

THE CLINICAL CANCER LETTER

Cancer research news for clinicians

Vol. 27 No. 8
August 2004

ASCO Recommends Against Routine Adjuvant Chemo For Stage II Colon Cancer

The American Society of Clinical Oncology has developed a set of recommendations to address whether patients who have had successful surgery for stage II colon cancer should be offered adjuvant chemotherapy in routine clinical practice.

The guideline, published in the August 15 issue of the Journal of Clinical Oncology, states that the routine use of adjuvant chemotherapy for medically fit, average-risk patients with stage II colon cancer is not recommended. Clinical trials have not established with certainty a significant degree of clinical benefit for adjuvant chemotherapy in patients with stage II colon
(Continued to page 2)

Cancer Survivorship:

Exercise Improves Function, Symptoms Of Cancer Survivors, AHRQ Report Finds

A new evidence report by the Agency for Healthcare Research and Quality concludes that exercise programs can improve cancer survivors' functional capacity and cardiopulmonary fitness, reduce their symptoms of fatigue, and improve their quality of life during and after cancer treatment.

Exercise also can reduce cancer patients' symptoms of anxiety and depression during treatment. The report suggests that physical activity may have other positive effects among cancer patients, but at this time there are too few studies to reach any conclusions.

In addition to examining the effects of exercise on cancer survivors, the report reviewed evidence from physical activity interventions in healthy populations.

Some behavior modification programs designed to increase exercise show continued effects for at least three months after they end, the report found. However, the review of existing evidence also demonstrated that it is difficult to achieve sustainable gains in increased physical activity because few studies looked at the effects of these programs for more than one year.

AHRQ's evidence review found that no specific behavioral intervention or setting appeared to be more effective than another and that shorter, less-intensive programs were just as successful at achieving behavior change as ones that lasted longer and involved more contacts with participants.

Interventions examined included face-to-face counseling, mailings, and check-ups by telephone. Settings for the interventions included clinics, community centers, schools, workplaces, child care centers, exercise centers,

(Continued to page 8)

© Copyright 2004
The Cancer Letter Inc.
All rights reserved.

Clinical Guidelines:
Guideline Adherence
Improves Early
Breast Cancer Survival
... Page 2

Chemosensitivity Assays
Not Ready For Use
In Clinic, ASCO Says
... Page 3

FDA Approvals:
Taxotere Approved
For Node+ Breast Ca.
... Page 4

Alimta Approved
For Metastatic NSCLC
... Page 5

PO Box 9905
Washington DC 20016
Telephone 202-362-1809

ASCO Stresses Evaluation Of Prognostic Markers

(Continued from page 1)

cancer, although most trials show a small benefit from adjuvant chemotherapy.

Specifically, patients who receive adjuvant chemotherapy have about a 4% to 5% greater chance of survival five years after surgery, compared with patients who had surgery alone. The exact benefit is not known with certainty because not enough stage II patients have been included in clinical trials involving this group of patients only.

Patients with stage II colon cancer also should be encouraged to participate in randomized clinical trials. The guideline includes a section on "Discussion Points" that advises oncologists on how to approach such a discussion with the patient.

"Patients and their families often want black-and-white guidance on how to treat their disease," said Al Benson III, director of the Robert H. Lurie Comprehensive Cancer Center's Clinical Investigations Program at Northwestern University's Feinberg School of Medicine and lead contributor to the guideline. "Unfortunately, that is not possible with stage II colon cancer. It is critical for each patient to weigh the risk of therapy and any potential benefit. The ASCO Discussion Points provide an opportunity for the patient and physician to discuss what is known about stage II colon cancer. By reviewing these points, we feel that

the patient will be better able to make an informed decision."

Doctors usually offer adjuvant chemotherapy to patients with stage III colon cancer because clinical trials have shown that it helps a proportionally larger number of patients live longer than patients who do not receive adjuvant chemotherapy. But, the data are not as definitive, the increase in cure rate is less in patients with stage II colon cancer. The reason for this is that even without adjuvant chemotherapy, most patients with stage II disease will be cured by surgery alone.

The guideline also discusses the importance of evaluating prognostic and predictive markers in high-risk stage II colon cancer. The guideline highlights the key role of the number of lymph nodes removed with the colon cancer during surgery, and examined by the pathologist, in making decisions about adjuvant chemotherapy. The greater the number of lymph nodes examined, the easier it is to have confidence that the cancer has not spread.

