For Early-Stage Cervical Cancer, Minimally Invasive Surgery Declining

More radical hysterectomies in women with early-stage cervical cancer are being performed by "open" surgery.

June 2, 2021 By National Cancer Institute

Nearly 3 years ago, results from a large clinical trial showed that minimally invasive surgery was inferior to traditional open surgery for women with early-stage cervical cancer. In the trial, called LACC, women with early-stage cervical cancer who had less invasive surgery, including robotic surgery, were more likely to have their cancer come back than those who had open surgery and were less likely to be alive 3 years after their surgery.

A new study shows that the LACC trial's results appear to have changed surgeons' treatment choices for women in the United States with early-stage cervical cancer. In the 18 months after the LACC results were published, the percentage of women who had minimally invasive surgery to remove the uterus and nearby structures, known as a radical hysterectomy, decreased from 58% to 43%, researchers reported April 29 in the New England Journal of Medicine.

The findings are in line with those from a study published last year, which showed a similar drop in the number of women with early-stage cervical cancer who underwent a minimally invasive radical hysterectomy since early 2018, when the LACC results were initially presented at a large research meeting.

The new study also found that the number of minimally invasive radical hysterectomies has dropped far more dramatically at large academic medical centers than at smaller hospitals.

Although not entirely unexpected, the discrepancy "suggests an opportunity to improve outcomes" for women with early-stage cervical cancer, study co-leader Patrick Lewicki, M.D., of New York-Presbyterian Hospital, and his colleagues wrote.

Several other large studies have linked minimally invasive radical hysterectomy with a higher risk of the cancer returning and death in women with early-stage cervical cancer, said Pedro Ramirez, M.D., professor of gynecologic oncology at the University of Texas MD Anderson Cancer Center, the LACC trial's lead investigator.

As a result, Dr. Ramirez explained, clinical guidelines from multiple US and European medical groups now recommend open surgery—known as a laparotomy—as the standard approach for

radical hysterectomy in women with early-stage cervical cancer.

At this point, for this group of patients, “I don’t think there is a role for minimally invasive surgery outside of a clinical study,” he said.

But that doesn’t mean minimally invasive surgery will never have a role in treating early-stage cervical cancer, said Emma Rossi, M.D., a gynecologic oncologist from the University of North Carolina School of Medicine.

“The LACC trial’s findings are valid and real,” Dr. Rossi said. But she noted that minimally invasive surgeries, particularly performed with robotic systems, have proven to be both safe and effective for numerous gynecologic conditions. And although the LACC trial and other studies consistently show worse outcomes with it in cervical cancer, she continued, “they failed to explain why.”

So, more research is needed, she said, “to see if we can find … ways to continue offering [minimally invasive surgery] while avoiding the negative effects.”

The Data on Open versus Minimally Invasive Radical Hysterectomy

Thanks to effective screening and prevention programs, cervical cancer has become fairly rare in the United States, with approximately 14,000 women diagnosed each year.

Nearly half of cervical cancers are diagnosed at an early stage, meaning the tumors are small and have not spread beyond the cervix.

Although there are other treatment options, radical hysterectomy is the most common treatment for early-stage disease, and cure rates for the disease are around 80%.

Minimally invasive surgery, which can also be called laparoscopic surgery, has been used to perform radical hysterectomies in women with early-stage cervical cancer for several decades. A minimally invasive procedure can be performed manually or with the use of robotic systems.

Its use for radical hysterectomies increased substantially in the late 2000s and 2010s, Dr. Rossi explained. That trend was driven by several factors, including the greater availability of robotic surgery and data indicating that it was as effective as open surgery and had some advantages for patients, including lower risk of complications during surgery and shorter postsurgical hospital stays.

By the time the LACC trial results were published in November 2018, robotic surgeries represented the lion’s share of radical hysterectomies in women with early-stage cervical cancer, Dr. Ramirez explained.

However, most (84%) of the minimally invasive procedures in the LACC trial were performed with traditional laparoscopic surgery rather than with robotic surgery. That led some oncologists who specialize in treating gynecologic cancers to argue that the trial did not reflect real-world practice.

Two population-based studies—conducted in Sweden and Denmark—appeared to offer some support for those criticisms. Neither found that robotic radical hysterectomy was linked with higher risk of recurrence or death in patients with early-stage cervical cancer.

