

Serum tumour markers

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There is always a risk in medicine that we treat the test result rather than the patient and I think that is especially true when it comes to tumour markers – we may be falsely reassured or unnecessarily alarmed. So what tests are useful and when should we consider doing them? And how do we interpret the result?

A recent audit, highlighted in this BMJ paper, suggested that:

- Over 50% of tumour markers requested (from primary and secondary care) were being used as an inappropriate form of screening.
- It was not uncommon for labs to receive PSA tests for women and CA125 tests for men!! This rather suggests those requesting them were not completely sure what they are doing!!

This BMJ clinical review helpfully summarised some of the answers to our questions about tumour markers...

Tumour markers are used in a number of ways:

- Screening asymptomatic individuals
- To aid diagnosis
- To assess prognosis
- To detect recurrence
- To monitor treatment

But not all tumour markers are useful for all these indications!

But first let's be clear which tumour markers we are talking about and what diseases they are used for...and then we will discuss which situation each tumour marker may be useful for.

Tumour marker	Cancer
PSA	Prostate
CA125*	Ovarian
CA15-3*	Breast
CA19-9*	Pancreatic
Carcinoembryonic antigen (CEA)	Colorectal
HCG	Germ cell and testicular cancers Gestational trophoblastic neoplasia
Paraproteins (M protein, Bence Jones protein) (can be measured in urine as well)	B cell proliferative disorders (eg. multiple myeloma)
α fetoprotein	Germ cell cancers/testicular cancers Hepatocellular carcinoma
Calcitonin	Medullary thyroid carcinoma
Thyroglobulin	Follicular or papillary thyroid

* CA stands for cancer antigen

The key points from the BMJ clinical review were that:

- **Measuring more than one serum tumour marker is not helpful** (the only exception is in germ cell tumours when both α fetoprotein and HCG should be measured).
- **Tumour markers are not helpful in those with non-specific symptoms, mainly because many tumour markers are also raised in benign disease, so sensitivity and specificity are low!**

- **The BMJ clinical review says that none of the tumour markers are helpful for screening asymptomatic individuals** except α fetoprotein for hepatocellular carcinoma (so primary liver cancer, not liver metastases). α fetoprotein should be measured 6 monthly in those at high risk of hepatocellular carcinoma (especially those with cirrhosis related to hepatitis B or C). (However, note that CA125 is being evaluated for ovarian cancer screening and PSA is widely used and the evidence for this is discussed in the prostate cancer section in the Men's Health chapter!)
- **All the tumour markers are helpful for both detecting recurrence and monitoring response to treatment**, although more work is needed in this area for many of the markers.
- So how helpful are they to **establish a diagnosis** or as a **prognostic indicator?**

Tumour marker	Useful to aid diagnosis?	Useful for prognosis?
PSA (prostate)	Yes	Yes
CA125 (ovarian)	Yes	Yes
CA15-3 (breast)	No	No
CA19-9 (pancreatic)	Yes	Yes
CEA (colon)	No	Yes
HCG (germ cell, testicular, trophoblastic disease)	Yes	Yes
Paraproteins (B cell proliferation)	Yes	No
A fetoprotein in germ cell/testicular Ca	Yes	Yes
A fetoprotein in hepatocellular Ca	Yes	Yes
Calcitonin (medullary thyroid)	Yes	No
Thyroglobulin (follicular/papillary thyroid)	No	No

- **Remember that many things can cause a tumour marker to be raised (other than cancer) and may lead to incorrect interpretation (false positives). Here are just a few of them!** (These lists are by no means exhaustive but you suddenly realise why interpreting the test without reference to the patient may result in all kinds of false anxiety!)

PSA

- Ejaculation, BPH, prostatitis, prostate massage (cycling!) prostate biopsy, cystoscopy cause an elevated PSA. However a rectal exam is not likely to cause a significant rise in PSA.
- 5α reductase inhibitors (eg. finasteride) lower PSA.

Remember: PSA is organ specific, not cancer specific, that it is it will rise with many diseases of the prostate, including benign hypertrophy, and not just cancer (indeed it can be normal in those with prostate cancer!)

PSA and prostate cancer screening are covered in some detail in the men's health chapter of The GP Update Handbook.

CA125

- Endometriosis, menstruation, IBS, pneumonia, arthritis, colitis, diabetes, laparoscopy, SLE all cause CA125 to rise.

CA125 and ovarian cancer are discussed in greater detail in the cancer chapter of The GP Update Handbook, where we have summarised the latest research on symptoms suspicious of ovarian cancer. **Please note that, current guidance from the Department of Health is to use the CA125 in conjunction with an ultrasound scan (DH, Key messages on ovarian cancer for health professionals, 2009).**

- **False negatives**

We would also add (although this was not mentioned in the BMJ Clinical Review) that tumour markers may be negative in the presence of cancer – so if you suspect ovarian cancer but the CA125 is normal do not be reassured – we think you should refer in these situations.

CPD Ideas

See the GP Update Revalidation Action Plans sent with this update update: designed to help you record your learning ready for your next appraisal and your revalidation folder.

Take home messages: Tumour markers

- **Measuring more than one serum tumour marker is not helpful.**
- **Tumour markers are not helpful in those with non-specific symptoms because of low sensitivity and specificity, and false negative may also occur. Do not be falsely reassured by a negative tumour marker in someone with suspicious symptoms.**
- **None of the tumour markers are helpful for screening asymptomatic individuals (although CA125 is being evaluated for ovarian cancer screening and PSA is widely used).**
- **Some, but not all, tumour markers give useful information that helps with diagnosis and prognosis.**
- **All the tumour markers are helpful for both detecting recurrence and monitoring response to treatment, although more work is needed in this area for many of the markers.**
- **Remember that many things can cause a tumour marker to be raised (other than cancer) and may lead to incorrect interpretation.**

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