MD ANDERSON'S REPORT TO PHYSICIANS July 2012 Vol. 57, No. 7

Geriatricians Play an Increasingly Important Role in Cancer Care

By Kathryn L. Hale

In the past, many elderly patients did not survive long after a cancer diagnosis. Even older patients who were healthy enough to undergo the standard treatment for their cancer often had a shorter life expectancy than younger people with the same cancer.

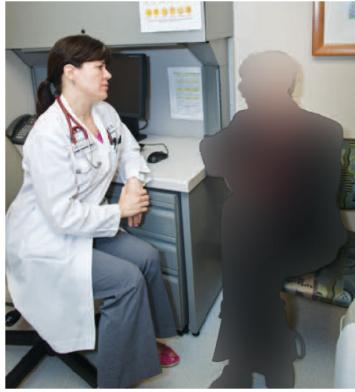
But as cancer treatments improve, many older patients are choosing more aggressive therapies, and they are surviving cancer in unprecedented numbers.

To meet the special needs of these patients, some physicians have begun to focus their practice on providing primary care for older patients before, during, and after cancer treatment.

Geriatrics and cancer

Holly Holmes, M.D., an assistant professor in the Department of General Internal Medicine at The University of Texas MD Anderson Cancer Center, is one of only a handful of practicing geriatricians in major cancer centers around the country—and she's busy. Nearly 7,000 new patients age 70 years or older register at MD Anderson every year.

To enable older patients to receive the most effective treatments possible, oncologic geriatricians focus on medical conditions typically associated with aging, such as chronic diseases and dementia, and on related health problems, such



, who has survived ovarian and breast cancers and is now being treated for a tumor near her spine, visits **Dr. Holly Holmes** for a geriatric assessment.

as motor disorders, polypharmacy, nutritional deficits, and geriatric syndromes. Geriatric syndromes is a term used to describe clinical conditions that affect older patients and do not fit into discrete disease categories—such as frailty, falls, weakness, memory loss, confusion, and mobility problems.



House Call

Exercise tips for cancer prevention and other health benefits



Geriatricians and Cancer Care

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"Geriatric syndromes don't go away just because a person has cancer," Dr. Holmes said. "I care for patients who are facing treatment for their cancer, and I try to reverse or control the other conditions to help them get through the treatment better."

Dr. Holmes and her peers at other institutions are working to fill a gap in what is known about how cancer and its treatment affect older people over both the short and long term. To that end, they participate in the Cancer and Aging Research Group, which designs and carries out trials that focus on clinical problems that are more common in older cancer patients than in younger patients. Dr. Holmes explained the need for such trials: "In the past, older people were underrepresented in the clinical trials that set the standards for cancer care. So we don't have as much systematic information about how they will respond to cancer therapy."

How old is "old"?

Dr. Holmes has been collaborating on a pilot study designed to predict how older patients with hematologic malignancies will tolerate and recover from allogeneic stem cell transplantation. At first, she resisted getting involved in the project because for the purposes of stem cell transplantation, "older" people are defined as those 60 years or older. In modern geriatrics, people are not considered old until they are in their 80s or 90s. Because people in their 80s and 90s are not candidates for stem cell transplants, Dr. Holmes at first did not see how this study had anything to do with her practice. But then she met a patient who changed her mind—a 55year-old man who, in the weeks following his stem cell transplant, developed multiple geriatric syndromes such as frailty, frequent falls, difficulty walking, weight loss, and weakness. Before his transplant, he had been strong and robust except for his cancer, but he had suddenly become a "geriatric" patient. This kindled Dr. Holmes's interest in developing a way to predict who, among older patients, would do well after a transplant and who would not.

Dr. Holly Holmes demonstrates tests of balance and grip strength for patient

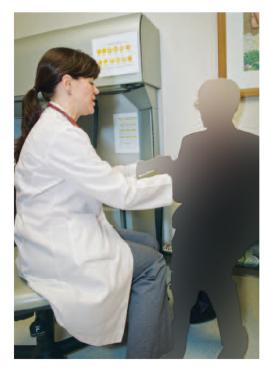
The study is investigating whether a comprehensive geriatric assessment a defined panel of parameters that includes the patient's physiologic age, comorbid conditions, medications, functional abilities, competence in activities of daily living, nutrition adequacy, physical performance status, mental and cognitive abilities, and social support—can be used to predict how well a patient will do during and after transplantation.

