

eISSN : 2579-8324

pISSN : 2579-8323

Alamat Korespondensi:

Ruang Redaksi Andalas Obstetrics and Gynecology Journal, Lantai 3 PPDS Obstetri dan Ginekologi Universitas Andalas, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127

Website:

<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

RESEARCH

ROMA and IOTA Score Comparison in Predicting Ovarian Tumour Malignancy

Yussya Aulia Malik¹, Andi Friadi²

Affiliations: 1. Resident of Obstetrics and Gynecology, Faculty of Medicine, Andalas University, Dr. M. Djamil Central General Hospital Padang; 2. Sub Division of Gynecological Oncology, Obstetrics and Gynecology Department, Faculty of Medicine, Andalas University, Dr. M. Djamil Central General Hospital Padang

Correspondence: Yussya Aulia Malik, email: nico_rico24@yahoo.com, Hp: 085274400300

Abstract

Ovarian cancer is the sixth most common cancer found among women. Incidence of ovarian cancer in Dr. M. Djamil Central Hospital had increased from 103 cases to 156 cases in 2011-2012. The Risk Of Ovarian Malignancy Algorithm (ROMA) consists of qualitative serum test where several variables including HE4 serum, CA125 serum, and menopausal status are turned into numerical score (Hye Yon Cho et al 2015). The latest diagnostic modalities developed by International Ovarian Tumour Analysis (IOTA) classifies tumour into four sub groups, based on ultrasound characteristics: unilocular, multilocular, adnexal mass with solid component without papilloma projection, adnexal mass with one or more papilloma projection. Based on this knowledge, author would like to investigate accuracy of ROMA and IOTA score in predicting malignancy status of early ovarian tumour.

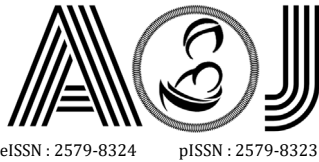
Objective: Determining ROMA and IOTA so thus can be utilised to predict whether the ovarian tumour is benign or malignant.

Method: This was analytical study, with cross sectional design and took place in Obstetrical and Gynaecological Outpatient Clinic of Dr. M. Djamil Central Hospital from August 2016 to January 2019. Sample was recruited using consecutive sampling method. Sixty one participants were recruited with CI 99%. Patients who met inclusion criteria would undergo Ca125 serum test and IOTA score. HE4 level was determined after surgery and the sample of a tumour was sent to pathology anatomy laboratory of Medical Faculty of Andalas University to investigate the malignancy status. Statistical analysis involved univariate and bivariate test. The variables included frequency distribution, ROMA, and IOTA score. Bivariate analysis included specificity, sensitivity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio.

Result: Thirty one patients (50,8%) from peri menopausal group had HE4 level ≤ 70 pmol/L and 30 patients (49,2%) from post menopause group had HE4 level ≤ 140 pmol/L. Eleven patients (18%) had CA125 level < 35 and 50 patients (82%) had CA125 level ≥ 35 . ROMA index showed low risk in 17 patients (27,9%) and high risk 44 patients (72,1%). IOTA with M Rules was 51 patients (83,6%) and B rules was 10 patients (16,4%). Diagnostic value for ROMA score had sensitivity of 71,9%; RMI of 84,2%; and IOTA 82,5%. ROMA and IOTA accuracy was 68,9% and 92,2%, respectively.

Conclusion: IOTA has better sensitivity in predicting ovarian tumour compared with ROMA. ROMA has higher positive predictive value compared with IOTA positive predictive value. ROMA negative predictive value is 5,9%, meanwhile for IOTA it is hard to determine

Keywords: ovarian cancer, ROMA, IOTA, Ca-125, HE4



eISSN : 2579-8324

pISSN : 2579-8323

Alamat Korespondensi:

Ruang Redaksi Andalas Obstetrics and Gynecology Journal, Lantai 3 PPDS Obstetri dan Ginekologi Universitas Andalas, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127

Website:

<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

INTRODUCTION

Ovarian cancer is the sixth most common cancer found among women. FIGO (federation of gynaecology and obstetrics) argues that two third of women with ovarian cancer presented with advanced stage of the disease and relatively lower five year survival rate for stadium III and IV, 23,9% and 37%, respectively, and closely related with the histopathology finding. World wide, ovarian cancer incidence is estimated at 204.499 annual cases with 124.860 death.¹

