticoduodenectomy
12. Treatment of desmoid tumors with sulindac; anti-estrogens (tamoxifen, toremifene); the combination of vinblastine and methotrexate; or the combination of doxorubicin and dacarbazine

Treatment/Management of Hereditary Nonpolyposis Colorectal Cancer

1. Patient and family counseling
2. Prophylactic total colectomy and ileorectal anastomosis with rectal surveillance
3. Hemicolectomy plus yearly colonoscopy
4. Total proctocolectomy and ileal pouch-anal anastomosis
5. Anterior proctosigmoidectomy
6. Prophylactic hysterectomy

MAJOR OUTCOMES CONSIDERED

- Risk of colorectal cancer
- Bowel function after surgery
- Number and size of colorectal adenomas
- Incidence of duodenal adenomas
- Risk for uterine cancer in female patients with hereditary nonpolyposis colorectal cancer
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A MEDLINE search of the English language literature was performed to determine the prevailing attitudes and favored treatments of several common but difficult clinical scenarios. These include choice and timing of surgery, management of extracolonic tumors, and the role of preoperative counseling.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Level I
Evidence from properly conducted randomized, controlled trials

Level II
Evidence from controlled trials without randomization
or
Cohort or case-control studies
or
Multiple times series, dramatic uncontrolled experiments

Level III
Descriptive case series, opinions of expert panels

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This manuscript was reviewed by the members of the Standards Committee of The American Society of Colon and Rectal Surgeons and by the Executive Committee of the Collaborative Group of the Americas on Inherited Colorectal Cancer and was approved by the Executive Council of The American Society of Colon and Rectal Surgeons.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The Levels of Evidence (I–III) are defined at the end of the "Major Recommendations" field.

SECTION 1. Familial Adenomatous Polyposis (FAP)

Guideline 1: Treatment Must Be Preceded by Thorough Counseling About the Nature of the Syndrome, Its Natural History, Its Extracolonic Manifestations, and the Need for Compliance With Recommendations for Management and Surveillance.
Level of Evidence: III. Dominantly inherited colorectal cancer syndromes show a striking pattern of cancer in affected families. This is because of the high penetrance (penetrance = percent of patients with the mutation who have the disease) and often-severe expression (expression = clinical consequences of the mutation) of the mutations involved. FAP has a penetrance of close to 100 percent, colorectal cancer occurs at an average age of 39 years, and every affected patient is guaranteed at least one major abdominal surgery. Despite these calamitous prospects, families with FAP adapt well to their disease. Most patients are compliant with recommended treatments, take a keen interest in the syndrome, and play an active role in encouraging relatives to undergo screening. However, when a relative has a bad outcome, either because of severe disease or complications of treatment, family psychology may be affected. Noncompliance, denial, or a refusal to accept recommendations may ensue. The best way of avoiding both bad outcomes and an unfortunate response to them is to provide comprehensive, integrated counseling, support, and clinical services. These sorts of services are best provided through a department, registry, or center with

personnel who have experience in managing patients and families with these syndromes.

Guideline 2: Prophylactic Colectomy or Proctocolectomy Is Routine. The Timing and Type of Surgery Depend on the Severity of the Polyposis Phenotype and to a Lesser Extent on the Genotype, Age, and Clinical and Social Circumstances of the Patient.
Level of Evidence: III. The recommendation for prophylactic colectomy or proctocolectomy in FAP is based on the very high rates of colorectal cancer seen in patients who are not screened. In unscreened patients the incidence of cancer is over 60 percent. Appropriate screening and timely surgery can minimize this. The risk of cancer is not uniform, however, and is related to the severity of the colonic polyposis. One study showed the rate of cancer for patients with >1,000 colonic polyps was twice that of patients with <1,000 colonic polyps. In its turn, the severity of the colorectal polyposis is often related to the site of the APC mutation in a family. The "hot spot" mutation at codon 1309 is in an area of the gene where mutations always cause severe disease. Mutations in codons 3 and 4 are classically associated with attenuated FAP, while mutations in the part of codon 15 that is 3´ of codon 1450 are usually associated with mild colorectal disease. Mutations in exons 5 to 15E have a variable colorectal phenotype, where some family members have relatively mild disease and others severe. The important aspects of surgery to consider are its timing, its type, and the technical options to be used.