"We're looking at the people who develop what might be called a frailty syndrome after transplantation: excessive fatigue, exhaustion, weakness, and weight loss," Dr. Holmes said. "We compare objective measures, such as grip strength, gait speed, weight loss, and self-reports of physical activity and energy level, with their pretransplant baseline assessments to find clues as to which parameters we could eventually use to make informed decisions about the risks and benefits of a transplant for an individual."

Improving patient assessment

There is no standard for geriatric assessment in cancer care; most oncologists continue to rely on simple scales of performance status that have been in use for years: the Eastern Cooperative Oncology Group scale and the Karnofsky scale. Both are useful for assessing patient status, but the goal of the Cancer and Aging Research Group is to develop assessment tools that offer more predictive value while remaining easy for busy clinicians to use. "As geriatricians who work with older cancer patients," Dr. Holmes said, "part of our job is to give the oncologists the information they need to improve their pretreatment assessment and selection of therapy for each patient."

The U.S. National Comprehensive Cancer Network (NCCN) has published guidelines on senior adult oncology, and Dr. Holmes was a member of the panel that developed the comprehen-



sive geriatric assessment recommendations for those guidelines.

For the stem cell transplant study, Dr. Holmes modeled her comprehensive geriatric assessment on one tested in a recent multicenter prospective study of how well such an assessment predicts chemotherapy toxicity in older adults. The results of that study, which were reported in the Journal of Clinical Oncology in 2011, indicated that among adults older than 65 years undergoing chemotherapy for a solid tumor, the risk of severe toxicity or death was higher in those older than 72 years. The risk was also high in those who had a gastrointestinal or genitourinary cancer and in those who received multiple chemotherapy drugs at standard doses. Patients who had a low baseline hemoglobin level or creatinine clearance, reduced hearing acuity, a fall in the last 6 months, limited ability to walk one block, a need for assistance in taking medications, or reduced social activities also had a high risk of severe toxicity or death.

Dr. Holmes acknowledged that it is not realistic to expect oncologists to incorporate a comprehensive geriatric assessment into their pretreatment evaluation because of the time required to





do so. "In its most recent guidelines for cancer care in older adults," she said, "the NCCN recommends that the oncologist perform a briefer assessment that nevertheless addresses the important domains of older patient resilience: sensory acuity, physical abilities, nutrition, urinary continence, mental status, activities of daily living, home environment, and social support."

It is often the patient's responses to these simple assessments that determine whether Dr. Holmes is consulted. Even a single question can clearly indicate the likely presence of some comorbid conditions and geriatric syndromes. "It can be difficult to get a meaningful answer from a general question, but if there's any red flag, the patient can be screened further or referred to a geriatrician," she said.

Dr. Holmes may be called in when an oncologist has concerns about an older patient's ability to undergo treatment. If the need is indicated, she can carry the assessment further, probing for the severity and underlying cause of conditions revealed by the initial assessment. She looks at both physical and mental status: "All older cancer patients should be screened for cognitive deficits because of the potential effect

of chemotherapy on cognition. I use simple tests to measure their physical functions: the 'sit-to-stand' test, grip strength, and gait speed. Gait speed is a terrific test because it reveals several different functions at once: cardiac and respiratory fitness, muscle strength, joint mobility, fall risk, and balance. You can capture all sorts of qualitative data just by watching someone walk." She also assesses the drugs and supplements the patient is taking, looking for side effects and interactions that might impair performance.

Dr. Holmes is sometimes consulted to offer an opinion on whether a patient should undergo standard therapy or an alternative. The NCCN recommends that oncologists approach these clinical decisions in terms of life expectancy. Dr. Holmes said this approach means considering a patient's likelihood of dying from the cancer in his or her remaining lifetime (i.e., how long this person would live if he or she did not have the cancer) and whether the cancer is likely to degrade the patient's quality of life.

Assessing the individual

Preliminary data from the stem cell transplant trial suggest that the more

rigorous comprehensive geriatric assessment is not much better than the traditional performance scales alone at predicting which patients will develop posttransplant geriatric syndromes. Dr. Holmes believes this is partly because oncologists already understand, and incorporate into their pretreatment assessment, the effects of comorbid conditions and physical abilities on a patient's response to treatment.

Dr. Holmes said, "In patients undergoing allogeneic transplant, a very aggressive therapy, the characteristics of the cancer itself and the events of the peritransplant period-infections, graftversus-host disease, number of hospitalizations, and complications and the medications needed to treat themseem to be more meaningful than any baseline characteristics in predicting geriatric syndromes."