The panel emphasizes that patients and their doctors should consider the number of lymph nodes that were examined when deciding about adjuvant chemotherapy. The guideline also pointed to other groups of stage II colon cancer patients—those with certain tumor characteristics that can be identified by a pathologist or by using specialized tests—who might be candidates for chemotherapy.

ASCO has collaborated with Cancer Center Ontario on this guideline and is publishing the guideline in conjunction with the Cancer Care Ontario group's systematic review on stage II adjuvant chemotherapy.

"This guideline represents one stop along a continuum," Benson added. "ASCO continually reviews relevant literature and updates guidelines as needed."

ASCO also released a new evidence-based patient guide, *Adjuvant Chemotherapy for Stage II Colon Cancer*. The guide is the patient version of the clinical practice recommendations.

Guideline Adherence Improves Early Breast Cancer Survival

The first study to compare survival between women with breast cancer whose treatment was based on consensus guidelines and those whose treatment was not shows that adhering to established guidelines improves survival and reduces the risk of recurrence.

The study retrospectively examined whether the systemic therapy prescribed after surgery for women with early-stage breast cancer was consistent

THE CLINICAL CANCER LETTER

Member,
Newsletter and Electronic
Publishers Association

World Wide Web: [http://
www.cancerletter.com](http://www.cancerletter.com)

Publisher: Kirsten Boyd Goldberg

Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 **Fax:** 202-318-4030

PO Box 9905, Washington DC 20016

Customer Service FAQ at www.cancerletter.com

Customer Service: 800-513-7042

PO Box 40724, Nashville TN 37204-0724

THE CLINICAL CANCER LETTER (ISSN 164-985X). Published monthly, subscription \$119 per year, by The Cancer Letter Inc. All rights reserved. None of the content of this publication may be reproduced, stored in a retrieval system, or transmitted in any form (electronic, photocopying, facsimile, or otherwise) without prior written permission of the publisher. Violators risk criminal penalties and \$100,000 damages.

with treatment guidelines established for at the time. Systemic therapy includes chemotherapy and hormonal therapy and is designed to reach cancer cells that may have spread beyond the original tumor site. The study was published online Aug. 2 in the Journal of Clinical Oncology at www.jco.org.

“Women treated for node-negative breast cancer according to consensus recommendations for systemic therapy experience a significant improvement in survival at 7 years,” said Nicole Hébert-Croteau, physician-epidemiologist at the Quebec National Institute of Public Health and lead author of the study. “Our associations support the current movement for developing, updating, and disseminating such recommendations.”

Using medical records from Canada’s national health care system, Hébert-Croteau and her colleagues compared survival between 1,002 women with early breast cancer whose systemic treatment was delivered according to guidelines developed at the 1992 St-Gallen conference in Switzerland, and 380 women whose treatment differed from those guidelines. The study also included 159 women whose guideline adherence was unknown. The women were diagnosed between 1988 and 1994 with invasive breast cancer that had not spread to nearby lymph nodes.

Developed by consensus with input from oncologists in Europe and North America, the St-Gallen guidelines continue to be updated regularly and are considered among the best guidelines available. The guidelines stipulate whether a woman with node-negative breast cancer should, after surgery, receive tamoxifen, chemotherapy, neither (as is the case for women at low risk of recurrence), or both, depending on her risk.

Researchers found that overall survival at 7 years was better among women whose systemic treatment complied with guidelines, especially for those at moderate risk of recurrence. Among those patients with moderate risk of recurrence, the 7-year survival was 88% for women who received treatment consistent with guideline recommendations vs. 79% among those whose therapy did not.

In addition, more women whose treatment differed from treatment guidelines experienced recurrence by 7 years than those whose therapy adhered to the guidelines. For those at moderate and high risk of recurrence, the recurrence rate at 7 years was 36% and 42% respectively when treatment did follow guidelines, versus 17% and 36% when treatment followed guidelines.

Underuse of systemic therapy exists to some degree at any cancer center due to the complex nature

of cancer care. For example, when a patient’s baseline prognosis is good, a physician may elect not to prescribe systemic therapy in efforts to avoid toxic side effects. Hébert-Croteau noted that patients may also have other medical problems that might influence the treatment recommendation.