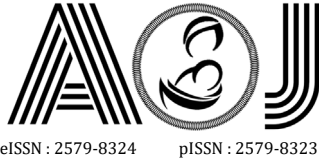
Indonesian Society of Gynaecology Oncology in 2012 stated ovarian cancer was the second most common cancer after cervix cancer. In 2012 there were 354 ovarian cancer in Indonesia and this number kept climbing with incidence of 7,1% in 2018. Most patients presented with stage II-IV (42,5%) which lead to poor treatment outcome.²

In 2011 to 2012, ovarian cancer incidence in M. Djamil Central Hospital had been increased from 103 cases to 156 cases, 50% percent higher. Seven patients (14%) and 11 patients (14%) had died due to ovarian cancer in 2011 and 2012, respectively. The treatment progress of ovarian cancer had been stagnant.

More than 70% patients presented with advance stage of the disease, where five year survival rate is lower than 30%. On the contrary, 25% patients presented with stage I where the 5 year survival rate was 90%, and stage II patients had 5 year survival rate of 70%. Early detection of ovarian cancer is very important for better treatment outcome. Ovarian tumour in early stage does not show specific symptoms which is the reason patients often come with advanced stage of the disease.³

Tumour marker for detection and early detection of ovarian cancer is crucial to learn about ovarian cancer.⁴ The Risk of Ovarian Malignancy Algorithm (ROMA) is qualitative serum test where HE4 serum level and CA 125 serum level are combined, then with menopause status this data is turned into numerical score. ROMA is able to assess wether a pre menopause and menopause women with ovarian adnexal mass has low or high risk to have malignancy during surgery.⁶

International ovarian tumor analysis (IOTA) is the latest diagnostic tool to classify ovarian tumour into four subgroup based on ultrasound characteristic: unilocular, multilocular, adnexal mass with solid component without papilloma projection, adnexal mass with one or more papilloma projection. There are various preoperative diagnostic tools to diagnose ovarian cancer, but good diagnostic value, effective, non invasive, affordable, and efficient need to chosen wisely. Based on this data, author would like to compare ROMA and IOTA in predicting early stage of ovarian malignancy.⁷



eISSN : 2579-8324

pISSN : 2579-8323

Alamat Korespondensi:

Ruang Redaksi Andalas Obstetrics and Gynecology Journal, Lantai 3 PPDS Obstetri dan Ginekologi Universitas Andalas, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127

Website:

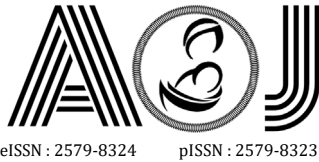
<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

METHOD

This was descriptive analytical study with cross sectional study approach. This study determined ROMA and IOTA score in predicting ovarian cancer malignancy in predicting ovarian cancer. This study took place in Gynaecological Outpatient Clinic of Dr. M. Djamil Central Hospital and Biomedical Laboratory of Medical Faculty Andalas University. Ovarian cancer patients data was collected from August 2016 to December 2019.

Study population was every patient with ovarian mass who will undergo surgery on Dr. M. Djamil Central Hospital. Sample was collected with consecutive sampling method and 61 patients were recruited with CI 99%. Ca125 serum level and IOTA score of patients who met inclusion criteria was collected and calculated. Subsequently, patient underwent surgery and HE4 from the tumour sample was sent to Pathology Laboratory of Medical Faculty Andalas University.

Univariate analysis was used to analyse every variable from this study. Data was presented with frequency distribution table with mean value. Distribution of ovarian tumour, risk of ovarian malignancy algorithm (ROMA), and IOTA score were analysed. Bivariate analysis was conducted to assess specificity, sensitivity, positive prediction value, negative prediction value, positive likelihood ratio, negative likelihood ratio, and accuracy.



eISSN : 2579-8324

pISSN : 2579-8323

Alamat Korespondensi:

Ruang Redaksi Andalas Obstetrics and Gynecology Journal, Lantai 3 PPDS Obstetri dan Ginekologi Universitas Andalas, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127

Website:

