CA 125 levels:

your guide

RESEARCH · AWARENESS · OUTREACH · EDUCATION

foundationforwomenscancer.org
Women who are suspected of having ovarian cancer and women who have been diagnosed with ovarian cancer may receive a blood test to measure their CA 125 level.

This association between ovarian cancer and CA 125 often leads to confusion and misunderstanding about what this test means for diagnosis of ovarian cancer and/or its impact on the clinical management of ovarian cancer.

This booklet will take you through the basics of what you need to know about CA 125 — what it is, what it’s measuring, and what the values mean. And hopefully, this information will help you better understand how this test is used and interpreted in your treatment and follow-up.

What is CA 125?

CA 125 is a substance found in the blood called a glycoprotein (a sugar-associated protein). It is commonly referred to as a “biomarker” — or “tumor marker” — because it provides information about the biological state of a disease (ovarian cancer) and is obtained by a blood sample from which a level can be measured. Measurement of CA 125 is the most commonly used test to assist in diagnosing and following ovarian cancer. However, it is not a perfect test because it is only elevated in approximately 50% of women who have early-stage ovarian cancer and 85% of women with advanced ovarian cancer.

In other words, CA 125 may not be elevated in someone who does have cancer and can be elevated in someone who does not have cancer. Additionally, the number itself does not correlate with how much disease a person has. Two patients with the same level can have a widely differently extent of cancer. As you’ll see or have personally experienced, this is certainly the case for ovarian cancer patients. Nevertheless, as a tool, serial changes in CA 125 levels, if elevated, can be fairly representative of disease status and frequently very helpful in the assessment of women with ovarian cancer.
The history of the CA 125 test

The current CA 125 blood test is the second generation of the test first introduced in the early 1980s’ as a possible treatment. Based on early experience with immune therapy for cancer, investigators started searching for something unique on the surfaces of ovarian cancer cells that could be used to trigger recognition of tumor cells by the immune system. After 125 attempts, an antibody was found that seemed to do the trick. The antibody was termed OC-125 (for the 125th antibody tested against ovarian cancer cells) and recognized a tumor cell surface signal termed CA 125. Unfortunately, attempts to use this antibody in treatment were not successful. However, creative researchers recognized an interesting phenomenon about the protein and antibody they were testing — the levels in the blood seemed to correlate with the status of the ovarian cancer.

New studies were launched to see if CA 125 might be useful as a test to diagnose and follow ovarian cancer patients. Eventually, a CA 125 level of 35 units was found to be a useful cutoff point, with 99% of healthy women having values less than 35. Levels above 35 units are certainly seen in healthy women, but beyond the cutoff point of 35, the higher the value, the more likely there is trouble somewhere in the body. Women with ovarian cancer often have levels measured in hundreds and even thousands of units.

So, the CA 125 test is helpful, but not perfect. Individual values are hard to interpret, so many physicians focus on the trend in values over a course of time rather than on any individual value. Time trends help to put the individual values into perspective to get a “picture” of what might be going on in a particular situation.
CA 125 and false elevation

Normal tissues, including ovarian, pancreatic, and breast cells, and the lining tissue of the abdomen and chest all make and release low levels of CA 125. Since the CA 125 test reflects the amount of protein (often called antigen) released into the bloodstream from specific organs, conditions that cause irritation or inflammation can change the test result. Ovarian cancer not only increases the number of cells that make CA 125, but also perturbs or inflames the abdominal lining, which contains “normal” cells that make and release CA 125. So, it’s not surprising that CA 125 is elevated in ovarian cancer and in some other cancers in the abdomen.

But other, noncancerous conditions can elevate the CA 125 value, such as inflammatory conditions of the abdomen (diverticulitis, peritonitis, pelvic inflammatory disease, inflammatory bowel disease, tuberculosis, and pancreatitis), cardiac conditions such as congestive heart failure, liver disease, recent surgery, and benign gynecologic conditions such as fibroids, endometriosis, ectopic pregnancy, or a ruptured cyst. In some situations, CA 125 is even used to monitor the effects of treatment for benign conditions such as endometriosis. These other diagnoses must be considered in the interpretation of an elevated CA 125 value.
Potential applications of the CA 125 test

The CA 125 test is used in a variety of situations during the course of diagnosis, treatment, and follow-up of ovarian and other closely related cancers, such as primary peritoneal and fallopian tube cancers.