An accompanying editorial by Rebecca Silliman, of Boston University Medical Center notes that translating clinical guidelines into practice is often a slow and complex process. She suggests that interventions that use small-group, case-based approaches that incorporate role-playing and discussion are needed to change provider behaviors.

“Although evidence-based guidelines are a necessary beginning, they are not sufficient in and of themselves to change practice,” Silliman said. “What is required is a much more comprehensive approach that incorporates not only knowledge, but also builds skills and affects attitudes.”

Silliman noted that the results of this study should be interpreted with caution, since they pertain to medical care that was delivered more than a decade ago.

Chemosensitivity, Resistance Assays Not Ready For Clinic, ASCO Tech Assessment Says

A new technology assessment from the American Society of Clinical Oncology states that the use of chemotherapy sensitivity and resistance assays to select chemotherapeutic agents for cancer patients should not be undertaken outside of the clinical trial setting.

CSRAs are an in-vitro laboratory analysis used to help determine whether a specific chemotherapy regimen might inhibit tumor growth in a specific patient. This type of analysis contrasts with so-called empiric therapy, where chemotherapy treatment is chosen based on clinical literature describing outcomes achieved through a specific clinical trial.

ASCO underscores that the idea of tailoring treatment to individual patients – using effective agents while sparing unnecessary ones – has obvious and great appeal, but ultimately found that limitations in the literature about CSRAs, including small sample sizes, a lack of prospective studies, low yield of assays, and newer chemotherapy drugs that continue to be developed, cast doubt as to their actual effectiveness of CSRAs in determining a course of treatment.

Furthermore, for technically challenging assays that require colony formation, such as the human tumor cloning assay, and for surgical procedures including the

sub-renal capsule assay, the success rate of the CSRA procedure is modest. In addition, preparation of the assay may involve complex laboratory work, limiting a broad application of the technology to routine clinical practice.

"I was glad to see that our technology assessment felt that clinical trial work on the use of chemotherapy and resistance assays should continue," said Daniel Von Hoff, director of Arizona Health Science Center Cancer Therapeutics Program and professor in the Department of Medicine, Molecular and Cellular Biology and Pathology, at University of Arizona College of Medicine. "Obviously there is a great need for these assays particularly with the more targeted therapeutic agents that are being developed."

ASCO recommends that oncologists instead make chemotherapy treatment recommendations based on published reports of clinical trials and a patient's health status and treatment preferences.

ASCO does recommend that research into the potential for using CSRAs as a tool for determining appropriate treatment should continue. "As laboratory procedures become more advanced, better assays will be developed," said Deborah Schrag, a medical oncologist and member of the Health Outcomes Research Group at Memorial Sloan Kettering Cancer Center. "In addition, as more chemotherapy drugs become available, and treatment choices for oncologists become more complex, the rationale for developing CSRAs becomes more persuasive."

ASCO defines a technology assessment as a process for determining whether a procedure is appropriate for broad-based use in clinical practices. Of an initial review of more than 1,100 articles, the ASCO Working Group found 12 articles that were relevant to include in a technology assessment of CSRAs and analyzed their results.

ASCO also released a new evidence-based technology assessment, Chemotherapy Sensitivity and Resistance Assays, the patient version of the clinical practice recommendations.

The new technology assessment is available on ASCO's patient website at www.PLWC.org.

Drug Approvals:

FDA Approves Taxotere For Node+ Breast Cancer

The U.S. Food and Drug Administration earlier this month approved Taxotere (docetaxel, Aventis) Injection Concentrate in combination with doxorubicin

and cyclophosphamide (TAC regimen) for the adjuvant treatment of patients with operable, node-positive breast cancer.

The supplemental New Drug Application received a Priority Review designation by the FDA, which is assigned to those applications that have the potential for providing a significant therapeutic advance. The additional indication also is under review by the European regulatory authorities.

The FDA based its decision on results from a second interim analysis from the pivotal Breast Cancer International Research Group (BCIRG) 001/TAX 316 study, which demonstrated that women with node-positive, early stage breast cancer who received a Taxotere-based chemotherapy regimen after surgery experienced a significant 25.7 percent reduction in their risk of relapse (or the chance of their cancer returning) as compared to women treated with another adjuvant combination regimen of 5-fluorouracil, doxorubicin, and cyclophosphamide (FAC).