<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

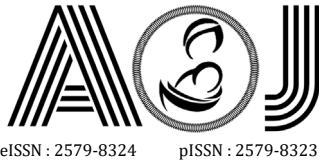
RESULT AND DISCUSSION**Characteristic of participant****Table 1.** Characteristic of participant

| Characteristic | Mean SD | Frequency | Percentage |
|-----------------------|-------------|-----------|------------|
| Age | 47,5 ± 13,7 | | |
| ≥ 45 | | 30 | 49.2 |
| <45 | | 31 | 50.8 |
| Pathology result | | | |
| Eptihelial carcinoma | | 57 | 93,4 |
| Non epithelial | | 4 | 6,56 |
| Menopause status | | | |
| Menopause | | 30 | 49.2 |
| Not menopause | | 31 | 50.8 |
| HE4 level | 47.8±18,9 | | |
| HE4 perimenopause | | | |
| ≤70 pmol/L | | 31 | 50.8 |
| >70 pmol/L | | 0 | 0 |
| HE4 in post menopause | | | |
| ≤140 pmol/L | | 30 | 49.2 |
| >140 pmol/L | | 0 | 0 |
| CA125 level | | | |
| <35 | | 11 | 18 |
| ≥35 | | 50 | 82 |
| ROMA index | | | |
| Low risk | | 17 | 27.9 |
| High risk | | 44 | 72.1 |
| IOTA | | | |
| B rules | | 10 | 16.4 |
| M Rules | | 51 | 83.6 |

Table 1 shows characteristic of participant. Table 1 shows 61 patients with cystic mass who will undergo surgery. Among 61 patients 30 patients and 31 patients are ≥ 45 years old (49,2%) and <45 years old (50,8%). Eleven patients (11%) have Ca125 serum level < 35 and 50 patients (82%) have Ca125 serum level > 35. Based on ROMA criteria, low risk patients and high risk patients are 17 (27,9%) and 44 (72,1%), respectively. IOTA result shows B rules (benign representation) and M rules as many as 10 patients (16,4%) and 51 patients (83,6%), respectively.

Table 2. Pathology result with ROMA

| ROMA index | Pathology anatomy | | Total |
|------------|----------------------------|---------|-------|
| | epithelial ovary carcinoma | non EOC | |
| High risk | 41 | 3 | 44 |
| Low risk | 16 | 1 | 17 |
| Total | 57 | 4 | 61 |



eISSN : 2579-8324

pISSN : 2579-8323

Alamat Korespondensi:

Ruang Redaksi Andalas Obstetrics and Gynecology Journal, Lantai 3 PPDS Obstetri dan Ginekologi Universitas Andalas, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127

Website:<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

Based on the table, ROMA had sensitivity of 71,9%; specificity of 25%; negative predictive value of 93,2%, negative predictive value of 5,9%; positive likelihood ratio of 0,96%; negative likelihood ratio of 1,12; and accuracy of 68,9%.

Table 3. Pathology result with IOTA

| IOTA | Pathology anatomy | | Total |
|----------------|----------------------------|---------|-------|
| | epithelial ovary carcinoma | non EOC | |
| M rules | 47 | 4 | 51 |
| B rules | 10 | 0 | 10 |
| Total | 57 | 4 | 61 |

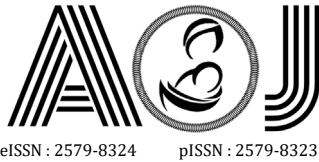
IOTA has sensitivity of 82,5%; negative predictive value of 92,2%; positive predictive value of 0,825; and accuracy of 92%.

DISCUSSION

This study predicted ovarian tumour prior to surgery. As many as 30 patients (49,2%) were ≥ 45 years old, and 31 patients were < 45 years old. Pathology anatomy investigation showed 57 samples (93,44%) were classified as epithelial ovarian carcinoma and 4 samples (6,56%) were non epithelial carcinoma. Thirty patients (49,2%) and 31 patients (50,8%) were menopause and premenopause, respectively. As many as 31 (50,8) premenopause group had HE4 level of ≤ 70 pmol/L and 30 patients (49,2%) from post menopause group had HE4 ≤ 140 pmol/L. Eleven patients (18%) and 50 patients (82%) had Ca125 level of < 35 and ≥ 35 , respectively. ROMA index showed 17 patients had low risk (27,9%) and 44 patients had high risk (72,1%). IOTA with M. Rules showed 51 patients (83,6%) and B Rules 10 patients (16,4%). Diagnostic value for ROMA score for sensitivity were 79,9%; RMI 84,2%; IOTA 82,5%; accuracy of ROMA score were 68,9%, and IOTA 92,2%.