Five primary roles for CA 125 assessment have been established, with varying degrees of clinical use and reliability. The five major roles are:

**Outcome prediction:** CA 125 has been studied for its ability to predict treatment outcome in women with ovarian cancer and closely related cancers, such as fallopian tube and primary peritoneal cancer.

**Detection:** CA 125 is widely used to detect recurrent ovarian cancer in women who have been previously treated.

**Monitoring:** CA 125 is used throughout the course of chemotherapy to monitor or assess treatment effectiveness.

**Screening:** CA 125 is often used to screen for ovarian, primary peritoneal, and fallopian tube cancers in high-risk women or in women with abnormal findings on examination or ultrasound.

**Pelvic mass triage:** CA 125 is included as a marker to help determine the risk of a malignancy preoperatively.
Recurrent disease detection

The CA 125 test is most reliable and useful for the detection of recurrent disease in women previously diagnosed with and treated for ovarian cancer. Also, CA 125 levels can be elevated even when an exam and scan (CT or PET) do not show any cancer. This is called “biochemical recurrence.”

The role of the CA 125 test results and when to start treatment for recurrent disease should be discussed with your gynecologic oncologist.

While there are certainly exceptions, generally, rising numbers over a series of tests strongly suggest that a woman is experiencing a recurrence of her disease. However, some women develop a recurrence without a rising CA 125 level. On the other hand, some women have a modest rise in the value but never develop recurrent disease.

Recent evidence has suggested that using CA 125 to diagnose recurrent disease sooner does not result in an overall improved survival. Furthermore, following these values more closely caused physicians to administer more chemotherapy, thus worsening quality of life without improving outcomes. The role of CA 125 in the setting of detecting recurrent disease should be discussed with your doctor.

Outcome prediction

While more research is needed to completely determine how well a CA 125 test can predict the outcome of cancer treatment, several recent studies have looked at this question. If, during the first time a woman is treated for ovarian cancer, her CA 125 level returns to “normal,” will she have a better chance of survival?

The answer seems to be “yes,” but with a note of caution. This conclusion only seems to be true when looking at the trends for large groups of women. CA 125 levels do not work as well as a predictor for individual women.
Treatment monitoring

The CA 125 test is a generally reliable tool to use along with a thorough history and physical exam to assess or monitor if a treatment is working. However, its usefulness depends on the starting value. Monitoring is most accurate when patients have an elevated initial CA 125 value. Some information is emerging suggesting that the trends in CA 125 values within what is generally considered the normal range may also provide clues to treatment success.

It is vital to stress that this test represents just a piece of the puzzle, and a number of other factors are considered in determining whether any given therapy is working to fight the cancer. It is also important to emphasize that CA 125 values may go up or down for a variety of reasons and, because of this, the test may not accurately reflect disease status. This is particularly true when the values are in the normal range or are only minimally elevated. Most clinicians rely on how the numbers change over time and not on one test result alone.

Monitoring changes in the CA 125 value while on treatment can provide some of the earliest clues that your therapy is working. However, it’s important not to over interpret the values. For instance, some chemotherapy and biologic agents used in recurrent disease treatment, such as pegylated liposomal doxorubicin (Doxil) and topotecan (Hycamtin), require closer scrutiny as a significant number of patients may have a rise in their CA 125 values — as much as 30% — after their first cycle of chemotherapy, and yet go on to respond to these drugs upon continued administration. Some patients even have a rise in CA 125 after their second or third cycle and still had a favorable treatment outcome. Similarly, bevacizumab, a targeted biologic agent, may cause elevated CA 125 values despite having a positive treatment effect. So, CA 125 values can and do fluctuate. Major treatment decisions, such as changing or discontinuing treatment, depend on multiple factors that you and your physician will consider. The trend in your CA 125 values is only one of these factors.
Ovarian cancer screening

However, researchers continue to look into other possibilities for ovarian cancer screening. One option that seems to hold promise is the use of several tests, including the CA 125 test, performed in sequence or together as indicators of the presence of ovarian cancer. Some recent research has shown promise using the CA 125 test over time to look for changes within an individual patient followed by ultrasound in those with elevated values. But it is too early to know if this approach will prove beneficial for the general population in terms of cost and lives saved.