With nearly five-years of follow-up (55 months), the significant reduction in the risk of relapse of this Taxotere-based regimen was observed regardless of a woman's hormone receptor status.

Also, at the time of this interim analysis, based on a total of 219 deaths, overall survival was longer for TAC than FAC (hazard ratio=0.69, 2-sided 95% CI=0.53, 0.90).

"The nearly five-year follow-up data from the study suggest that by substituting Taxotere for 5-fluorouracil in a standard chemotherapy regimen in the adjuvant setting, we now have a treatment that may be able to benefit more women with early stage breast cancer," said Dennis Slamon, chairman of the BCIRG Scientific Committee and director of clinical and translational research at UCLA's Jonsson Comprehensive Cancer Center.

The primary endpoint of the BCIRG study was to compare the disease-free survival after treatment with Taxotere in combination with doxorubicin (Adriamycin) and cyclophosphamide (Cytosan), (TAC), to a standard regimen of 5-fluorouracil, doxorubicin and cyclophosphamide, (FAC). The nearly five-year follow-up results of the study were presented at the San Antonio Breast Cancer Symposium last December.

The study enrolled 1,491 pre- and post-menopausal women with node-positive, early stage breast cancer from 112 sites in 20 countries between June 1997 and June 1999. Women were randomized to receive either TAC or FAC in the adjuvant (post-surgery) setting.

Follow-up data (55 months) of women on the

study did not identify unexpected safety concerns and confirmed the results already presented at the time of the first interim analysis (33 months).

The TAC regimen was associated with a higher rate of febrile neutropenia (low white blood cell count that can lead to infections) compared with FAC (24.7 percent versus 2.5 percent). However, incidence of severe infection were similar (3.9 percent versus 2.1 percent) and there were no treatment-related deaths due to infection in the study. Patients in the study were not treated with primary prophylactic use of G-CSF (granulocyte colony-stimulating factor), but G-CSF was required for subsequent cycles following the first episode of febrile neutropenia and/or infection.

Other severe adverse events occurring in 5 percent or more of patients treated with TAC included neutropenia, nausea, stomatitis and asthenia, and with FAC included neutropenia, nausea, vomiting and asthenia.

The study compared an approximately equal number of treatment cycles for both treatment groups and more than 90 percent of patients in both treatment groups received all six cycles of treatment.

Taxotere is approved in the U.S. to treat patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy, and patients with unresectable locally advanced or metastatic non-small cell lung cancer in combination with cisplatin, who had not received prior chemotherapy. It also is approved for patients with unresectable locally advanced or metastatic NSCLC after failure of prior platinum-based chemotherapy. Last May, FDA approved Taxotere for use in combination with prednisone as a treatment for men with androgen-independent (hormone-refractory) metastatic prostate cancer.

FDA Approves Lilly's Alimta For Metastatic NSCLC

The U.S. Food and Drug Administration earlier this month granted Eli Lilly and Co.'s Alimta accelerated approval for the treatment of locally advanced or metastatic non-small cell lung cancer in previously treated patients.

In February, Alimta was approved, in combination with cisplatin (a common chemotherapy agent), for the treatment of malignant pleural mesothelioma, a cancer often associated with asbestos exposure.

Alimta is an antifolate that simultaneously blocks three separate enzyme targets vital to the survival of cancer cells. Alimta's administration includes vitamin supplementation with folic acid and vitamin B12. A

team of researchers led by Lilly discovered that this vitamin regimen significantly reduces the drug's side effects without negatively impacting its ability to kill cancer cells. The administration cycle for Alimta is a 10-minute infusion, once every three weeks.

"Alimta represents a medical advance in the treatment of lung cancer," said Paul Bunn, director of the University of Colorado Cancer Center. "The benefits Alimta offers patients are clear, and it is much better tolerated than the current standard, and is conveniently administered."

The FDA accelerated approval is based on Alimta's efficacy and safety profile as evidenced in one of the largest phase III studies to date in the second-line setting that compared Alimta directly to Taxotere. In July, the study was the basis for a unanimous recommendation for accelerated approval by the FDA's Oncologic Drug Advisory Committee.

Alimta's approval was based on the drug's ability to reduce tumor size in advanced non-small cell lung cancer patients.