While it is still not clear whether a comprehensive geriatric assessment should be incorporated into all older cancer patients' pretreatment evaluations, the role of oncologic geriatricians continues to expand as physicians seek to balance effective treatments with quality of life for their patients. "Cancer care is not a 'one size fits all' matter for older patients any more than it is for younger patients," Dr. Holmes said. "We need to look at each person and each cancer individually and decide what information is pertinent to the clinical decision-making for that person." ■

FOR MORE INFORMATION

Dr. Holly Holmes713-563-4485

FURTHER READING

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Quarterly discussion of cancer types for which there is no standard treatment or more than one standard treatment

Early-Stage Cervical Cancer

Treatment choices vary according to disease stage and patientspecific factors

By Sunni Hosemann

Introduction

This discussion addresses early-stage squamous cell carcinomas and adenocarcinomas of the uterine cervix. Although other histologic types of cervical cancer, including clear cell and glassy cell carcinomas, neuroendocrine carcinomas, and other cancers such as sarcomas, melanomas, or lymphomas may arise in the cervix, these are rare and may require different treatment approaches and considerations; thus, they are not included in this discussion.

Several treatment options have proven to yield equivalent oncologic outcomes in patients whose cervical cancers are discovered in the early stages. However, the effects of the treatments themselves are not equivalent among individual patients, and considerable analysis and discussion are needed to help patients determine their best option for care.

Traditionally, treatment options for early-stage cervical cancers have included surgery and radiation therapy. For both modalities, advances in technology and techniques have given rise to less aggressive treatment options aimed at reducing treatment morbidity and long-term complications while achieving oncologic outcomes that are equivalent to those achieved with more aggressive procedures.

Primary treatment options

Surgery

All treatment options for patients who have stage IA1 cervical cancers are surgical. The decision to use a specific procedure depends on several key factors. The standard treatment is an extrafascial (simple) hysterectomy, in which only the cervix and uterus are removed. If a cone biopsy has been performed and had negative margins, observation is also an acceptable option, particularly if the patient desires to preserve her fertility or is a poor surgical candidate because of medical comorbidities. For certain patients with stage IA1 cancer and high-risk prognostic factors, radical hysterectomy or trachelectomy may be performed as described below.

Radical hysterectomy, in which the uterus, cervix, parametrium, vaginal cuff, and pelvic lymph nodes are removed,

is the standard treatment for patients with stage IA2 or IB1 cancer. In patients who desire fertility preservation, a radical trachelectomy, in which the cervix, parametrium, vaginal cuff, and pelvic lymph nodes are removed but the fundus of the uterus is retained, can be performed. A radical trachelectomy is a more complex operation than a radical hysterectomy, and the increased risk is justified only in women who want to preserve their ability to bear children. Because of its complexity, a radical trachelectomy is a surgery best performed by a gynecologic oncologist who sees a high volume of cases.

Candidates for radical trachelectomy are patients who have tumors less than 2 cm in diameter, no high-risk tumor histologies, and no evidence of lymph node or distant metastases, according to Kathleen Schmeler, M.D., an assistant professor in the Department of Gynecologic Oncology and Reproductive Medicine at The University of Texas MD Anderson Cancer Center. "The oncologic outcomes of radical trachelectomy are similar to those of radical hysterectomy," Dr. Schmeler said, "and about 80% of women who have undergone a radical trachelectomy and later attempt pregnancy are successful." However, compared with pregnancies in the general population, post-trachelectomy pregnancies carry higher risks of miscarriage (particularly during the second trimester) and preterm labor.

Radical hysterectomy and radical trachelectomy can be done as open procedures, laparoscopically, or robotically. According to Michael Frumovitz, M.D., an associate professor in the Department of Gynecologic Oncology and Reproductive Medicine, open surgery for cervical cancer is rare at MD Anderson. He said that for radical hysterectomy, the robotic and laparoscopic approaches are equivalent, and the procedure is usually determined by the surgeon's preference. For radical trachelectomy, robotic surgery is the only minimally invasive approach performed at MD Anderson.

Most surgeries for cervical cancer are accomplished using minimally invasive means. The exceptions are patients whose uterus is too large to remove intact or whose respiratory reserve would be compromised by the abdominal insufflation necessary for laparoscopic or robotic access. Dr. Frumovitz noted that patients with medical conditions that increase the risk of intraoperative and postoperative complications, such as obesity or diabetes, are the patients most likely to benefit from a minimally invasive procedure. Such patients are also more likely to benefit from the supportive care available at a large center.