Timing of Surgery. Even in patients with severe disease, cancer is rare under the age of twenty. At-risk family members start screening (either genetic or with flexible sigmoidoscopy) at around puberty. If there is a positive genotype or an adenoma is seen on sigmoidoscopy, colonoscopy is recommended. The risk of cancer of any individual patient can be estimated from the size and number of the adenomas seen on colonoscopy and surgery planned accordingly. For patients with mild disease and low cancer risk, surgery can be done in mid teen years (15–18 years). Where there is severe disease, or if the patient is symptomatic, surgery is done as soon as convenient after diagnosis.

Type of Surgery. There are three main surgical options: colectomy and ileorectal anastomosis (IRA), proctocolectomy with ileostomy (TPC), and proctocolectomy with ileal pouch-anal anastomosis (IPAA). For any of these options there are choices of technique. The ileal pouch-anal anastomosis can be stapled, leaving 1 to 2 cm of anal transitional epithelium and low rectal mucosa, or it can be handsewn after a complete anal mucosectomy. The operation can be done conventionally (i.e., open), laparoscopically, or laparoscopically assisted. The ileostomy may be a regular end stoma or one of the varieties of continent ileostomy (K or T).

Choice of Procedure. TPC is almost never done as a first operation except when a proctocolectomy is required and there is a contraindication to a pouch-anal anastomosis (e.g., a mesenteric desmoid tumor prevents the pouch from reaching the pelvic floor, a low rectal cancer invades the pelvic floor, or poor sphincters mean inability to control stool).

There is debate among authorities on which of the other two options should be preferred. Some recommend IPAA for all or almost all FAP patients, basing their

recommendation on the risk of rectal cancer after IRA and equivalent quality of life after the two operations. Others have shown better functional outcomes after IRA and recommend it for patients with mild colorectal polyposis. However, the risk estimates of rectal cancer that are an overriding concern for the proponents of universal IPAA are based on data collected before restorative proctocolectomy was an option and may well be overestimates, especially when applied to patients with mild disease. The risk of rectal cancer after IRA is strongly related to the severity of colorectal polyposis at presentation, and IRA is a reasonable option in mildly affected patients (<20 rectal adenomas, <1,000 colonic adenomas). Retrospective data show that such patients have a very low risk of rectal cancer and include all those with attenuated FAP. Bowel function is usually good after IRA, the operation is simple, and complication rates are relatively low. Bowel function after a stapled IPAA is almost as good as with an IRA, and the anastomosis is usually safe enough to allow consideration of the option of avoiding a temporary ileostomy.

There is no argument that patients with severe rectal (>20 adenomas) or colonic (>1,000 adenomas) or those with a severely dysplastic rectal adenoma, a cancer anywhere in the large bowel, or a large (>3 cm) rectal adenoma should have a primary IPAA. A stapled IPAA is associated with a risk of anal transitional neoplasia in 30 percent of patients, although if serious neoplasia occurs (high-grade dysplasia or carpeting of the mucosa), the transitional zone can usually be stripped transanally and the pouch advanced to the dentate line. Even mucosectomy and handsewn IPAA is associated with anal neoplasia, although at a lower rate. The disadvantage of anal mucosectomy is worse function and increased complication rates. Both IRA and IPAA require lifelong surveillance of the rectum or pouch, because both are at risk of developing adenomas.

Choice of Technique. Mobilization of the colon using minimally invasive techniques such as laparoscopy or a Pfannenstiel incision is ideal for performing colectomy in children, because it minimizes the trauma of the surgery and the pain of the incisions. Its cosmetic result is appealing and it allows an early return to full activities. Whether minimally invasive techniques lower the risk of postoperative intra-abdominal desmoid tumors is unknown, but the concept is attractive. A preoperative erect abdominal x-ray will usually show the position of the flexures and indicate whether use of a Pfannenstiel incision for mobilizing the colon is feasible.