The FDA also cited Alimta's significantly improved safety profile as compared to Taxotere as a supporting basis for approval. Patients on Alimta also experienced less grade 3 or 4 neutropenia (a decrease in infection-fighting white blood cell counts); less neutropenia with fever; less diarrhea; fewer hospitalizations due to adverse events and less hair loss. As with all chemotherapy agents, patients on Alimta and Taxotere experienced low-blood cell counts. Patients treated with Alimta experienced higher rates of grade 3 or 4 Alanine Transaminase (ALT), a laboratory measurement of liver function. Some of the most common grade 3 or 4 toxicities associated with Alimta (regardless of causality) include anemia (8 percent vs. 7 percent for Taxotere); fatigue (16 percent vs. 17 percent for Taxotere); anorexia (5 percent vs. 8 percent for Taxotere); and infection without neutropenia (6 percent vs. 4 percent for Taxotere).

In accordance with the FDA's accelerated approval, Lilly will continue to gather data for Alimta in non-small cell cancer.

Breast Cancer: Reduced Risk of Metastasis When Screening Finds Cancer

Women who have breast cancer detected by mammography screening have a reduced risk of distant tumor recurrence than women with breast cancer detected outside of screening, according to a study in

the Sept. 1 issue of the Journal of the American Medical Association.

The incidence of cancerous tumors detected by mammography screening is increasing due to its expanding use, according to background information in the article. Selection of therapies for women diagnosed as having breast cancer is based on risk estimations for cancer recurrence.

Heikki Joensuu, of Helsinki University Central Hospital, Helsinki, Finland, and colleagues compared the survival outcomes of women with cancerous tumors detected by mammography screening with women whose tumors were detected outside of screening. The study included 2,842 women identified from the Finnish Cancer Registry as having breast cancer in 1991 or 1992. The average follow-up time was 9.5 years. The clinical, histopathological and biological features of the tumors were compared.

The researchers found that women with cancerous tumors detected by mammography screening had better estimated 10-year distant (other location in the body) disease-free survival than women with tumors found outside of screening. In analysis that included factors related to the biological aspects of the cancers, women with tumors detected outside of screening had a 90 percent increased risk for distant recurrence than women with tumors detected by mammography screening.

"Cancerous tumor detection in mammography screening was a favorable prognostic variable independent of the number of axillary lymph nodes, the primary tumor size, age at cancer detection, and the histological grade," the authors write. "Further research on factors related to cancer invasiveness and metastasis formation needs to be performed. For women with cancerous tumors detected by mammography screening, the risk of distant metastases may be overestimated unless the method of detection is taken into account in risk estimations."

Ellence Has Lower Risk Of Heart Damage, Study Finds

Two chemotherapy regimens using different doses of Ellence are associated with a low risk of heart damage in women with breast cancer, according to a study published in the Aug. 2 issue of the Journal of Clinical Oncology.

This is the first sub-study to evaluate patients more than eight years after they completed adjuvant treatment with Ellence and builds upon results of the FASG-05 study which demonstrated significant 5 and

10 year disease-free and overall survival benefits in patients treated with Ellence. In this sub-study, which was funded by Pharmacia Corp., investigators evaluated the long-term effects of two different doses of Ellence on cardiotoxicity--a standard dose of 50 mg/m² and a higher dose of 100 mg/m².

This sub-study, evaluating long-term cardiac function, enrolled 150 relapse-free patients from the FASG-05 trial who had received either standard FEC 50 (fluorouracil 500 mg/m², epirubicin 50 mg/m², cyclophosphamide 500 mg/m²) or higher dosed FEC 100 (same regimen with epirubicin 100 mg/m²) every 21 days for six cycles during adjuvant therapy for node-positive breast cancer. The blinded assessment for long-term cardiac injury was performed by a peer-review committee, comprised of three cardiologists and three medical oncologists, and included an evaluation of cardiac events occurring after the end of chemotherapy, vital signs, and concomitant disease among other cardiac parameters. This assessment occurred at a median follow-up of 102 months.

Following the treatment phase of the FASG-05 study, researchers found that at a median follow-up of 67 months, FEC 100 produced a statistically significant improvement in 5-year disease-free (66.3% v 54.8%, $P = .03$) and overall survival (77.4% v 65.3%, $P = .007$) compared with FEC 50. A recently presented 10-year update of the FASG-05 trial showed that FEC 100 remained significantly superior to FEC 50 in terms of disease-free ($P = .036$) and overall survival ($P = .038$).