CONTRIBUTING FACULTY, THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER



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Radiation therapy

Although standard treatment guidelines still list radiation therapy as a primary treatment option with oncologic outcomes equivalent to surgery, at MD Anderson, primary radiation therapy is now rarely considered the best choice for patients with early-stage cervical cancer. Anuja Jhingran, M.D., a professor in the Department of Radiation Oncology, said, "There was a time when radiation was the preferred treatment for many older or obese patients with early cervical cancers because it caused less morbidity than surgery. But new surgical techniques have changed the equation." With the advent of minimally invasive surgeries, which are associated with shorter recovery times than open hysterectomies, an increasing

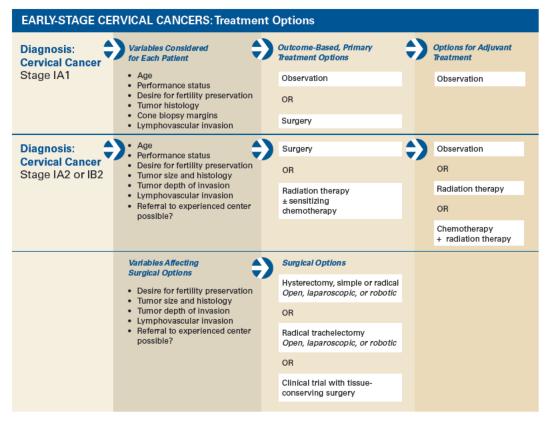
number of patients with cervical cancer undergo surgery. "This is true even for patients with comorbidities—diabetic patients, for example, in whom the preferred treatment was radiation because of the problems they had with postoperative wound healing, are now undergoing surgery," Dr. Jhingran said.

In addition, Dr. Jhingran noted that ovarian function is lost when the pelvis is irradiated, eliminating the possibility of preserving fertility and hormone production. Long-term effects of hormonal deprivation, such as osteoporosis and pelvic fractures, are especially important because many of the patients who are treated for cervical cancer are young.

Other long-term health considerations factor into treatment decisions. "Losses of bladder and bowel function are concerns in patients who receive radiation therapy and those who undergo surgery for this disease," Dr. Jhingran said. "It used to be that these complications were less common with radiation, but with newer surgeries, this too has shifted in favor of surgery."

Radiation therapy remains the treatment of choice in patients with locally advanced cervical cancer (stages IB2-IVA) and those with stage IA2 or IB1 disease who have medical conditions that put them at high risk of surgical complica-

Definitive radiation therapy for cervical cancer includes



whole-pelvis external-beam radiation and brachytherapy, which is performed by implanting radioactive pellets into the uterus and/or vagina and is customized according to the size and location of the tumor. "Both treatments are required to give the patient a sufficient radiation dose as a primary treatment," said Dr. Jhingran. Sensitizing chemotherapy with cisplatin typically is given on a weekly basis during radiation therapy.

Adjuvant treatment

Cervical cancers are initially staged clinically rather than surgically; therefore, surgical findings can indicate the need for additional treatment. Patients should receive adjuvant radiation therapy—and possibly concurrent chemotherapyif they are found to have disease-positive lymph nodes, positive surgical margins, or parametrial involvement. Patients are also considered for adjuvant treatment if they have a combination of high-risk pathologic features, including poorly differentiated tumors, large tumor size, deep stromal invasion, or lymphovascular space invasion.

Dr. Jhingran said that many factors that would indicate a need for adjuvant radiation therapy often are known in advance of initiating treatment. "For the most part, thanks to advances in imaging, we are able to determine ahead of time whether radiation therapy will be needed," she said, "If so, it



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should be given as a definitive treatment instead, so the patient would not have to undergo surgery as well, which may increase long-term complications such as bowel obstruction and lymphedema."

Incidental diagnosis

Cervical cancer is most often initially detected by a Papanicolaou test, with follow-up colposcopy and biopsies, and occasionally by investigation of symptoms. However, occasionally cervical cancer is discovered incidentally by pathologic analysis after a simple hysterectomy has been performed for unrelated reasons. When that is the case, criteria similar to those described above for adjuvant treatment based on surgical findings—pathologic status of surgical margins and the presence of risk factors—are used to guide further treatment.

