[News * Analysis * Commentary * Controversy]

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Big Concerns about Inadvertent Use of Morcellation in Previously Undiagnosed Uterine Leiomyosarcoma

BY ED SUSMAN

"[At gynecologic surgical meetings], you can't go to a session without seeing a morcellator for a fibroid or uterus or a new technique. It is so widely accepted, and you get away with it most of the time, but it doesn't make it right."

ORLANDO, FL—Women who have among the rarest of cancers—leiomyosarcoma—have far better outcomes when the tumors are excised en bloc than when the cancer undergoes morcellation, usually as part of a laparoscopic procedure. That was the conclusion of a report here at the Meeting on Women's Cancer of the Society of Gyncologic Oncology.

The mortality rate among women whose tumors were removed en bloc during a complete hysterectomy was 19.4% after a mean of 63 months of follow-up while in cases where morcellation—i.e., piecemeal removal of lesions and organs—occurred the mortality rate was 44% after a mean follow-up of 39 months, Jeong-Yeol Park, MD, Clinical Assistant Professor of Medicine at Asan Medical Center in Seoul, said in his plenary talk. "Tumor morcellation and spillage during surgery may adversely affect treatment outcomes in patients with these highly malignant tumors."

Ed Susman

PETER LIM, MD: "We have to identify these patients, and as we do more and more robotic and minimally invasive surgery, I think we are going to see a bigger population. We have to better refine our tests."

In the retrospective study, Dr. Park and colleagues identified 56 patients who underwent surgery that involved removal of leiomyosarcomas: 31 of the women were treated with non-morcellation hysterectomy while morcellation occurred in 25 other women.

The non-morcellation group underwent total abdominal hysterectomy as initial surgery without morcellation; the other women underwent surgery that included abdominal, vaginal, or laparoscopic morcellation.

The researchers narrowed their study population to include just women with early leiomyosarcoma confined to the uterus during surgical management. Also included were patients who were referred to the institution after initial surgery had been performed, and the researchers reviewed the medical records of patients treated between 1989 and 2010.

"We sought to compare treatment outcomes and patterns of recurrence in patients with apparently early uterine leiomyosarcoma who did and did not undergo tumor morcellation during surgery," Dr. Park said.

The surgery often begins as treatment for uterine leiomyoma—fibroids—and advances in minimally invasive surgery may involve morcellation to eliminate the fibroids or perform a hysterectomy with less scarring. There are few symptoms or diagnostic tests that can alert the physician that the "benign lesion" is actually a rare but deadly tumor, Dr. Park explained.

"As a result, many patients with early uterine leiomyosarcoma are diagnosed only after surgical management, which may include tumor morcellation."

Ed Susman

NADEEN ABU-RUSTUM, MD: "Most of us would agree that if you knew there is a leiomyosarcoma you would not do a morcellation dissection for this tumor. The problem is that with increasing minimally invasive approaches and the benefits of removing big tumors with morcellation, this has become very popular as the majority of patients will do well and will not have a problem."

When the treating surgeon recognizes that a leiomyosarcoma has been morcellated during surgery, the surgeon often reaches out for help to the gynecologic oncology specialist, but by then fatal damage may have been done. "Once or twice a year we get these phone calls: 'We morcellated a leiomyosarcoma—what should we do next?,'" said Nadeen Abu-Rustum, MD, Director of Minimally Invasive Surgery in the Gynecology Service at Memorial Sloan-Kettering Cancer Center, the Discussant for the study.

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confirmed in a substantially larger population of women.

New Targets & Biomarker Studies

Although Dr. Dannenberg agrees the results need to be confirmed and extended in a larger group of women, he also thinks the observations could be incorporated into ongoing trials as a biomarker for risk. For example, he hypothesizes that studies that examine the impact of adjuvant exercise or weight loss on recurrence risk might find greater benefit in overweight or obese women whose tissue have crown-like structures, relative to women with similar BMI whose tissues don't carry evidence of inflammation.

