A TECHNICAL REVIEW

LabCorp

Risk for Ovarian Malignancy Algorithm (ROMA®) Calculation Tool Using Elecsys® Assays

In the presence of adnexal mass

The ROMA® (Risk of Ovarian Malignancy Algorithm) Calculation Tool Using Elecsys® Assays combines the results of the Roche Elecsys HE4 assay, Elecsys CA 125 II assay and menopausal status into a numerical score. The ROMA® Calculation Tool is intended to aid in assessing whether a premenopausal or postmenopausal woman who presents with an ovarian adnexal mass is at high or low likelihood of finding malignancy on surgery. The ROMA® Calculation Tool is indicated for women who meet the following criteria: older than age 18; ovarian adnexal mass present for which surgery is planned; and not yet referred to an oncologist. ROMA values must be interpreted in conjunction with an independent clinical and radiological assessment. The test is not intended as a screening or stand-alone diagnostic assay.[1]

Clinical Review

An estimated 21,290 women in the United States were diagnosed with ovarian cancer in 2015, and approximately 14,180 women died of the disease.[2] Symptoms of ovarian cancer are related to the presence of adnexal masses and are often vague and unspecific. The primary goal of diagnostic evaluation of an adnexal mass is to determine whether it is benign or malignant. Estimates are that 5% to 10% of women in the US will have surgery for a suspected ovarian neoplasm during their lifetime, and 13% to 21% of these women will be diagnosed with an ovarian malignancy.[3] Because the majority of adnexal masses are benign, it is important to try to determine before surgery whether a patient is at a high likelihood for ovarian malignancy, in order to ensure proper management.[3] The American College of Obstetricians and Gynecologists Practice Bulletin 174 published in November 2016 states that consultation with or referral to a gynecologic oncologist is recommended for women (both premenopausal or postmenopausal) with an adnexal mass who meet certain criteria, including women who have an elevated score on a formal risk assessment test such as the ROMA.[4]

According to the package insert, the ROMA® Calculation Tool score is used to stratify women into likelihood groups for finding cancer on surgery.[1] To improve the management of patients presenting with adnexal mass, the ROMA® Calculation Tool results may be used in conjunction with Initial Cancer Risk Assessment (ICRA) in assessing the likelihood of finding malignancy on surgery in premenopausal and postmenopausal women presenting with an adnexal mass.[1] Several studies have evaluated the sensitivity of the ROMA score at a predefined specificity for identifying ovarian cancer in women presenting with a pelvic mass and found that the use of ROMA increases sensitivity compared with CA 125 or HE4 alone.[5-9] In 2014, Moore and colleagues published the findings of a prospective, multicenter trial evaluating women with a pelvic mass who had an initial clinical risk assessment (ICRA) performed by a generalist. Adjunctive use of ROMA with an ICRA improved the stratification of women with a pelvic mass into low- and high-risk groups for ovarian cancer. According to the study, this combination was found to be effective in ruling out malignant disease.[9] The cut-off points in Table 1 were used in order to provide a specificity level of 75%. Women whose ROMA results are equal to or above these cut-off points are at a high likelihood of finding malignancy on surgery.[1]

Table 1 — ROMA Score Cut-off points[1]

	ROMA Score	Likelihood of Malignancy
Premenopausal Women	≥ 1.14	High
	< 1.14	Low
Postmenopausal Women	≥ 2.99	High
	< 2.99	Low

The performance of the ROMA® Calculation Tool for stratification into low-likelihood and high-likelihood groups for premenopausal and postmenopausal women for harboring epithelial ovarian cancer only is shown in Table 2[1]:

Table 2 — Estimated Performance of the ROMA Clinical Trial[1]

	Premenopausal	Postmenopausal
Sensitivity	100.0%	89.5%
Specificity	77.6%	82.8%
Positive Predictive Value	15.0%	57.6%
Negative Predictive Value	100.0%	96.7%

The performance for the adjunctive use of ROMA Calculation Tool Using Elecsys Assays with ICRA (ROMA Calculation Tool Using Elecsys Assays and/or ICRA being positive for high likelihood of finding malignancy on surgery) was evaluated by calculating sensitivity, specificity, positive predictive value and negative predictive value. The prevalence was 14.9%.[1] The adjunctive use of ICRA and ROMA for diagnosis of EOC including LMP showed sensitivity for malignancy increasing from 76.9% to 90.8%. Specificity for malignancy decreased from 84.4% to 70.4%. Positive predictive value for the adjunctive use of ICRA and ROMA decreased from 46.3% to 34.9% due to an increase in the number of false-positive tests. However, negative predictive value of the adjunctive use of ICRA and ROMA increased from 95.4% to 97.8% (Table 3).[1]

Table 3 — Estimated Performance of ROMA With ICRA[1]

	ICRA	ROMA	Adjunctive
Sensitivity	76.9%	86.2%	90.8%
Specificity	84.4%	79.5%	70.4%
Positive Predictive Value	46.3%	42.4%	34.9%
Negative Predictive Value	95.4%	97.0%	97.8%

Clinical Limitations

According to the package insert, the ROMA® Calculation Tool Using Elecsys® Assays uses the combination of Elecsys HE4 and Elecsys CA 125 II values that depend on the premenopausal or postmenopausal status of a woman.[1] The premenopausal or postmenopausal status must be based on ovarian function determined with information available from clinical evaluation and medical history.[1]

The ROMA® Calculation Tool result cannot be used as absolute evidence for the presence or absence of malignant disease. The ROMA® Calculation Tool result should not be used as a cancer screening test. The ROMA® Calculation Tool result has only been evaluated in women who will undergo a surgical intervention and is only intended for use in this population. The ROMA® Calculation Tool should not be used without an independent clinical evaluation and is not intended to determine whether a patient should proceed to surgery. A low-likelihood ROMA result, in the setting of a positive initial cancer risk assessment, should not preclude oncology referral.[1]

The ROMA® Calculation Tool has not been validated for the following groups: women previously treated for malignancy; women currently being treated with chemotherapy; pregnant women; and women under 18 years of age.[1]

The ROMA® Calculation Tool has been validated only with HE4 and CA 125 results produced with assays from specific manufacturers. The ROMA performed by LabCorp employs the Roche Elecsys HE4 and CA 125 assays as specifically indicated in the FDA-cleared manufacturer's package insert.

Relevant Assays*

Test Name	Test Number
Ovarian Malignancy Risk (ROMA®)	140045
Specimen 1 mL serum in a red-top or gel-barrier tube. If a red-top tube is used, transfer separated serum to a plastic transport tube.	

*For the most current information regarding test options, including specimen requirements and CPT codes, please consult the online Test Menu at www.LabCorp.com.

References:
1. ROMA Calculation Tool: ROMA Calculation Tool Using Elecsys Assays [package insert]. Indianapolis, IN: Roche Diagnostics; 2016-08, V 1.0 English.
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