



Focus on

Ovarian cancer

HE4 & ROMA score



Ovarian cancer

Many women are or will be affected by suspected ovarian cancer. The symptoms for this type of cancer are non-specific and occur late.

The prognosis is basically determined by the stage of the disease at the time of diagnosis.

The risk of recurrence after 5 years is 80% and most recurrences appear within the first 3 years of treatment.

Early diagnosis and the detection of recurrence are the only means to improve the prognoses in the short term.

The diagnosis

Diagnosis is based on the medical history, a clinical examination and imaging (ultrasound, MRI).

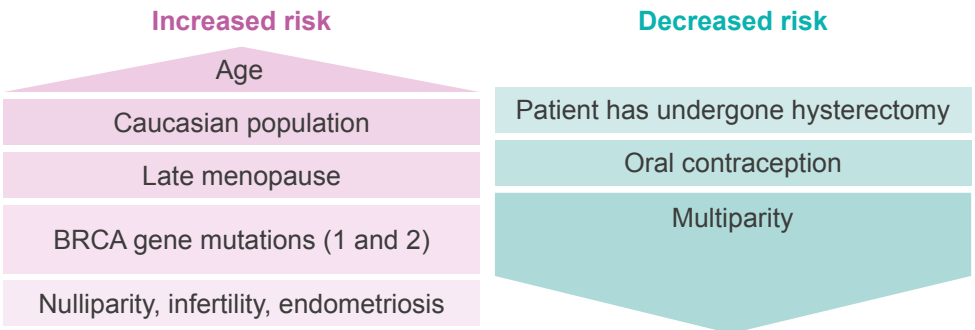
The definitive diagnosis of cancer is obtained via anatomical pathology and requires the taking of histological samples.

In the case of the diagnosis of ovarian cancer, screening for a BRCA1 or 2 mutation should be offered (source FNCLCC*):

- in women with isolated or hereditary ovarian cancer, which occurred before the age of 70,
- in women with ovarian cancer which occurred after 70, with a first-degree relative with breast or ovarian cancer (or even second-degree if the intermediary is a man).

Case history

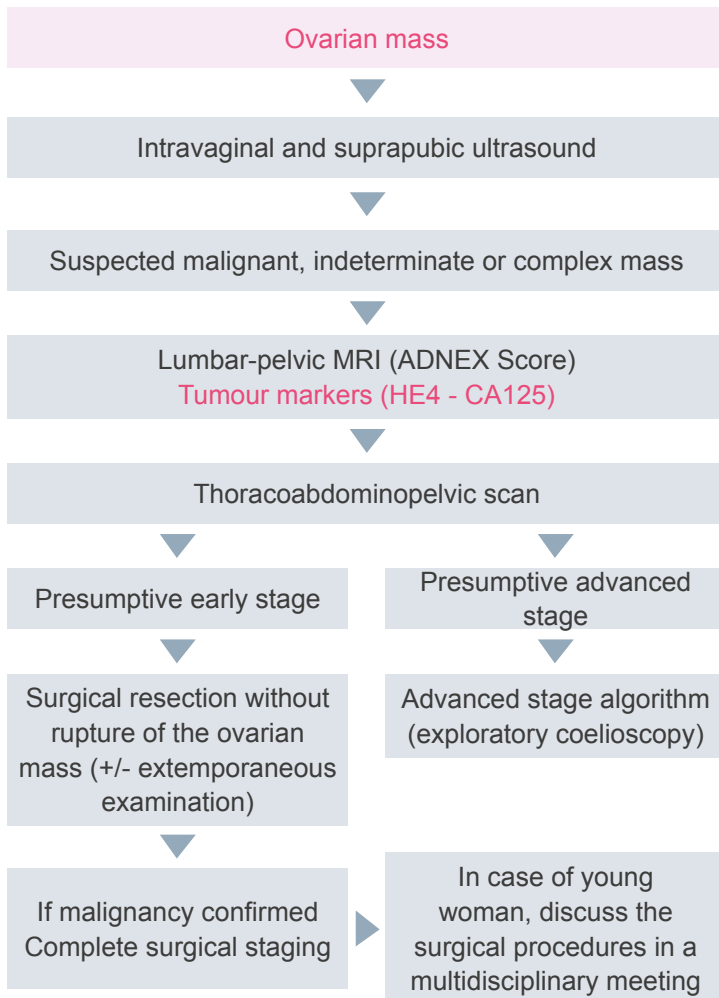
Screening for risk factors, including a personal and family history of cancer and of comorbidities.



