

Ovarian Cancer Markers

Indications for Ordering

Adjunct tests for evaluation of an ovarian mass

Test Description

Cancer Antigen 125 (CA 125)

- Quantitative electrochemiluminescent immunoassay

Human Epididymis Protein 4 (HE4)

- Quantitative enzyme immunoassay

Risk of Ovarian Malignancy Algorithm (ROMA)

- Quantitative enzyme immunoassay
- Quantitative electrochemiluminescent immunoassay

Tests to Consider

Primary tests

[Cancer Antigen 125 0080462](#)

- Evaluate and monitor ovarian cancer (usually epithelial subtype)
 - Monitoring requires elevated pretreatment value of CA 125
 - Combination with HE4 may enhance sensitivity
- Not recommended for monitoring breast cancer or germ cell tumors
- Not a stand-alone test for ovarian cancer screening or diagnosis

[Human Epididymis Protein 4 \(HE4\) 2003020](#)

- Use with CA 125 to monitor ovarian cancer, usually epithelial subtype, post therapy if pretreatment level was elevated
- Not recommended for monitoring mucinous or germ cell ovarian cancer
- Not a stand-alone test for ovarian cancer screening or diagnosis

[Risk of Ovarian Malignancy Algorithm 2012618](#)

- Assess cancer risk, particularly epithelial cell ovarian cancer, in pre- and postmenopausal women with an adnexal mass
- Combines CA 125 and HE4, together with menopausal status, to classify adnexal mass patients into high- or low-risk epithelial ovarian cancer groups
- Not intended as a screening, stand-alone, or tumor-monitoring test
- Tumor monitoring using HE4 and/or CA 125 test should be ordered separately

Related tests

Granulosa cell tumors

- [Inhibin B 0070413](#)
- [Total Inhibin, Serum 2014109](#)
- [Estradiol, Adult Premenopausal Female, Serum or Plasma 0070045](#)

Germ cell tumors

- [Alpha Fetoprotein, Serum \(Tumor Marker\) 0080428](#)
- [Neuron Specific Enolase 0098198](#)
- [Beta-hCG, Quantitative \(Tumor Marker\) 0070029](#)

Disease Overview

Incidence

- Ovarian cancer – >22,000 new cases and >14,000 deaths annually
 - Epithelial subtype – 40/100,000 for postmenopausal women

Diagnosis

- Markers cannot be used to diagnose ovarian cancer
- Markers may be useful in evaluation of a pelvic mass in postmenopausal women

Prognosis

Pretreatment CA 125 and HE4 levels are highly predictive of overall survival

Pathophysiology

- CA 125
 - Secreted in tumors of epithelial origin (~80% of tumors)
 - Frequency of elevation of CA 125 correlates with
 - Clinically detected stage of cancer (higher elevation of CA 125 levels in later stages)
 - Tumor burden (correlates with stage)
 - Type of tumor (usually in epithelial tumors)
- HE4
 - Secreted in tumors of epithelial origin (~80% of tumors)
 - Relapse
 - HE4 increases by $\geq 25\%$ in 60% of women with ovarian cancer relapse or progression
 - HE4 remains constant in 75% of women without progression of ovarian cancer

Monitoring

- CA 125
 - Uses
 - Evaluate ovarian mass
 - Determine pretreatment level for use in monitoring
 - Assess patient response to chemotherapy
 - Detect early relapse
 - Suggested monitoring is every 2-4 months for the first 2 years
 - Absolute serum value of CA 125 before third cycle of chemotherapy is most important factor for predicting progression at 12 months
 - Persistent postoperative elevation suggests poor prognosis
- HE4
 - May be complementary for monitoring when used in conjunction with CA 125
 - May be useful because some individuals do not have elevated CA 125 level but will manifest with elevated HE4 level

Test Interpretation

Results

- CA 125
 - Normal – <35 U/mL
 - Ovarian cancer less likely but not ruled out
 - In patients with ovarian cancer, a rising level from individual's baseline level may reflect progression of disease
 - Abnormal – ≥35 U/mL
 - Ovarian cancer possible if clinical suspicion is high
 - The higher the level, the more probable the mass is malignant
- HE4
 - Normal – ≤150 pmol/L
 - HE4 remains constant in 75% of women without disease progression
 - An elevation in HE4 concentration of ≥25% is clinically significant even if within the normal range
 - An increase of this magnitude suggests recurrence or disease progression
 - Abnormal – >151 pmol/L
 - An increase of ≥25% suggests recurrence or disease progression
 - HE4 increases by ≥25% in 60% of women with ovarian cancer relapse or progression
 - The higher the level, the more probable the mass is malignant
 - A decrease of ≥25% suggests therapeutic response

- ROMA
 - Premenopausal
 - >1.30 high likelihood of finding epithelial ovarian cancer
 - ≤1.30 low likelihood of finding epithelial ovarian cancer
 - Postmenopausal
 - >2.76 high likelihood of finding epithelial ovarian cancer
 - ≤2.76 low likelihood of finding epithelial ovarian cancer

Limitations

- CA 125 and HE4 tests are not useful in cancer screening
- Individuals with confirmed ovarian carcinoma may have pretreatment CA 125 values in the same range as healthy individuals
- CA 125 levels may be elevated in patients with nonmalignant disease
- Test values for CA 125 are not interchangeable between different laboratories or test platforms
 - Sequential monitoring should be performed at the same laboratory
- ROMA should not be used without an independent clinical/radiological evaluation and is not intended to be a screening test or to determine whether a patient should proceed to surgery