Future directions

For many cancers, research aims to find more effective ways of eradicating disease and bringing about cures. For cervical cancer, particularly early-stage cervical cancer, there are already well-established, effective treatments. The emphasis of many current trials is to achieve the best oncologic outcomes with the least invasive treatments. At MD Anderson, such study initiatives consider not only the rigors of treatment a patient must undergo for her cancer but also her future health and quality of life. To that end, most clinical trials in gynecologic oncology have a companion study to evaluate and monitor quality-of-life issues.

Quality of life

According to Dr. Schmeler, all cervical cancer patients enrolled in robotic surgery trials, which assess oncologic and surgical outcomes, are concurrently enrolled in a study by Pamela Soliman, M.D., an assistant professor in the Department of Gynecologic Oncology and Reproductive Medicine, to monitor quality-of-life outcomes. Similarly, patients in prospective trials of radical trachelectomy will be monitored for quality-of-life issues, along with oncologic and fertility results. "We do these procedures to retain fertility, so it is reasonable to try to establish whether women actually do go on to attempt pregnancies, and if so, whether they are successful," said Dr. Frumovitz. These trials could help establish the value of radical trachelectomy and identify which patients are the most likely to benefit from the procedure.

Drs. Schmeler and Jhingran are also conducting a study of long-term sequelae of definitive radiation therapy for cervical cancer. Of particular interest are bone density changes and pelvic fractures.

Is even less aggressive surgery possible?

Although considerable advances have been made in minimally invasive surgery, investigators have begun to explore whether even less aggressive surgical approaches could be used in patients with early-stage cervical cancers. Removal of the

About Cervical Cancer

A ccording to the World Health Organization, the cervix is the second most common cancer site in women worldwide. Each year, more than 500,000 new cases of cervical cancer are diagnosed, and approximately 250,000 deaths are attributed to cervical cancer. About 80% of cervical cancers occur in low-income countries.

In the United States, where cervical cancer was once one of the deadliest cancers, death rates have declined by 70% since the advent of screening by the Papanicolaou test in 1955 and the test's subsequent widespread use. Women who are not screened regularly are at higher risk of developing and dying of invasive cervical cancer than are those who undergo regular screening.

Virtually all cases of cervical cancer are linked to genital infection with the human papillomavirus (HPV). According to Michael Frumovitz, M.D., an associate professor in the Department of Gynecologic Oncology and Reproductive Medicine, this is of particular note as women become sexually active at early ages. "We believe it takes about 10 years for HPV-related cancers to develop," he said, "and we are seeing young women—in their 20s and 30s—who have invasive cervical cancers." The U.S. Preventive Services Task Force recommends that Papanicolaou screening begin at 21 years of age.

Approximately 80% of cervical cancers are squamous cell carcinomas, and the majority of the remainder are adenocarcinomas. Treatment recommendations are currently the same for both types. Recently, despite the decline in the overall incidence of invasive cervical cancer and squamous cell carcinomas, the incidence of adenocarcinoma appears to be increasing, particularly in younger women. One possible reason for this is improved detection techniques. Adenocarcinomas tend to occur higher up in the cervix or in the uterus itself, beyond the transformation zone where squamous cancers arise, and thus are more difficult to sample; newer collection methods for Papanicolaou screening may be better able to detect adenocarcinomas at their earlier stages.

parametrium, which is part of both radical hysterectomy and radical trachelectomy, is the cause of many of the undesirable sequelae of these procedures, such as bladder, bowel, and sexual problems. The parametrium contains autonomic nerve fibers that are vital to these functions.

"There may be patients in whom removal of the parametrium is not necessary," Dr. Schmeler said, citing a recent study conducted by Dr. Frumovitz. The study found no parametrial involvement in pathologic specimens from patients who had favorable pathologic characteristics, specifically patients with negative lymph nodes, no lymphovascular

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Exercise and Cancer Prevention

Benefits of exercise apply to a variety of cancers



People who engage in regular, moderate exercise are less likely to develop some forms of cancer than are people who do not exercise regularly, according to recent studies. The evidence is strongest for colon, endometrial, and postmenopausal breast cancers.

Connecting the dots

"Although the connections between exercise and cancer prevention are not entirely clear yet, there are some probable explanations," said Karen Basen-Engquist, Ph.D., a professor in the Department of Behavioral Science at The University of Texas MD Anderson Cancer Center. One explanation relates to weight control. Regular exercise can prevent obesity, which is associated with many types of cancer. Obesity can cause the body to produce too much estrogen, which is a factor in some cancers, such as breast cancer. Obesity can also cause the body to produce too much insulin. Excess insulin can lead to the overproduction of cells, which, in turn, can lead to cancer.