Guideline 3: Lifetime Follow-Up of the Rectum (After IRA), Pouch (After IPAA), and Ileostomy (After TPC) Is Required; Increasing Neoplasia in the Rectum Is an Indication for Proctectomy.
Level of Evidence: III. The combination of a germline APC mutation, stasis of stool, and glandular epithelium is potent at producing epithelial neoplasia. Adenomas and carcinomas have been described in the rectum, the ileostomy, and the ileal pouch itself, with the risk and severity of neoplasia increasing with time. The risk of severe neoplasia is mainly determined by the position of the mutation in the gene, as reflected by the severity of the polyposis. Severely affected patients have such a high risk of rectal cancer after IRA that subsequent proctectomy is almost routine and initial IPAA is to be preferred. Yearly endoscopic surveillance of the bowel after the index surgery for FAP is standard. Two thirds of patients undergo spontaneous regression of rectal polyps after IRA, an effect that lasts three to four years. Subsequent surveillance will give a picture

of the stability of the rectal mucosa. Small (<5 mm) adenomas can be watched, although random biopsies are done to exclude severe dysplasia. Increasing number and size of adenomas are indications for more frequent surveillance, and adenomas >5 mm should be removed cleanly with a snare. Repeated fulguration of rectal polyps over many years can cause dense scarring that makes cancers flat and hard to see, and rectal dissection during proctectomy can be very difficult. Chronic rectal scarring makes rectal biopsy difficult, because the forceps tend to "bounce off" the scarred mucosa. Furthermore, scarring leads to reduced rectal compliance, increased stool frequency, and a tendency to seepage and incontinence. Severe dysplasia, or villous adenomas >1 cm, are indications for proctectomy. Proctoscopy is best done with a video endoscope, because comfort is enhanced and the view is better. Excellent preparation and a good view are essential to pick up early cancers that can be flat and subtle.

Sulindac (Clinoril®; Merck & Co., Inc., West Point, PA), either by mouth or by suppository, is effective in making polyps disappear. Celecoxib reduces polyp load, as does the sulindac metabolite exisulind. However, cancers have been reported in cases where sulindac had been effective in minimizing rectal polyps in the rectum of FAP patients who had had IRA, and these anecdotal cases make the long-term use of chemoprevention for rectal polyposis suspect. If it is used in patients who cannot tolerate rectal polypectomy, or who are unwilling or unable to have a proctectomy, close surveillance (every 6 months) with random biopsies to look for severe dysplasia is needed.

There have been at least three recent reports describing adenomas in ileal pouches, with a frequency and severity that depend on time from the initial surgery. Two prospective studies have independently calculated the rate of pouch polyposis as 42 percent at seven years. There have been anecdotal reports of large adenomas and over 100 adenomas in an ileal pouch. In general these have been treated successfully by oral sulindac, in a dose of 150 to 200 mg twice daily. The full impact of pouch polyposis will not be obvious until the cadre of FAP patients with ileal reservoirs reaches a mean follow-up of 20 years. This is the time to most ileostomy cancers and to the highest rates of rectal cancers after IRA.

Guideline 4: Use of Chemoprevention as Primary Therapy for Colorectal Polyposis Is Not Proven and Is Not Recommended.
Level of Evidence: I to II. Sulindac, celecoxib, and exisulind are nonsteroidal anti-inflammatory drugs that have been shown to reduce the number and size of colorectal adenomas in patients with FAP. While many studies are short-term, two show effectiveness of sulindac maintained over four years. These studies were in patients who had undergone colectomy and IRA. A recent randomized, placebo-controlled, double-blind study of sulindac in genotype-positive, phenotype-negative FAP patients failed to show any effect of sulindac on polyp progression. Furthermore, there have been case reports of cancers occurring in patients with sulindac-mediated ablation of polyps, and the only report of a permanent, complete resolution of rectal polyposis comes from researchers who used sulindac suppositories. The effect on polyps is dependent on continued compliance, and there are significant side effects with each medication. These medications should not be used as an alternative to surgery, except in patients with pouch polyposis or in selected patients with rectal polyposis after IRA in whom surgery is risky or

unwanted by the patient. In these groups of patients, close surveillance (proctoscopy or pouchoscopy every 6 months) is indicated.