During the assessment for long-term cardiac injury, the cardiotoxicity observed after adjuvant treatment with the higher dosed regimen (FEC 100) comprised two cases of well-controlled CHF that were possibly linked to treatment. An additional 18 patients experienced clinically asymptomatic left ventricular dysfunction (LVD), eight where treatment causality was probable. None of these asymptomatic patients developed further cardiac symptoms. In the patients treated with the standard dose regimen (FEC 50), one patient presented with a mild (grade 1) and asymptomatic LVD for which the causality was doubtful.

Prostate Cancer: Modality Combo Decreases Prostate Cancer Recurrence

High-risk prostate cancer patients who undergo a combination of hormonal therapy, radioactive seed implant (brachytherapy) and external beam radiation therapy have a decreased chance of recurrence,

according to a study published in the Aug. 1 issue of the International Journal of Radiation Oncology-Biology-Physics, the journal of the American Society for Therapeutic Radiology and Oncology.

Historically, high-risk prostate cancer has been a therapeutic challenge for physicians, despite efforts to cure patients by aggressively treating them with either surgery, brachytherapy or external beam radiation. Previous studies have shown the 5-year freedom from recurrence rates for high-risk patients treated with just one of these treatments to be between 0 and 50 percent, with up to half of these failures occurring where the original tumor was found.

To see if combining therapies would decrease recurrence rates for men with high-risk prostate cancer, 132 patients with high Gleason scores, with high prostate-specific antigen scores or who were at an advanced clinical stage of prostate cancer were studied. A three-pronged approach that included brachytherapy, external beam radiation therapy and hormonal therapy produced an 86 percent rate of freedom from recurrence after five years. Also, 47 of the original 132 patients in the study had a prostate biopsy performed two years after the end of treatment and 100 percent of them showed no evidence of the cancer recurring.

Hormonal Therapy Improves Prostate Cancer Survival

Researchers from Brigham and Women's Hospital and Dana-Farber Cancer Institute found that adding six months of hormone therapy to external beam radiation therapy for localized prostate cancer increased patients' likelihood of surviving to five years by 10 percent.

These findings challenge the current treatment gold standard--two months of radiation followed by three years of hormone therapy--a regimen associated with negative side effects significantly impacting quality of life. The study was published in the Aug. 18 issue of the Journal of the American Medical Association.

"This is the first study to provide evidence that 3D conformal radiation therapy combined with six months of AST provides a survival benefit for those with early-stage prostate cancer," said lead investigator Anthony D'Amico, a radiation oncologist with BWH and DFCI and professor of radiation oncology at Harvard Medical School. "These results should prompt physicians evaluating treatment options to prescribe six months of hormone therapy as opposed to a three-year regimen. Six months of hormonal therapy now becomes the preferred duration of hormonal therapy if used for patients with

localized prostate cancer treated with external beam radiation."

The researchers randomly assigned 206 patients to receive either two months of radiation therapy in conjunction with six months of AST or two months of radiation therapy alone. Patient follow-up averaged four and a half years. The patients treated with the combination therapy had a two-fold reduction in risk of death compared to those treated only with radiation therapy (12 percent compared to 22 percent). They also were less likely to require salvage AST five years following randomization.

"Patients with prostate cancer face a wide variety of decisions regarding their treatment, each with its own distinct benefits and risks," said senior author Philip Kantoff, chief of Solid Tumor Oncology at DFCI and BWH and professor of medicine at HMS. "That six months of hormone therapy combined with radiation therapy is an effective treatment provides patients with an important option if they are concerned about hormone therapy related side effects."

While this study answers an important question about the duration of AST in patients with localized prostate cancer undergoing radiation therapy, Kantoff and D'Amico said the next question is whether chemotherapy (Taxotere), in conjunction with AST and radiation therapy, can further improve survival in men with localized but high-risk prostate cancer.

Colon Cancer: Study Suggests Surveillance Colonoscopies Overperformed

Physicians appear to be performing surveillance colonoscopies at frequencies higher than those recommended by evidence-based medical guidelines, according to results of a survey conducted by the National Cancer Institute.

Surveillance colonoscopies are follow-up colonoscopies given to patients who already have had a colorectal abnormality detected and removed. These results, which appear in the Aug. 17 Annals of Internal Medicine, suggest that as the demand for colonoscopies in the U.S. increases, overperformance could use up limited physician resources and cause unnecessary risk to patients.

