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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Marwa

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List of Abbreviations

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

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

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***Protocol** of Thesis*

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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