

# **Evaluation of Serum HE4 in Malignant and Benign Ovarian Masses**

*Thesis*

*Submitted for partial fulfillment of Master Degree in  
Obstetrics and Gynecology*

*By*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبِّحْكَ لَا إِلَهَ إِلَّا مَا  
عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

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*✍️ Marwa*

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## *List of Abbreviations*

<b>AUC</b>	:	Area under the curve
<b>BMI</b>	:	Body mass index
<b>CA125</b>	:	Cancer antigen 125
<b>CEA</b>	:	Carcinoembryonic antigen
<b>CSF-1</b>	:	Colony stimulating factor 1
<b>CT</b>	:	Computed tomography
<b>DM</b>	:	Diabetes mellitus
<b>EOC</b>	:	Epithelial ovarian cancer
<b>FIGO</b>	:	Federation of Gynecology and Obstetrics
<b>GI</b>	:	Gastrointestinal
<b>HE4</b>	:	Human Epididymis Protein 4
<b>HRT</b>	:	Hormone replacement therapy
<b>HT</b>	:	Height
<b>IAP</b>	:	Immunosuppressive acidic protein
<b>IV</b>	:	Intravenous
<b>LPA</b>	:	Lysophosphatidic acid
<b>LR+</b>	:	Positive likely hood
<b>LR-</b>	:	Negative likely hood
<b>MAGE</b>	:	Mucoviscosity associated gene A
<b>MCS-F</b>	:	Macrophage colony-stimulating factor
<b>MRI</b>	:	Magnetic resonance imaging

*List of Abbreviations*

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<b>NACB</b>	:	National Academy of Clinical Biochemistry
<b>NPV</b>	:	Negative predictive value
<b>PCOS</b>	:	Polycystic ovarian syndrome
<b>PET</b>	:	Positron emission tomography
<b>PID</b>	:	Pelvic inflammatory disease
<b>PPV</b>	:	Positive predictive value
<b>RMI</b>	:	Risk of malignancy index
<b>ROC</b>	:	Receiver operator characteristics
<b>ROMI</b>	:	Risk of Ovarian Malignancy Algorithm
<b>SMRP</b>	:	Soluble mesothelin related peptide
<b>SN</b>	:	Sensitivity
<b>SP</b>	:	Specificity
<b>TATI</b>	:	Tumor-associated trypsin inhibitor
<b>TVUS</b>	:	Trans vaginal ultrasonography
<b>US</b>	:	Ultrasonography
<b>VEGF</b>	:	Vascular endothelial growth factor
<b>WFDC2</b>	:	Wap four- disulphide core domain protein 2
<b>WT</b>	:	Weight

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## **Introduction**

Ovarian cancer is the second diagnosed gynecologic malignancy in the United States; it is also the most deadly because over 70% of women are diagnosed with advanced stage disease. In advanced stage disease cure rates are only 20-30% (*Jemal et al, 2007*).

According to current estimates, 1.4% (1 in 72) of women born today will be diagnosed with ovarian cancer at some point in their lifetime (*Ries et al, 2008*).

Early stage ovarian cancer has an excellent prognosis if treated. Given the limitation of treatment for advanced ovarian cancer and the success of treatment for early stage disease, a screening test is intuitively appealing (*Schink, 1999*).

Prior attempts to establish population based screening protocols for ovarian cancer have employed CA125, ultrasound and new biomarkers and statistical approaches (*Bast et al, 1981; Bast et al, 1990*).

Transvaginal ultrasound has proven useful as a secondary screening tool; however its utility as a screening tool remains questionable given its demonstrated low positive predictive value and clinically insufficient levels of sensitivity (*Van Nagell et al, 2007*). Advanced imaging techniques such as CT or MRI have proven too expensive for widespread use given their limited sensitivity & specificity.

CA125 is the current "gold standard" biomarker for diagnosis of ovarian cancer. It is a high molecular weight mucin type glycoprotein that is expressed by ovarian tumors and other cancers such as breast cancer( *Berruti et al, 1994; Norum et al, 2001*), mesothelioma (*Hedman et al, 2003*), non-Hodgkin lymphoma (*Bairey et al, 2003; Zidan et al, 2004*), leukemia (*Camera et al, 2000*), gastric cancer (*Yamamoto et al, 2007*), leiomyoma and leiomyosarcoma of gastrointestinal origin ( *Whiteley et al, 1993*).It is also elevated in benign conditions such as cirrhosis, benign gynecologic conditions, endometriosis, pregnancy, ovulation, liver disease and congestive heart failure.

CA125 has very low sensitivity in identifying patients with early stage ovarian cancer( *Terry et al, 2004*).Thus to improve the sensitivity & specificity of ovarian cancer