Guideline 5: Treatment of Duodenal Adenomas Depends on Adenoma Size and the Presence of Severe Dysplasia. Small Tubular Adenomas With Mild Dysplasia Can Be Kept Under Surveillance, But Adenomas With Severe Dysplasia Must Be Removed.
Level of Evidence: II to III. The incidence of duodenal adenomas in FAP patients is in the range of 80 to 90 percent. All FAP patients therefore undergo screening esophagogastroduodenoscopy starting at age 20 years. The risk of invasive cancer developing in a duodenal adenoma, or in the duodenal papilla, is considerably higher than that for the average population, but in absolute terms it is still low. The aim of endoscopy is not to eradicate all neoplasia but to make sure that there is no severe dysplasia. Studies of the natural history of duodenal neoplasia in FAP show that rapid progression of dysplasia is uncommon, occurring in only 11 percent of cases over a mean follow-up of seven years. Prospective, randomized studies have shown that treatment with nonsteroidal anti-inflammatory drugs is ineffective in treating duodenal adenomas, although a recent report indicates that celecoxib (see Note from NGC below) may have some effect. If they are not medically treated, low-risk adenomas (small, tubular, low grade dysplasia) may be biopsied and left alone. High-risk adenomas (>1 cm, villous) are treated. Adenomas with confirmed high-grade dysplasia must be removed. As endoscopic or even transduodenal excision or destruction is ineffective in the long term; duodenectomy has to be considered for duodenal adenomas with high-grade dysplasia after the diagnosis has been confirmed on review by an experienced gastrointestinal pathologist.

Guideline 6: Duodenectomy or Pancreaticoduodenectomy Is Recommended for Patients With Persistent or Recurrent Severe Dysplasia in the Papilla or Duodenal Adenomas.
Level of Evidence: III. A review of literature reporting treatment of advanced duodenal adenomas shows that recurrence is almost guaranteed unless the duodenum is removed. Transduodenal polypectomy or endoscopic polypectomy may be temporarily effective, but does not offer a permanent cure. The results of pancreas-preserving duodenectomy or pancreaticoduodenectomy for benign or early malignant disease are good, with low recurrence and acceptable morbidity. The outcome of surgery for established cancer is not good with recurrence and death the usual outcome. Although the risk of duodenal/periampullary cancer is relatively low in patients with FAP, patients with persistent high-grade dysplasia in the duodenum or papilla are a high-risk group. Careful surveillance is needed, and conservative surgery or endoscopic therapy may be tried. If the severe dysplasia returns or persists, consideration must be given to duodenectomy.

Guideline 7: Surgery for Intra-Abdominal Desmoid Tumors Should Be Reserved for Small, Well-Defined Tumors With a Clear Margin; Abdominal Wall Desmoid Tumors Should Be Excised Whenever Possible.
Level of Evidence: III. Desmoid tumors are histologically benign overgrowths of fibroaponeurotic tissue occurring rarely in the general population but in 12 to 17 percent of patients with FAP. In the general population desmoids are usually found in limbs or limb girdles; in FAP desmoids are usually (80 percent) intra-abdominal and often (80 percent) present within two to three years of an abdominal surgery. Intra-abdominal desmoid tumors usually involve the

mesentery of the small bowel, where they are intimately involved with the mesenteric vessels. They tend to infiltrate diffusely and kink adjacent bowel loops and may obstruct the ureters. Attempts at excision are often unsuccessful, involve removal of a variable length of small intestine, and are associated with a high morbidity and a high recurrence.

Intra-abdominal desmoid tumors may affect prophylactic colorectal surgery by limiting the length of the small bowel mesentery. This will sometimes prevent an ileal pouch-anal anastomosis. The most common scenario in which this occurs is in patients with Gardner's variant of FAP who need proctectomy after a previous ileorectal anastomosis. Patients need to be warned about this possibility and the likelihood of ileostomy before undergoing the surgery. The second most common site for desmoids in FAP is in the abdominal wall. Abdominal wall desmoid tumors are easier to excise than intra-abdominal tumors, recurrence rates are lower, and the morbidity associated with excision is less. They should be excised with a 1-cm margin. It is often necessary to use mesh to cover the defect in the abdominal wall.