"Wouldn't you like to know at time zero, if a person has inflammation and how severe it might be, so you can see if they derive bigger benefit?" he said.

"I think the discovery has potentially important implications for future trials and, ultimately, for personalizing therapy, be it behavioral or pharmacologic interventions." Additionally, he notes that the insights might go part way to explaining why aromatase inhibitors appear to be less effective in overweight and obese women, relative to lean women.

Perhaps, most important, though might be the identification of potential targets for intervention, given the growing number of overweight and obese individuals in the population. In addition to the non-steroidal anti-inflammatory drugs that block the COX-2 pathway, there are numerous small molecules and dietary substances that impact the activation of NF-κB, which resides at the top of a signaling cascade in mammary tissue.

Dr. Dannenberg declined to talk about specifics, because the studies are ongoing, but said that his research group is actively exploring ways to either reduce the number of crown-like structures or render them functionally inert. He predicts either outcome could lead to an improvement for breast cancer prevention or treatment.

"You might say there is cause for optimism," he concluded.

→MORCELLATION

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"This paper from Korea shows us that morcellating smooth muscle tumors is more problematic for an already very high-risk group of patients. Most of us don't see this tumor at the time of diagnosis. We see it after myomectomy and by that time the patient is referred to us. We know that if there is perforation of the tumor or adjacent soft tissue or there is peritoneal dissemination, these patients do extremely poorly.

"Most of us would agree that if you knew there is a leiomyosarcoma you would not do a morcellation dissection for this tumor. The problem is that with increasing minimally invasive approaches and the benefits of removing big tumors with morcellation this has become very popular as the majority of patients do well and will not have a problem."

Dr. Park, in response to questions from Dr. Abu-Rustum, said that once morcellation of the leiomyosarcoma has been done, no additional workup has been shown to be effective in changing the outcome of the patient.

"This paper shows us that morcellating smooth muscle tumors is more problematic for an already very high-risk group of patients."

Spirited Discussion

In a spirited discussion, several doctors expressed concerns over the use of morcellation. "I feel that I am hovering on the brink of safety at all times," said Bobbie Gostout, MD, Chief of Obstetrics and Gynecology at the Mayo Clinic.

She said that gynecologic oncologists have advocated careful removal of suspicious lesions because they

Ed Susman

BOBBIE GOSTOUT, MD: "We are exposing our patients to a risk that to me seems out of bounds....I don't think there is an acceptable, safe morcellator out there....It is time to go back to our industry partners and say we need a new alternative. We need a contained system so that we can advance the goal of minimally invasive surgery, which I fully embrace.

understand that missteps can change the women's prognosis. "But we are also the group that seems to have accepted morcellation. As a surgical tool I don't think there is an acceptable, safe morcellator out there.

"That's different than saying "Are we getting away with it? We are getting away with it most of the time. I think it is time to go back to out industry partners and say we need a new alternative. We need a contained system so that we can advance the goal of minimally invasive surgery, which I fully embrace.

"We are exposing our patients to a risk that to me seems out of bounds," Dr. Goustout said.

Session moderator Pedro Ramirez, MD, Director of Minimally Invasive Surgical Research and Education and Associate Professor in the Department of Gynecologic Oncology at the University of Texas MD Anderson Cancer Center, agreed: "That is certainly a very valid comment. At our institution we don't own a morcellator so those cases are not performed."

Dr. Abu-Rustum noted that in attending other societies' meetings that are associated with gynecology, "you can't go to a session without seeing a morcellator for a fibroid or uterus or a new technique. It is so widely accepted, and you get away with it most of the time, but that doesn't make it right."

He suggested that doctors devise an algorithm that can give surgeons an idea of what the risk is, based on various imaging and clinical signs so they can determine if a woman is at high risk for having a malignancy.