Physical activity may also prevent cancer in other ways. It can boost the immune system and reduce inflammation; these help the body fight cancer development. Exercise also speeds the passage of food through the digestive system, possibly reducing how long cancer-causing substances spend in the colon. Finally, exercise can help regulate cell death (a normal process), preventing the uncontrolled growth associated with cancer.

Getting enough exercise

The American Institute for Cancer Research recommends that people get at least 30 minutes of moderate physical activity every day; 60 minutes of daily activity is even more beneficial. Anything that gets your heart beating more quickly and makes you breathe more deeply can count as moderate exercise. Participating in a mix of strength training and cardiovascular activities, such as

jogging or brisk walking, will help you get the most out of exercise. Although studies have suggested that incidental or occupational activities such as taking the stairs may have some benefits, the cancer prevention benefits of deliberate exercise are much clearer.

If you find the prospect of 30 minutes of sustained exercise daunting, take heart: researchers have found that breaking those 30 minutes into smaller blocks of time can be just as beneficial.

Starting out

Dr. Basen-Engquist suggested several ways to ease the transition into regular exercise. Before starting out, think about the kinds of activities you enjoy. These might be things you don't traditionally think of as exercise—dancing or walking the dog. If you start with something you enjoy, your exercise program is more likely to last.

Start slowly and work your way up. Don't be disappointed if you're not exercising 30 minutes every day from the outset. And for support, look to friends or other groups who also participate in the physical activities you enjoy.

Keeping motivated

Dr. Basen-Engquist offered three principles for maintaining the motivation to exercise: setting goals, monitoring progress, and rewarding yourself.

Your goal might be to increase the distance you cover, the time you spend exercising, or your repetitions of an activity (such as laps of the pool).

A range of devices allow you to monitor your progress. Wearing a pedometer will allow you to count your steps both during exercise and throughout the day. You might also time your exercise sessions, adding them up at the end of the month and aiming for longer sessions in the next month. New applications for smart phones and Web sites such as MapMyRun.com can help measure distances and speed. If you would rather keep things simple, you might chart your progress on a calendar, where you can also set new targets for speed, distance, calories burned, or other measures.

For rewards, you might try fruits such as berries. Dr. Basen-Engquist suggested allowing yourself to download a new song or buy some new reading materials if you meet your goals. And by only allowing yourself to engage in a certain fun activity (perhaps reading a favorite magazine) while exercising, you'll come to associate exercise with enjoyment instead of self-denial.

Vacations, bad weather, and other disruptions to your routine can derail your exercise plans. So, if your exercise program is going well but you see a high-risk situation ahead, take preventive action: pack your exercise clothes for a vacation, or have an indoor activity in mind for days when the outdoors look unappealing.

Even though the mechanisms that connect exercise with cancer prevention are not well understood, Dr. Basen-Engquist said, "You can confidently say that being active will benefit your health more than being sedentary."

-A. Scholtz

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- · Talk to your physician
- Visit www.mdanderson.org
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space invasion, and tumors 2 cm or smaller in diameter. "Based on those observations, it's reasonable to investigate whether conization or a simple hysterectomy with lymph node dissection would be adequate treatment for this group of patients," Dr. Schmeler said. A prospective multicenter trial is currently under way to find out. For patients whose tumors are larger or have less favorable pathologic characteristics and require a radical hysterectomy, Pedro Ramirez, M.D., a professor and the director of Minimally Invasive Surgical Research and Education in the Department of Gynecologic Oncology and Reproductive Medicine, is conducting a prospective study comparing the surgical, oncologic, and quality-of-life outcomes of minimally invasive and open surgery.

Is clinical staging enough?

A recent MD Anderson study compared surgical findings with pretreatment positron emission tomography findings and found that 24% of patients with locally advanced cervical cancers had disease in the para-aortic lymph nodes that was not detected by preoperative imaging. "This indicates that positron emission tomography analysis may not be enoughit may be leading us to understage and thus undertreat some cervical cancers." said Dr. Frumovitz. A new trial will use a laparoscopic extraperitoneal approach to examine the para-aortic nodes in patients in whom such involvement is suspected.

Is concurrent chemotherapy enough?

The standard treatment for patients with positive lymph nodes after a hysterectomy is concurrent chemotherapy with pelvic or extended-field radiation therapy. However, the incidence of distant metastasis among patients with more than one positive node is 15%-20%. To address this issue, an international trial is evaluating the addition of four cycles of chemotherapy after the completion of radiation therapy in this group of patients.

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