Guideline 8: Intra-Abdominal Desmoid Tumors Involving the Small Bowel Mesentery Are Treated According to Their Rate of Growth and Their Presentation. Clinically Inert Tumors Should Be Treated With Sulindac or Not Treated at All. Slowly Growing or Mildly Symptomatic Tumors May Be Treated With Less Toxic Regimens Such as Sulindac and Tamoxifen or Vinblastine and Methotrexate. Rapidly Growing Tumors Need Aggressive Therapy With Either Very High-Dose Tamoxifen or Antisarcoma-Type Chemotherapy. Radiation Is an Option if Collateral Damage Is Not a Big Concern.
Level of Evidence: III. Intra-abdominal desmoid tumors vary in their clinical behavior from aggressive, relentless growth to indolent, asymptomatic coexistence. There is no single, predictably effective way of managing intra-abdominal desmoids. Evidence suggests that sulindac is partially effective but that a response to this nonsteroidal anti-inflammatory agent may not be noticeable for up to two years. The role of high-dose antiestrogens is uncertain, with one report describing good results in aggressive desmoids with tamoxifen in a dose of 120 mg/day. Toremifene, a more potent antiestrogen than tamoxifen, has some effect on desmoid tumors but seems to be work better in non-FAP desmoids than FAP. A pilot study of the antifibrosis agent pirfenidone resulted in some modest responses. Most aggressive desmoids receive chemotherapy, and there are two regimens reported. The combination of vinblastine and methotrexate has low toxicity and produces some responses. Non-FAP desmoids seem more likely to respond to this combination, although no prospective studies have been done. Antisarcoma therapy, such as doxorubicin and dacarbazine, is much more toxic but seems to be more effective for rapidly growing intra-abdominal desmoid tumors associated with FAP. Radiation is effective in destroying tumors but its effect on the small bowel can be disastrous, causing fistulas and necrosis.

Intra-abdominal desmoids that are not growing may be treated by sulindac alone. If they are growing slowly or causing symptoms it is reasonable to add tamoxifen in a dose range of 80 to 120 mg/day. The dose should be gradually escalated to these levels over a few weeks. If the tumor continues to grow, chemotherapy is appropriate. Really rapid growth is an indication for antisarcoma therapy, while a slower growth rate means vinblastine/methotrexate can be tried. A recent report of successful intestinal transplantation after resection of abdominal desmoids

reinforces the extent of the surgery needed to remove them, but also offers some hope for tumors that fail to respond to anything else.

SECTION II: Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

Guideline 1: Treatment Must Be Preceded by Thorough Counseling About the Nature of the Syndrome, Its Natural History, Its Extracolonic Manifestations, and the Need for Compliance With All Recommendations for Management and Surveillance.

Level of Evidence: III. Hereditary nonpolyposis colorectal cancer is a dominantly inherited syndrome due to an inactivating mutation in one of the human deoxyribonucleic acid (DNA) mismatch repair genes. The syndrome is more complex than FAP because more genes are involved, penetrance is less complete, and expression is more varied. Furthermore, the clinical criteria defining HNPCC are arbitrary and not particularly accurate, and the yield of testing for germline mutations is lower than for FAP. HNPCC has a penetrance of at least 80 percent, and colorectal cancer occurs at a mean age of 46 years. Affected patients usually have at least one surgery and are committed to lifelong surveillance of several organs. Careful counseling is necessary to allow patients and their families to understand the implications of these complexities.

Guideline 2: When Patients With HNPCC as Defined by Genotype or Compliance With Amsterdam I Criteria Are Diagnosed With More Than One Advanced Adenoma or a Colon Cancer, They Should Be Offered the Options of Prophylactic Total Colectomy and Ileorectal Anastomosis (IRA) or Hemicolectomy Plus Yearly Colonoscopy. The Choice of IRA Assumes the Anal Sphincter and Rectum Function Normally.