Pauline Mysliwiec, formerly of NCI, now at the University of California-Davis School of Medicine, and colleagues sought to learn how well physicians followed recommended guidelines for surveillance colonoscopies, and what factors most influence a physician's decisions.

The U.S. Preventive Services Task Force sets federal government guidelines for preventive disease screenings, based on cost-effectiveness, evidence from scientific research, and clinical trials.

The authors surveyed both gastroenterologists and general surgeons about their opinions and practices regarding the use of surveillance colonoscopy in various clinical scenarios. The aim was to find out how often physicians would recommend a colonoscopy and/or other procedures following an initial discovery of a colorectal abnormality in a healthy and asymptomatic 50-year-old patient. The possible abnormalities included a small, benign, hyperplastic polyp, a single small adenoma, a single large adenoma, or multiple adenomas. A physician could recommend a colonoscopy, fecal occult blood testing, a double-barium enema, flexible sigmoidoscopy, or a general rectal exam.

The study found that both groups of physicians recommended a colonoscopy in a follow-up session at a higher frequency than guidelines would require, especially in situations where the initial findings were considered low-risk.

In the lowest risk scenario--a patient diagnosed with only a small, hyperplastic polyp--24 percent of gastroenterologists and 54 percent of general surgeons recommended a colonoscopy, either alone or in conjunction with another procedure, at a frequency of at least every five years. Medical guidelines do not recommend any follow-up colonoscopy for hyperplastic polyps because the presence of these polyps has not been shown to increase the risk of colorectal cancer. Among those patients with a single, small adenoma--which is considered a low-risk abnormality--the authors reported more than one-half of physicians surveyed would recommend repeat colonoscopy every three years or sooner.

More than 80 percent of the physicians in the study cited clinical evidence in scientific journals as having a major influence in their decisions, and said scientific evidence was significantly more influential than medical guidelines. Information obtained at medical conferences or meetings also was perceived as influential. The authors noted that one problem may be that different medical groups have somewhat differing recommendations, so doctors do not have one single source to turn to for practice guidelines.

"Forces in the doctor's own practice may play a role, as well," said co-author Martin Brown, of NCI. "This includes concerns about liability, community influence, and financial incentives."

In a statement, the American Gastroenterological

Association said it disputed the validity of the study's conclusion.

"The Annals study is based on physician's self-reporting practice patterns based on hypothetical cases," the AGA said. "Because this study does not contain clinical detail, physicians may over or underestimate their own clinical behavior. Many guidelines currently exist for colon polyp surveillance. The appropriate time interval for surveillance is influenced by many factors (type of polyp, size, number and the adequacy of the colonic prep).

"An important issue raised in the study is what is the clinical significance of the small polyp? The guidelines proposed by the AGA and a consortium of GI societies could not provide recommendations for their surveillance due to the lack of scientific studies to define the appropriate behavior. Therefore, it is wrong to judge inappropriate the actions of physicians who performed surveillance colonoscopies on patients with small polyps.

"The National Cancer Institute, which funded this study, should take the logical next step and fund a long-term study of the natural history of the small polyp," the AGA said. "Applying the knowledge generated by such a study could positively impact the very real public health issues of the cost of colorectal cancer surveillance and clinical care strategies for small polyps."

Cancer Survivorship: **Exercise Interventions Reduce Anxiety, Fatigue, Report Says**

(Continued from page 1)

churches, and participants' homes.

"This report provides good information about increasing physical activity through interventions delivered in a variety of settings," said AHRQ Director Carolyn Clancy. "Hopefully it will help us to identify programs that can lead to sustained behavior change."

The report was prepared by a team of researchers led by Jeremy Holtzman, at AHRQ's University of Minnesota Evidence-Based Practice Center in Minneapolis.

A summary of the report, Effectiveness of Behavioral Interventions to Modify Physical Activity Behaviors in General Populations and Cancer Patients and Survivors, can be found at www.ahrq.gov/clinic/epcsums/pacansum.htm. For the full report, go to www.ahrq.gov/clinic/evrptfiles.htm#pacan. Printed copies may be ordered by calling (800) 358-9295 or by sending an e-mail to ahrqpubs@ahrq.gov.