Location of tumour markers in the case of a suspected ovarian mass^[1]

1. Diagnosis

Early stage (FIGO I to IIA)



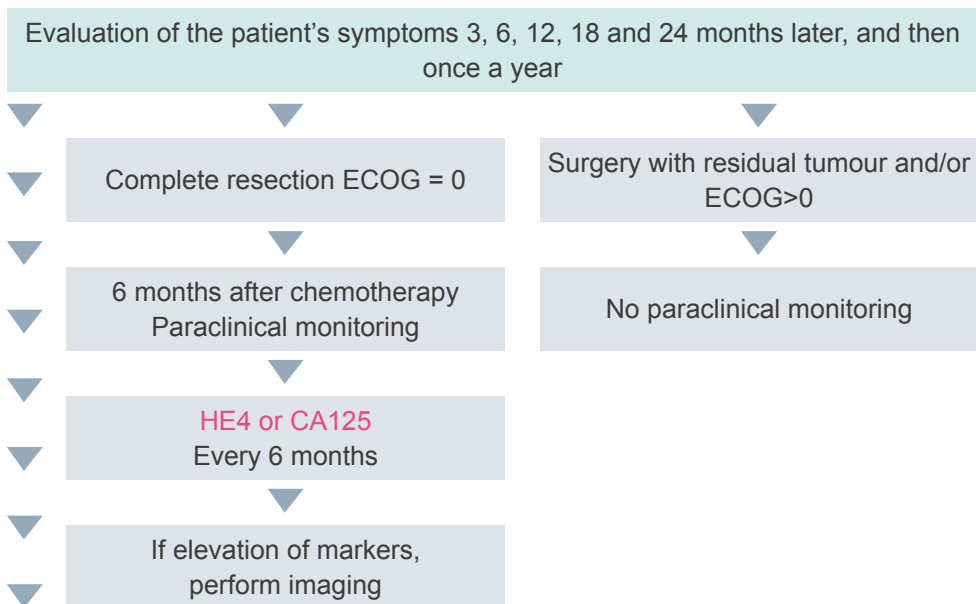
NB: tumour markers (HE4 and CA 125 are also recommended in advanced stages (FIGO III and IV)



Key point

- A serum CA125 assay is recommended to diagnose an ovarian tumour that is suspected to be malignant on basis of imaging (Grade A).
- A serum HE4 assay is recommended to diagnose an indeterminate ovarian mass identified imaging (Grade A).
- In the case of a single serum marker, no recommendation on the choice between the CA125 and HE4 assay
- In the case of an undetermined ovarian mass identified in imaging, use of the ROMA score is suggested.

2. In post-therapeutic monitoring



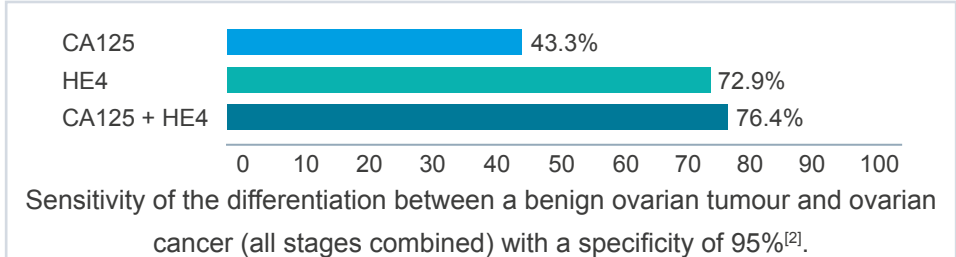


Key point

- If paraclinical monitoring is indicated, a serum HE4 assay can be offered (Grade C) (...). In the absence of possible monitoring for HE4, a serum CA125 assay can also be suggested (Grade B).
- In the case of serum elevation of HE4 or of CA125 after treatment of epithelial ovarian, fallopian tube or primitive peritoneal cancer, an imaging examination is recommended (Grade B).

HE4: *Human epididymis-specific protein 4*

HE4 is an epididymis-specific protein known of since 1991. Its overexpression has been identified in patients suffering from ovarian cancer from the initial stages (I and II) of the cancer, especially in cancers of the serous type. Its expression is independent of CA125 expression and occurs in 50% of cancers that do not express CA125.



