

Gynaecological Oncology News

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HE4 – New Tumour Marker

Promising new tumour marker for ovarian cancer

HE4 (human epididymis protein 4) may improve our ability to triage women with pelvic masses. In the US it has been approved by the Food and Drug Administration for the follow-up of patients with a diagnosis of ovarian cancer.

HE4 is expressed in serous, clear cell and endometrioid ovarian cancer cell types, but not in mucinous or germ cell types. It is also negative in endometriosis.

For the differential diagnosis of women with pelvic masses, we know that CA125 is quite unspecific and ovarian endometriosis expresses high levels of CA125.

The Risk of Ovarian Malignancy Algorithm (ROMA) uses the combination of HE4 and CA125 and calculates the risk of ovarian cancer in women with a pelvic mass. Literature suggested that HE4 plus CA125 outperform every other tumour marker in regards to the prediction of malignancy.

Where can HE4 help?

Ovarian endometriosis often mimics ovarian cancer. Instead of a referral for a gynaecological oncology opinion, they can be operated on by general gynaecologists.

Elderly patients with pelvic masses often are medically unfit for surgery. A reliable assessment of the risk of malignancy allows us to reassure and spare these patients surgery.

CA125-negative patients with ovarian cancer could be correctly recognised prior to surgery with HE4 and referred for a gynaecological oncology opinion.

The new test is already used in the US and is now slowly introduced in Australia. American experience demonstrates that it may allow determining with greater accuracy what the most appropriate recommendation for women with a pelvic mass is.

- Patients with endometriosis may benefit from a referral to a dedicated gynaecological (endometriosis) surgeon.
- Patients with a low risk of malignancy and high co-morbidity profile may avoid surgery all together.
- Patients with low serum CA125 but high HE4 may benefit from gynaecological oncology input.

An example: A postmenopausal woman with a pelvic mass and a CA125 of 60 U/ml, HE4 of 6 pM has a 2.5% risk of malignancy according to ROMA. If the patient's HE4 is 40 pM, the same numbers indicate a risk of malignancy of 22%.

Ovarian Borderline Tumours

Ovarian Borderline Tumours (tumours of low malignant potential) represent a group of tumours with signs of atypia (similar to invasive ovarian cancer) but lack of invasion. Patients with Borderline tumours frequently present at a young age.

The majority of patients do well after surgery but up to 10% of patients may recur or even die as a consequence of the disease. Until now, we were unable to predict who is at risk of recurrence and thus needs to be followed closely.

New research from Queensland suggests that the tumour marker CA125 (measured preoperatively) identifies patients who are at high risk of relapse or to die from the disease. Survival was 91% at 5 years for women with low CA125 and 78% for women with elevated CA125.

Even more importantly, LMP patients who had high CA125 prior to surgery were found to develop recurrences far beyond 5 years from surgery.

SUMMARY: High-risk patients need to be monitored closely and life-long and may need a total pelvic clearance once family planning is completed. In contrast, patients at low risk don't need to be followed. Their life expectancy is that of the normal population.

Recommendations:

HE4 is not routinely measured by any Australian lab as yet and I am currently negotiating a service for patients with Sullivan & Nicolaides Pathology. No Medicare rebate number exists as yet; the costs for the HE4 test will be around \$30.

ROMA requires CA125 and HE4 and its algorithm is available as an app on iPhones (CA125 and HE4 Ovarian Biomarker Tool) or on the internet (www.taketherightpath.com) for free.

I will discuss the suitability of the HE4 test with patients individually.

LAPAROSCOPIC HYSTERECTOMY

A radio interview recorded for eCancer Radio at the IGCS meeting about Laparoscopic Hysterectomy is available for listening on www.obermair.info/newsletters/AndreasObermair [PODCASTeCancerLoRes.mp3](#) (5 mins).

Please do not hesitate to give me a call if you wish to discuss an aspect of the above or a specific patient with me.

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*Merry Christmas and a Fantastic New Year to you all!
I look forward to continue working together in 2011.*