However, most other studies have reported findings that are consistent with those from the LACC trial. A large US study involving 2,400 women and another US-based study conducted at three Mayo Clinic hospitals reached the same conclusion: women who had robotic radical hysterectomies for early-stage cervical cancer had a higher risk of the cancer returning and worse survival.

The LACC trial's findings were "shocking" to many gynecologic oncologists, Dr. Rossi said. But the consistency of the findings with those from other population-based studies can't be dismissed, and, given the attention the research received in the medical community and in news stories, she noted, doctors and patients were going to respond.

Rapid, but Uneven, Change in Surgical Choice

To conduct the new study, Dr. Lewicki and his colleagues looked at data on nearly 2,500 women with early-stage cervical cancer from a large database that covers approximately 25% of the hospitals in the United States.

Their review included women treated between November 2015 and March 2020, spanning several years before and approximately 1.5 years after the publication of the LACC trial's results. To compensate for the time it can take for clinicians to learn about newly published research findings, the review excluded the 3 months immediately following the publication of the trial results.

In the period before the results were published, 58% of radical hysterectomies for early-stage cervical cancer were performed with minimally invasive surgery. By March 2020, use of the minimally invasive procedure had dropped to 45%.

Academic centers were far more likely to change practice, with a much steeper decline in minimally invasive radical hysterectomy compared with what was seen at smaller community hospitals.

It will likely take some time for practice to change among surgeons at smaller hospitals, said David Sheyn, M.D., of the Case Western Reserve University School of Medicine, and part of the research team.

"It can sometimes take 5 to 6 years for [research] findings to make their way down to the community setting," Dr. Sheyn said. Nevertheless, some surgeons who feel they get the best results with the robotic procedure may be "less likely to pivot" from their usual patterns of care, he continued, or at least not as quickly.

The slow pace of change at nonacademic centers may also reflect the different practice environment at smaller hospitals, said Dr. Rossi, where continuing education and collaborative

efforts such as tumor boards are less common.

Why Worse Survival with Minimally Invasive Surgery?

One burning question on many researchers' minds is why minimally invasive surgery would be less effective than open surgery in this particular situation and not for other gynecologic conditions (e.g., uterine cancer).

One of the most prominent theories places the blame on devices called uterine manipulators, which are sometimes used during minimally invasive procedures to improve surgeon's ability to access and visualize the uterus and surrounding structures. This disruption to the uterus, the thinking goes, may be causing some cancer cells to become dislodged and escape into adjacent areas.

Drs. Ramirez and Sheyn agreed that this idea of cancer cell "spillover" is a theoretical concern that would be difficult to prove.

Dr. Rossi echoed a sentiment that other gynecologic oncologists have proposed: the problem may be the surgeons. Unlike drugs, which are consistent in how they are made and delivered, "that's not true for surgery," she said. "Different surgeons can have different outcomes, even with the same technique."

And compared with open surgery, minimally invasive radical hysterectomy is a much more technically challenging procedure, she said, raising the question: "Is this possibly a technique-driven effect?"

That's a subject for more research, Dr. Rossi continued, one that could open the door to reintroducing minimally invasive surgery for early-stage cervical cancer "in a safe way."

Increasing Open Surgery at Smaller Hospitals?

For the time being, Dr. Ramirez stressed, the overwhelming evidence of worse outcomes with minimally invasive surgery for women with early-stage cervical cancer makes changing clinical practice an imperative.

He expressed concerns at the slow transition from minimally invasive to open radical hysterectomy at smaller hospitals. What will it take to speed things up?

"We have to continue to educate the public and educate doctors," Dr. Ramirez said. "It's also the responsibility of hospitals to ensure that standard practices are being followed."

Dr. Sheyn said he expects surgeons at smaller hospitals to continue to decrease their use of minimally invasive procedures for early-stage cervical cancer. But, for a variety of reasons, he continued, "there may still be some holdouts."

One important source of change will be younger surgeons, Dr. Rossi said. Because many younger

surgeons at smaller hospitals are often trained at large academic centers, they are likely to be taught to perform open surgeries for this particular procedure.

“That tells me that this is going to be an enduring effect,” Dr. Rossi said, because academic centers “are where the [gynecologic surgeons] of tomorrow are going to be training.”

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