Level of Evidence: III. When patients known to be affected with HNPCC are diagnosed with advanced neoplasia, they can be offered a choice of conventional partial colectomy with surveillance of the remaining large bowel or total colectomy with rectal surveillance. Surveillance involves colonoscopy or proctoscopy (after IRA) every one to two years for life. There is evidence that cancers can occur in HNPCC within two years of a negative colonoscopy, but that cancers found on screening exams performed with a three-year interval can be cured. The risk of metachronous cancer after conventional treatment of an index cancer is 45 percent in patients with HNPCC, high enough to make prophylactic colectomy a reasonable option. The downside of colectomy and IRA lies in its effect on bowel function and quality of life. In a study of patients having IRA for FAP, quality of life was maintained, although stool frequency increased. These patients were younger than typical HNPCC patients having surgery, but even older patients can do well after IRA provided their anal sphincters and rectums are normal. The outcome of partial colectomy and effective surveillance can be similar to that of colectomy and IRA in terms of minimizing metachronous cancers. Likely patient compliance, the anticipated quality and frequency of colonoscopy, and the relative costs and reimbursement of the two options therefore influence the choice. Even after IRA, the risk of rectal cancer is 12 percent in 12 years, so continuing surveillance of the rectum is mandatory.

HNPCC patients diagnosed by genotype with a normal colon are also candidates for prophylactic colectomy. If penetrance of the mutation in the family approaches 100 percent, this should be strongly considered. There have been two attempts to discern the relative benefits of surgery vs. surveillance using decision analysis

methods. One study showed that prophylactic colectomy/proctocolectomy performed at the time of diagnosis led to a greater benefit in years of life expectancy gained than surveillance, but that this benefit decreased the longer surgery was delayed. Furthermore, if prophylactic surgery is performed at the time of diagnosis of a cancer, the gain in life expectancy is only four days for colectomy/IRA and six days for proctocolectomy. The advantage of surgery is further reduced if the gain in years is discounted. When the outcome of the analysis was quality-adjusted life years, surveillance was the most effective strategy, with a gain of 14 quality adjusted life years (QALYs) compared with no surveillance, 3.2 QALYs compared with prophylactic proctocolectomy at diagnosis of HNPCC, and 0.3 QALYs compared with colectomy. A similar phenomenon was seen when comparing colectomy with proctocolectomy. Use of QALYs improved the relative value of the lesser operation. A decision analysis reported that prophylactic colectomy at age 40 conferred an increase in life expectancy over surveillance of 8 to 18 months. In the same scenario, other researchers calculated a benefit for surgery of 9.6 months. These analyses do not take costs into account, however, and they assume a level of compliance and quality of endoscopy that may not be realistic. In the absence of a randomized comparison of surveillance and surgery, both options must be explained to the patient and individual circumstances, such as comorbidity, gastrointestinal physiology, likely compliance and ease of colonoscopy, taken into account.

Guideline 3: Patients With HNPCC Who Have a Rectal Cancer Should Be Offered the Options of Total Proctocolectomy and IPAA or Anterior Proctosigmoidectomy, Assuming That the Sphincters Can Be Saved.
Level of Evidence: III. Rectal cancer is an uncommon index cancer in patients with HNPCC. Surgical options, assuming the sphincters can be saved, are restorative proctocolectomy (with ileal pouch-anal anastomosis) and anterior resection. There are substantial differences in bowel function after these two procedures, but the risk of metachronous colon cancer after a primary rectal cancer is not known. The decision to preserve the proximal colon and commit to a program of intensive surveillance is therefore based on likely compliance of the patient with surveillance and the likely impact of the surgery on quality of life.

Guideline 4: Female Patients With HNPCC and Uterine Cancer in Their Family May Be Offered Prophylactic Hysterectomy Once Their Family Is Complete or When Undergoing Surgery for Other Intra-Abdominal Conditions.
Level of Evidence: III. The lifetime risk of uterine cancer in HNPCC is 42 percent, and although it is most common in families with hMSH6 mutations, it is also associated with hMSH2 and hMLH1 mutations. Screening for endometrial cancer in females with HNPCC has been shown in at least one study to be ineffective in detecting cancer, and so where uterine cancer is a feature in families, affected females should be offered prophylactic hysterectomy. Oophorectomy should be done at the same time, because the risk for ovarian cancer associated with HNPCC is high and in a multi-institution review of HNPCC-associated ovarian cancer, synchronous endometrial cancer was present in 21.5 percent of 80 patients.

One report has shown that an increased risk for gynecologic cancer begins by age 25 years. Although the mean age at gynecologic cancer in their series of 67 affected females (43 uterine, 24 ovarian) was 49.3 years, five gynecologic cancers were diagnosed before age 35. The timing of prophylactic hysterectomy and

oophorectomy is therefore debatable. It is tempting to offer surveillance during the childbearing years and delay surgery until the patient has had a chance to have her family. Until more data are available, this is the best option. Surgery can be done at the time of another abdominal surgery, or as a separate operation once the patient's family is complete.