"I think the challenge for gynecologic oncologists is that we get referral from gynecologists who say that they have seen only one such case in their lifetime, and 'it doesn't matter anyway because the patient is going to die,'" said Peter Lim, MD, Medical Director for Robotic Surgery and Minimally Invasive Surgery at Center of Hope in Reno, Nevada.

"That is typical of the comments I have gotten. As we do more and more robotic and minimally invasive surgery, I think we are going to see a bigger population.

"We have to identify these patients," Dr. Lim continued. "We have to better refine our tests. We can't just say, 'Well, we don't hava a test. Let's just go ahead and do it.'"

Morcellation is likely to increase as minimally invasive surgery goes toward smaller and smaller incisions—"You have to morcellate, because you can't get a big piece out," he explained.

He noted that when a surgeon morcellates a leiomyosarcoma, "you have Stage 1 disease that is now Stage 4 disease." Morcellating these tumors can create a "tumor seeding" that becomes even more difficult because there are no chemotherapy treatments that are known to work in the disease.

"Fibroids are very common, and the estimated incidence of leiomyosarcoma in fibroids is one in 200,000," said Dr. Gostout. "Minimally invasive surgery has made such a difference for the thousands of women each year who require this surgery. Right now the tools to take out the uterus involve morcellation of some sort, and these tools are just inadequate."

The patients in Dr. Park's study were about the same age—47.9 in the non-morcellation group and 46.4 in the morcellation group. Patients had an average of two children; 33% of the non-morcellation group were menopausal compared with 16% of the morcellation group. One of the non-morcellation patients required reoperation compared with six patients who had morcellation.

More than 90% of the patients were diagnosed with Stage1 disease; the tumors were about 9.8 cm in the non-morcellation patients and 7.3 cm in the morcellated group, and about 905 of the tumors were found to be high grade.

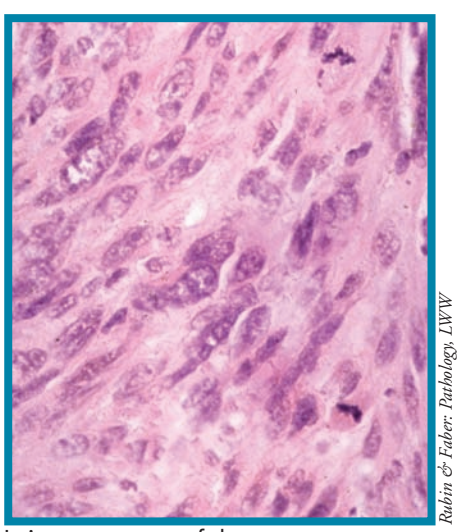
About 60% of the patients in the study received chemotherapy or chemoradiation therapy. The rest of the women did not receive adjuvant therapy.

The five-year overall survival among the non-morcellation patients was 73% compared with 46% for patients in which morcellation occurred.

"Not only complete excision of the tumor but also an en bloc excision without tumor injury is important in the management of patients with apparently early uterine leiomyosarcoma," he said.

Ed Susman

JEONG-YEOL PARK, MD: "Not only complete excision of the tumor but also an en bloc excision without tumor injury is important in management of patients with apparently early uterine leiomyosarcoma"



Rubin & Faber: Pathology, LWW

Leiomyosarcoma of the uterus, showing the moderately disorganized arrangement of malignant cells, irregular in shape and displaying numerous mitoses

Gynecologic Cancer Foundation Changes Name

The Gynecologic Cancer Foundation has changed its name to the Foundation for Women's Cancer (foundation forwomenscancer.org).

"With this straightforward new name, the Foundation celebrates its 20th anniversary committed to its core mission: to increase awareness and education, support expanded research and training, and provide knowledge and hope for women diagnosed with cancers specific to them," according to a posting on the website.

The new name "reflects our desire to continue supporting crucial research and knowledge of reproductive cancers, as well as our renewed effort to reach even more women."