When Ovarian Cancer Returns, Surgery May Be a Good Choice for Selected Patients

For some people with access to skilled surgeons, surgery plus chemotherapy improves survival compared to chemotherapy alone.

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In more than 7 of 10 people with ovarian cancer, the cancer comes back after initial treatment. When ovarian cancer does recur, patients may have additional surgery to remove as much of the cancer as possible before starting chemotherapy again.

But it's been unclear whether this additional, or secondary, surgery improves how long people live. Several large studies have set out to resolve this question.

So far, two of them have reached different conclusions.

In one clinical trial, conducted mainly in the United States and Asia, secondary surgery did not improve how long people lived overall or without their cancer progressing, researchers reported in 2019. These results, from a trial called GOG-0213, led some experts to strongly question the role of secondary surgery.

Now, results from the second large clinical trial, known as DESKTOP III, show that, among patients who meet a strict set of criteria, secondary surgery followed by chemotherapy can improve survival compared with chemotherapy alone.

Initial results from a third trial, called SOC-1, which was conducted in China, showed that people who had secondary surgery lived longer without their cancer progressing than those who did not have surgery. Researchers are awaiting final results of the SOC-1 study.

But the patient populations that participated in each of the three studies were very different.

The eligibility criteria for DESKTOP III, which was conducted mainly in Europe, were developed to help doctors identify those patients most likely to benefit from a second operation upon recurrence, explained Yovanni Casablanca, M.D., a gynecologic oncologist at Walter Reed National Military Medical Center. The patients most likely to benefit are those for whom secondary surgery can remove all visible disease, said Dr. Casablanca, who was not involved with any of the trials.

“The biggest takeaway [from these studies] is that there is not a one-size-fits-all approach to treating recurrent ovarian cancer,” said gynecologic oncologist Sarah Temkin, M.D., associate director for clinical research in NIH’s Office of Research on Women’s Health, who was not involved with any of the trials.

Results of DESKTOP III, which were published December 2, 2021, in the New England Journal of Medicine, mean that “surgery is back on the table as an important part of treatment in a select group of patients” with recurrent ovarian cancer, Dr. Casablanca said.

For individuals who meet strict criteria, surgery “could or even should be considered—but only if a patient has access to an experienced and skilled surgeon,” said Elise Kohn, M.D., head of Gynecologic Cancer Therapeutics in NCI’s Cancer Therapy Evaluation Program, who was not involved with the studies. That’s because secondary surgery can be challenging to perform if the cancer has spread more widely.

If a patient’s care team feels that secondary surgery is not likely to be successful in removing all signs of the cancer, “patients … should not be exposed to a potentially harmful surgical treatment,” wrote the DESKTOP III researchers, led by Philipp Harter, M.D., Ph.D., a gynecologic oncologist at Kliniken Essen-Mitte in Germany.

Identifying patients most likely to benefit from secondary surgery

When ovarian cancer does return, how and where tumors grow and spread in the body can vary widely from patient to patient, said Ginger Gardner, M.D., a gynecologic oncologist at Memorial Sloan Kettering Cancer Center (MSKCC), who also was not involved with any of the three studies. “[So], we need to have as many strategies as we can to best eliminate or control it.”

Sometimes the cancer is in one or two spots, but sometimes tumors are sprinkled across multiple organs, which requires a longer and more complicated operation, Dr. Gardner said.

Most people with recurrent ovarian cancer will have had surgery and chemotherapy when their disease was first diagnosed. And questions like whether the patient can physically handle secondary surgery and whether the cancer is in one or more spots that the surgeon can access start to come into play, she continued.

The DESKTOP III clinical trial enrolled 407 people with recurrent ovarian cancer, nearly all of whom had received chemotherapy after their initial diagnosis. To be eligible for the study, patients had to have been in remission and not receiving chemotherapy for at least 6 months.

In addition, trial participants had to meet three criteria that were chosen to maximize the chances that secondary surgery would be successful: First, when they were initially treated for cancer, surgery must have removed all visible disease. Second, they had to be fully active and able to carry out daily activities without restrictions. And third, they had to have little or no buildup of fluid in their abdomen. A large buildup of this fluid, known as ascites, is a sign that the cancer has

spread more widely, Dr. Casablanca explained.

All participants were treated at specialized medical centers that do many surgeries on people with ovarian cancer. They were randomly assigned to receive either surgery followed by chemotherapy or chemotherapy alone.

People in the surgery group lived for a median of about 54 months after starting treatment, compared with 46 months in the no-surgery group. People in the surgery group also lived longer without their cancer progressing than those in the no-surgery group.

Surgeons were able to completely remove visible disease in 75% of patients who underwent the procedure. Median survival in such patients was more than double that of patients who did not have all the cancer removed (62 months versus 28 months).

The investigators in DESKTOP III "were doing very hard surgeries with good results," Dr. Casablanca noted. Patients experienced few complications of surgery, indicating that the overall quality of surgical care was high. And overall quality of life was similar among people in the surgery and no-surgery groups.

No one-size-fits-all approach for treating recurrent ovarian cancer

Although not everyone will be able to tolerate and benefit from secondary surgery, the results of DESKTOP III indicate that "surgery should be part of our toolbox for achieving the best result for our patients," Dr. Gardner said.

"We need to use precision in the selection of medical and surgical options—the right treatment for the right patient," Dr. Gardner and Dennis Chi, M.D., a gynecologic surgeon at MSKCC, wrote in an editorial accompanying the DESKTOP III results.

A few factors could explain the differing results of the three trials, Dr. Gardner and others said. One key difference is that, whereas the DESKTOP III and SOC-1 investigators used standardized criteria for selecting participants, "the patient selection criteria in GOG-0213 were much more fluid," Dr. Gardner said. In that trial, whether a patient was eligible to undergo surgery was based on an individual surgeon's judgment of whether their cancer could be completely removed surgically.

Although differences between the studies make it hard to compare them head-to-head, "the results from both the DESKTOP and SOC-1 trials define criteria where surgery is valuable and warn against its use in broader circumstances," Dr. Kohn said.

As Dr. Casablanca emphasized, "When someone has their first recurrence of ovarian cancer, we need to pause and ask if they meet the selection criteria" outlined by DESKTOP III. Those judgments should be made by a gynecologic oncologist—a specialist trained in managing ovarian cancer with both surgery and drug therapy, she and other experts said.

Findings may not apply in all settings

If surgery is indeed an option, Dr. Casablanca said, “we should be thoughtful about where that surgery is performed and who performs it.”

“We may not see the same outcomes [of secondary surgery] in community practice if we don’t have the same level of surgical quality,” Dr. Casablanca cautioned.

Indeed, said Dr. Temkin, few US women with ovarian cancer are treated at hospitals or medical centers that do a high volume of surgery for recurrent ovarian cancer. And many never see a gynecologic oncologist, even at the time of diagnosis, because they lack access to specialized care. As a result, Dr. Temkin said, “I think that the DESKTOP III trial results are applicable to [only] a small number of US patients with ovarian cancer.”

Finally, she noted, “we’ve seen a widening of disparities” in ovarian cancer survival in recent decades, due mainly to lack of access to high-quality medical care. “Survival for white patients with ovarian cancer has improved significantly over the last few decades because we have new treatments and new drugs. But for Black patients and those living in rural settings, ovarian cancer survival hasn’t really improved,” she said.

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