Definitions:

Level of Evidence

Level I
Evidence from properly conducted randomized, controlled trials

Level II
Evidence from controlled trials without randomization
or
Cohort or case-control studies
or
Multiple times series, dramatic uncontrolled experiments

Level III
Descriptive case series, opinions of expert panels

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations.).With the exception of some chemoprevention studies, the majority of parameters are supported by level III evidence, derived from retrospective case-controlled studies.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate choice and timing of surgery for individuals affected with dominantly inherited colorectal cancer

POTENTIAL HARMS

- A stapled ileal pouch anal anastomosis (IPAA) is associated with a risk of anal transitional neoplasia in 30 percent of patients, although if serious neoplasia occurs (high-grade dysplasia or carpeting of the mucosa), the transitional zone can usually be stripped transanally and the pouch advanced to the

dentate line. Even mucosectomy and handsewn IPAA is associated with anal neoplasia, although at a lower rate.
- The disadvantage of anal mucosectomy is worse function and increased complication rates.
- Antisarcoma chemotherapy may cause toxic side effects.
- Repeated fulguration of rectal polyps over many years can cause dense scarring that makes cancers flat and hard to see, and rectal dissection during proctectomy can be very difficult. Chronic rectal scarring makes rectal biopsy difficult, because the forceps tend to "bounce off" the scarred mucosa. Furthermore, scarring leads to reduced rectal compliance, increased stool frequency, and a tendency to seepage and incontinence.
- The downside of colectomy and ileorectal anastomosis lies in its effect on bowel function and quality of life.
- A review of literature reporting treatment of advanced duodenal adenomas shows that recurrence is almost guaranteed unless the duodenum is removed. Transduodenal polypectomy or endoscopic polypectomy may be temporarily effective, but does not offer a permanent cure. The outcome of surgery for established cancer is not good with recurrence and death the usual outcome.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are inclusive, and not prescriptive. Their purpose is to provide information on which decisions can be made, rather than dictate a specific form of treatment. These guidelines are intended for the use of all practitioners, health care workers, and patients who desire information about the management of the conditions addressed by the topics covered in these guidelines.
- The practice parameters set forth in this document have been developed from sources believed to be reliable. The American Society of Colon and Rectal Surgeons makes no warranty, guarantee, or representation whatsoever as to the absolute validity or sufficiency of any parameter included in this document, and the Society assumes no responsibility for the use or misuse of the material contained here.
- Many of the parameters discussed in the guideline concern the choice and timing of surgery, topics for which no prospective, randomized studies are available. Similarly, there are no randomized studies dealing with desmoid tumors or the role of counseling in these syndromes. With the exception of some chemoprevention studies, the majority of parameters are therefore supported by level III evidence, derived from retrospective case-controlled studies.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Church J, Simmang C. Practice parameters for the treatment of patients with dominantly inherited colorectal cancer (familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer). Dis Colon Rectum 2003 Aug;46(8):1001-12. [108 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Aug

GUIDELINE DEVELOPER(S)

American Society of Colon and Rectal Surgeons - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society of Colon and Rectal Surgeons

GUIDELINE COMMITTEE

The Standards Task Force

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: James Church, MD; Clifford Simmang, MD; on Behalf of the Collaborative Group of the Americas on Inherited Colorectal Cancer and the Standards Committee of The American Society of Colon and Rectal Surgeons

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Society of Colon and Rectal Surgeons Web site.

Print copies: Available from the American Society of Colon and Rectal Surgeons, 85 W. Algonquin Rd., Suite 550, Arlington Heights, IL 60005

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on October 8, 2004. The information was verified by the guideline developer on October 25, 2004. This summary was updated by ECRI on January 12, 2005 following the release of a public health advisory from the U.S. Food and Drug Administration regarding the use of some non-steroidal anti-inflammatory drug products. This summary was updated on April 15, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs).

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public

or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2006 National Guideline Clearinghouse

Date Modified: 9/25/2006