Pelvic mass triage

CA 125 has been used as part of a panel of biomarkers to determine the likelihood that a mass on imaging or exam is malignant. CA 125 is one of several markers in multianalyte platforms. These tests estimate the risk of a malignancy preoperatively to allow proper triage of a patient to a gynecologic oncologist in the event of an elevated risk score.
In September 2016 the U.S. Food & Drug Administration (FDA) issued a safety communication that recommends against using tests that are currently marketed for ovarian cancer screening. According to the statement, “The Agency is especially concerned about delaying effective preventive treatments for women who show no symptoms, but who are still at increased risk for developing ovarian cancer. Based on currently available information, the FDA recommends against using currently offered tests to screen for ovarian cancer.”

The FDA made the following recommendations regarding ovarian cancer screening tests for women, including those at increased risk of developing ovarian cancer:

- Be aware that there is currently no safe and effective ovarian cancer screening test.
- Do not rely on ovarian cancer screening test results to make health or treatment decisions.
- Talk to your doctor about ways to reduce your risk of developing ovarian cancer, especially if you have a family history of ovarian cancer, or have the BRCA1 or BRCA2 genetic mutations.
Future interventions

Many novel applications for CA 125 are emerging including using this test to assess response to neoadjuvant chemotherapy and predict the ability of the surgeon to cytoreduce. Additionally, CA 125 can be used in dynamic modeling to assess the efficacy of drugs in early development.

A final note

We urge women diagnosed with ovarian cancer to keep in mind that the CA 125 test is only one indication of how well the treatment is working. Gynecologic oncologists, who are obstetrician-gynecologists with an additional three to four years of training in the comprehensive treatment of women with gynecologic cancers, are specifically knowledgeable about how to interpret a CA 125 test result in the treatment of ovarian cancer.

For information on how to find a gynecologic oncologist and general information about ovarian and other women’s cancers, please visit foundationforwomenscancer.org.

For more information on ovarian and other gynecologic cancers, please call or e-mail the Foundation for Women’s Cancer at 312-578-1439 or info@foundationforwomenscancer.org.
What can you do to help us End Women's Cancer?

Raise awareness about gynecologic cancers.

Donate to the Foundation for Women’s Cancer online.

Participate in the National Race to End Women’s Cancer by running, walking or donating to a team. endwomenscancer.org

Host your own fundraising event or partner with the Foundation.

Give a Matching Gift through your employer to the Foundation.

Give gifts of stock or securities to the Foundation.

Designate a planned gift to the Foundation.

To make a gift or for additional information, please email the Foundation at info@foundationforwomenscancer.org or call 312.578.1439.

Connect with us on social media

/foundationforwomenscancer  @GYNCancer  @foundationforwomenscancer

The Foundation for Women’s Cancer offers many resources for women, advocates and the general public, including Survivor Courses around the U.S. and online. Find more about all of them on our website.

Donate & Learn More foundationforwomenscancer.org
The Foundation for Women’s Cancer (FWC) is a 501(c)3 nonprofit organization dedicated to increasing research, education and awareness about gynecologic cancer risk, prevention, early detection and optimal treatment.

foundationforwomencancer.org
info@foundationforwomencancer.org

phone 312.578.1439
fax 312.235.4059

Foundation for Women’s Cancer
230 W. Monroe, Suite 710
Chicago, IL 60606–4703

The FWC is the official foundation of the Society of Gynecologic Oncology.

Printing of this brochure made possible by generous educational sponsorship from Morphotek, Inc. Sponsorship excludes editorial input. Content developed by the Foundation for Women’s Cancer (FWC).

© 2017 Foundation for Women’s Cancer. All rights reserved.