

REDUCING THE RISK OF GYNAECOLOGICAL CANCERS

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ABSTRACT

- Amongst the top 10 commonest female cancers in Singapore are: breast (1st); ovarian (4th); cervical (5th) and uterine cancers (7th).
- Risk factors of cervical cancer are smoking, early sexual exposure, multiple sexual partners and immunosuppression. Risk factors common to both ovarian cancer and uterine cancer are age, family history and nulliparity.
- The potential role of a tumour marker in epithelial ovarian cancers, include: (1) Cancer Screening; (2) Diagnosis; (3) Prognostication; (4) Monitoring Response to Treatment and (5) Detecting Recurrence. At present, CA-125 lacks sufficient specificity to be a suitable screening test when used in isolation. However, when combined with pelvic ultrasound in post-menopausal women, both can achieve high specificity (99.9%), sensitivity of 78.6%. CA-125 has been a clinical useful marker for predicting response to treatment, prognostication and detecting tumour recurrence.
- Prevention of gynaecological cancers lies in patients reducing risk factors and going for Pap smear screening to prevent cervical cancer.

OVERVIEW

The top 10 commonest female cancers in Singapore are: Breast(1st), Colorectum(2nd), Lung (3rd), Ovarian cancer (4th), Cervix cancer (5th), Stomach (6th), Uterus (7th), Skin (8th), Thyroid (9th) and Lymphoma (10th).

RISK AND PROTECTIVE FACTORS FOR GYNAE-COLOGICAL CANCERS

The risk and protective factors for Gynaecological Cancers are shown in Table 1.

TUMOUR MARKERS

A tumour marker is defined as a biologic substance produced by malignant tumours, which enters the circulation in detectable amounts. For it to be clinically useful, a tumour marker should :

1. be tumour-specific
2. be produced in sufficient amount to be detectable even in minimal disease.
3. quantitatively reflects the tumour burden.

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Table 1. Risk and protective factors for gynaecological cancers

Cervix cancer	Ovarian cancer	Uterine (Endometrial) Cancer
	Risk Factors	
Smokers Immunosuppressed Early sexual exposure Multiple sexual partners	After 50 years old Family History or personal history of breast, ovarian, endometrial and colonic cancers. Nulliparity Subfertility treatment	After 40 years old Family History or personal history of breast, ovarian, endometrial and colonic cancers. Nulliparity Metabolic Syndrome Anovulatory menstrual cycles Unopposed estrogen Tamoxifen
	Protective Factors	
Pap smear screening	Combined Contraceptive Pills Parity Breastfeeding	Combined Contraceptive Pills Parity

Various ovarian cancers may produce tumour markers:

Epithelial Ovarian Cancer:

CA125

CEA (*Carcinoembryonic antigen*)

Germ Cell Tumours:

AFP (*alpha-FetoProtein*)

beta-hCG (*human chorionic gonadotropin*)

LDH (*lactate dehydrogenase*)

The potential role of a tumour marker in epithelial ovarian cancers, include: (1) Cancer Screening; (2) Diagnosis; (3) Prognostication; (4) Monitoring Response to Treatment and (5) Detecting Recurrence.

CA125 – a glycoprotein, normally present during embryonic/ fetal development of coelomic epithelium, present in adult structures that are derived from it, namely: (1) mesothelial cells of the pleura, pericardium, peritoneum; (2) tubal, endometrial and endocervical epithelium; (3) ovarian epithelium.

Measuring CA125 – CA-125 is measured by immunoassays. A 99 percentile cut-off of serum value, at 35 U/ml, is used to denote an abnormal value, i.e. values >35 U/ml representing 1% of healthy females population and 35U/ml is accepted as the upper limit of normal in clinical practice.

Specificity – CA-125 has a lower specificity in pre-menopausal than post-menopausal women presumably. It can be elevated in other malignancies (pancreatic, breast, colon, and lung) and

benign as well as physiologic conditions such as endometriosis, pelvic inflammatory disease, menstruation, pregnancy, etc.

Facts about CA-125 & epithelial ovarian cancer

- About 85% of patient with epithelial ovarian cancer have elevated CA-125 of >35 U/ml.
- Elevated more often in advanced stage compared to early stage ovarian cancer (50% for stage 1 vs >90% in advanced stages).
- Less often elevated in mucinous, clear cell and borderline tumours.

Screening and Diagnosis of an Adnexal Mass

At present, CA-125 lacks sufficient specificity to be a suitable screening test when used in isolation. However, when combined with pelvic ultrasound in post-menopausal women, both can achieve high specificity (99.9%), sensitivity of 78.6%. The Risk Malignancy Index (RMI) predicts risk of malignancy of an adnexal mass and is calculated by:

$$\text{RMI} = \text{U} \times \text{M} \times \text{CA125}$$

CA125 value in U/ml;

M = Menopausal status (1,3) :

U = Ultrasound features (0,1,3)

RMI of more than 200 is a strong indication for gynaecological oncology review.

CA-125 has been a clinical useful marker for predicting response to treatment, prognostication and detecting tumour recurrence.

Carcinoembryonic antigen (CEA)

- is often associated with colon and pancreatic carcinoma.
- serum CEA levels are elevated in 25-50% of women with ovarian cancer.
- usually elevated in advanced stage, mucinous, endometrioid and clear cell tumours.
- elevated in not more than 20% of serous carcinoma.

PRIMARY PREVENTION & SCREENING FOR GYNAECOLOGICAL CANCERS

If I am woman, what would I do to reduce my risk of developing a gynaecological cancer?

The 10 things to do are:

1. avoid smoking & maintain good general health
2. avoid developing the Metabolic Syndrome
3. avoid having multiple sexual partners
4. go for yearly gynaecological examination
5. have regular Pap smears & regular Mammography (as recommended)
6. use the combined contraceptive pills in between pregnancy
7. ensure I menstruate regularly
8. have two or more children
9. breastfeed my children
10. Consider regular CA125 & Ultrasound Pelvis screening especially if I have a family history (above)

LEARNING POINTS

- **Of the 10 commonest female cancers in Singapore, breast, ovarian, cervical, and uterine cancers occupy first, fourth, fifth and seventh positions respectively.**
 - **Risk factors of cervical cancer are smoking, early sexual exposure, multiple sexual partners and immunosuppression.**
 - **Risk factors common to both ovarian cancer and uterine cancer are age, family history and nulliparity.**
 - **At present, CA-125 lacks sufficient specificity to be a suitable screening test when used in isolation. However, when combined with pelvic ultrasound in post-menopausal women, both can achieve high specificity (99.9%), sensitivity of 78.6%.**
 - **CA-125 has been a clinical useful marker for predicting response to treatment, prognostication and detecting tumour recurrence.**
 - **Prevention of gynaecological cancers lies in patients reducing risk factors and going for Pap smear screening to prevent cervical cancer.**
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