- **The HE4 protein offers greater sensitivity and specificity than CA125 proteins, especially in early forms.**
- **The combination of HE4 and CA125 improves the sensitivity and specificity of the detection of ovarian cancers and recurrence of these.**

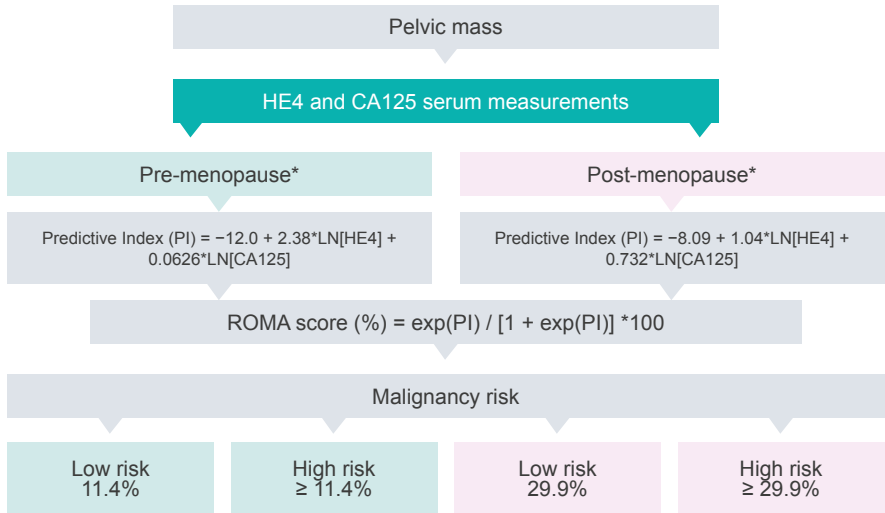
Furthermore, the concentration of HE4 increases **2 to 5 months before a clinical recurrence**, which makes it a useful marker for therapeutic monitoring^[3].

As no protein considered in isolation is totally specific or sensitive to ovarian tissue, combining markers and grouping them with clinical information has been proposed, to improve reliability.

ROMA score

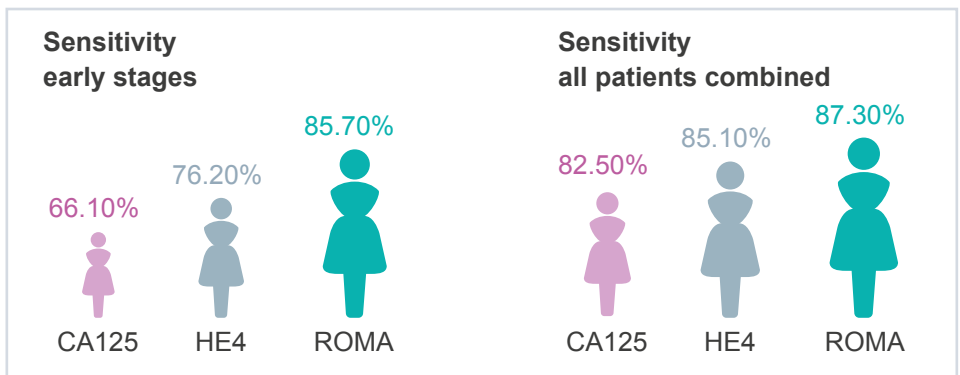
The Roma score is an algorithm combining the biomarkers CA125, HE4 and the patient's menopausal status (pre- or post-menopause).

The score thus calculated classifies pelvic mass according to the probability of malignancy or benignity, which is decisive as the basis for patient treatment.



Performance

According to a study on 1975 patients (meta analysis Dayani et al.)^[4]





The Roma score has an excellent **negative predictive value** (NPV), and constant in all studies, 98 to 100%, i.e. Gives strong assurance that a pelvic mass is benign if the Roma score indicates a low risk^[5, 6].



“The ROMA score (...) is superior in diagnosis of suspected malignant ovarian tumour in the form of an indeterminate ovarian mass identified in imaging in terms of sensitivity, specificity, AUC than the data from serum CA125 and HE4 assayed in isolation....” INCA – November 2018^[1]

Clinical benefits HE4 and ROMA Score

In combination with the patient case history, clinical examination and imaging, the ROMA score improves:

quick referral
of a patient with a high risk to a specialist team.

or a **reduction** of the number of unnecessary surgical interventions

the long-term survival rate and provides rapid reassurance to concerned patients.



Practical details

Indications

- 1. CA125, HE4 and Roma Score:** Supports early diagnosis of ovarian cancer in combination with clinical examination and imaging
- 2. HE4 - CA125:** Monitoring of treatment effectiveness - Detection of relapses
- 3. HE4:** Differential diagnosis of endometriosis

Test

HE4 + CA125 + ROMA score

To be specified:

Pre-menopause or post-menopause

Note: For the ROMA algorithm, HE4 and CA125 must be assayed from the same sample and with the same equipment, which means that a result for CA125 obtained from another sample or with a different system cannot be used.

Pre-analysis

- 1 mL of frozen serum 4 h

For more information

www.eurofins-biomnis.com >

Examinations > Test code: **HE4**

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References

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