Cancer Antigen 125 (CA 125)

CA 125 is a surface antigen on a high molecular weight glycoprotein recognised by a monoclonal antibody (produced using an ovarian cancer cell line). It is most useful as a marker for non-mucinous ovarian epithelial cancer and indeed is present in up to 80% of cases of advanced ovarian cancer - but is often negative earlier in the disease.

Conditions which may cause elevated cancer antigen 125

**Malignant disease**
- Ovarian cancer.
- Uterine cancer.
- Fallopian tube cancer.
- Other intra-abdominal cancers (pancreas, stomach, colon, rectum) and metastases from other sites (eg, breast, lung).

**Non-malignant conditions**
- Benign ovarian tumour (eg, Meigs' syndrome).
- Endometriosis.
- Pelvic inflammatory disease/salpingitis.
- Pregnancy and menstruation. (CA 125 can increase two- to three-fold during menstruation.)
- Leiomyoma, including fibroids.
- Ascites with non-malignant causes eg liver disease (cirrhosis).
- Diverticulosis.
- Pleural and pericardial disease.
- Pancreatitis.
- Heart failure.

**Uses of cancer antigen 125**

Elevated CA 125 is associated with many conditions - listed above. However, currently it is mainly used when ovarian cancer is suspected and for monitoring after treatment.

**Investigation of female patients with symptoms suggestive of ovarian cancer**

CA 125 can be used in the assessment of patients presenting with a pelvic mass. It is, however, a nonspecific test, ie raised in other conditions, many of which are benign (see above). The National Institute for Health and Care Excellence (NICE) estimates only 1 in 100 women with a raised CA 125 or abnormal ultrasound will have ovarian cancer. So for every 100 women referred, 99 will not have cancer, which results in economic and psychological cost. Nevertheless, NICE advocates that CA 125 should be the first-line investigation for women (particularly over the age of 50) with symptoms suggestive of ovarian cancer. See the separate Ovarian Cancer article for more details on symptoms, signs and early detection of this condition.

Sensitivity of CA 125 is also relatively low. Approximately 80% of patients with advanced ovarian cancer have raised levels of CA 125 but no more than 50% of patients with clinically detectable stage I disease have raised CA 125 levels. If ultrasound results are combined with menopausal status, a risk of malignancy index (RMI) can be calculated. Guidelines advise using a cut-off level of 200 to indicate malignancy.

The test is more sensitive for ovarian cancer in postmenopausal women. Royal College of Obstetricians and Gynaecologists (RCOG) guidelines advise that if serum CA 125 level is raised in a premenopausal patient but less than 200 units/mL, further investigation may be required to exclude or treat differential diagnoses. A level of more than 200 units/mL should prompt referral to a gynaecologist.
CA 125 level is not necessary when a simple ovarian cyst has been diagnosed by ultrasound. Also if a woman presents with a suspicious pelvic mass or ascites then an urgent referral should be made.

Since NICE guidelines were published in 2011 advocating symptom-triggered testing of CA 125 leading to ultrasound scan where raised, studies have shown that cancers are not detected at an earlier stage but that it may increase the chance of complete tumour removal at surgery.\[6, 7, 8]\n
**Monitoring known patients with ovarian cancer for relapse**

A number of reviews have failed to identify survival advantage for the process of monitoring CA 125 in asymptomatic women after treatment.\[9, 10\] It has often traditionally been used to try to pick up relapse early but current evidence is not sufficient to support this practice.\[4\]

**Screening for ovarian cancer**

The relatively low prevalence of ovarian cancer means that the positive predictive value of CA 125 as a screening test is extremely low. CA 125 is unreliable in differentiating benign from malignant ovarian masses in premenopausal women because of the increased rate of false positives and reduced specificity.\[5\] This is because an elevated CA 125 level is also found in so many other conditions. When levels are elevated, serial monitoring can be helpful, as rapidly rising levels are more likely to be associated with malignancy than high levels which are static.

Large studies have evaluated CA 125 as a screening tool in combination with ultrasound scanning to detect ovarian cancer early but results so far have failed to demonstrate benefit.\[11\] Therefore, it is not recommended outside research settings.\[4\]

However, CA 125 is still being evaluated as a screening tool for patients at high risk of ovarian cancer, in combination with other tests. The UK Familial Ovarian Cancer Screening Study (UKFOCSS) recruited women over a number of years with strong family histories or mutations in BRCA1 or BRCA2, to be screened with transvaginal ultrasound scan of the ovaries combined with a CA 125 level regularly and continue to follow this up.\[12, 13\] A second study, the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) study reports encouraging early results but further follow-up is awaited before conclusions can be reached.\[14\]

**Further reading & references**

- Sundar S, Neal RD, Kehoe S; Diagnosis of ovarian cancer. BMJ. 2015 Sep 1;351:h4443. doi: 10.1136/bmj.h4443.
- UK Familial Ovarian Cancer Screening Study

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