This study showed Ca125 had high sensitivity (95,2%) but insufficient specificity (57,5) to be utilised as tool to predict ovarian malignancy. Ca124 level was found increased in more than 80% advanced stage of epithelial ovarian malignancy and only found increased in 50% of early stage of ovarian malignancy. High level of Ca125 is also found in other condition including inflammation as endometriosis, hip inflammatory disease, pregnancy, non gynaecological cancer as breast cancer, lung cancer, and gastrointestinal cancer. Sensitivity and specificity Ca125 to predict ovarian malignancy is 56-100% and 60-92%, respectively.

Sebastian Szubert (2016) conducted a study in Poland and argued that ultrasound to estimate IOTA had sensitivity of 95% and specificity of 88,3%. Vit Weinberg (2016) from Czech Republic suggested ultrasound for diagnosing ovarian malignancy had sensitivity of 84%, specificity of 96%, positive predictive value 96%, negative predictive value 83%, and total accuracy of 89%.



eISSN : 2579-8324

pISSN : 2579-8323

Alamat Korespondensi:

Ruang Redaksi Andalas Obstetrics and Gynecology Journal, Lantai 3 PPDS Obstetri dan Ginekologi Universitas Andalas, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127

Website:

<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

J. Yazbek et al (2017) recruited 166 women with adnexal mass based on ultrasound found that diagnosis based on the pattern showed sensitivity of 0.69 (95% CI, 0.52–0.81), specificity of 0.94(95% CI, 0.88–0.97), positive likelihood ratio of 11.3 (95% CI, 5.53–22.8) and negative likelihood ratio of 0.34(95% CI 0.21–0.55). This study concluded that ultrasound had high specificity meanwhile the risk of misdiagnosed was still present.

Study by Ahmad Sayanesh in 2015 suggested if ultrasound is performed by experienced operator the sensitivity and specificity to diagnose ovarian tumour may be up to 77-86% and 94-100%, respectively. However, distinguishing a cyst and cancer with ultrasound is very complicated.¹¹

Our study showed ultrasound was performed by beginner operator, therefore recognising from the mass pattern had not yet been standardised and may lead to significant discrepancy. IOTA SR approach is designed for beginners operator so thus the result may be more accurate.

CONCLUSION

International Ovarian Tumour Analysis (IOTA) has better sensitivity in predicting ovarian malignancy compared to The Risk Of Ovarian Malignancy Algorithm (ROMA). ROMA positive predictive value is higher compared with IOTA positive predictive value. ROMA negative predictive value is 5,9%, meanwhile for IOTA it is hard to determine

REFERENCES

1. Chan DW, et al. Use of Tumor Markers in Testicular, Prostate, Colorectal, Breast, and Ovarian Cancers. Washington, United State: the American Association for Clinical Chemistry, Inc. 2009
2. Anton C, et al. A comparison of CA125, HE4, risk ovarian malignancy algorithm (ROMA), and risk malignancy index (RMI) for the classification of ovarian masses. Sao Paolo: CLINICAL SCIENCE, 2012. 437-41.
3. Bianca Ortiz, et al. HE4, Ca125, and ROMA Algorithm for Differential Diagnosis Between Benign Gynaecological Diseases and Ovarian Cancer. 2014.
4. Yamamoto Y, et al. Comparison of 4 Risk-of-Malignancy Indexes in the Preoperative Evaluation of Patients With Pelvic Masses. Clinical Ovarian and Other Gynecologic Cancer, 2014. 8-12.
5. Daniel W. Chan, José Carlos Campos Torres, et al. Risk-of-Malignancy Index in preoperative evaluation of clinically restricted ovarian cancer. São Paulo Medical Journal. 2009. p; 73-5
6. Hye Yon Cho et al. Comparison of HE4 ,CA125 and Risk Of Ovarian Malignancy Alogaritm in the Prediction of Ovarian Cancer in Korean Woman. 2015



eISSN : 2579-8324

pISSN : 2579-8323

ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL

Alamat Korespondensi:

Ruang Redaksi Andalas Obstetrics and Gynecology Journal, Lantai 3 PPDS Obstetri dan Ginekologi Universitas Andalas, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127

Website:

<http://jurnalobgin.fk.unand.ac.id/index.php/JOE>

7. Fujirebio Diagnostics AB. ROMA, HE4 EIA + ARCHITECT CA 125 II™.; 2011.
8. Budiana, I. N. TUMOR OVARIUM: PREDIKSI KEGANASAN PRABEDAH. JURNAL ILMIAH KEDOKTERAN, 44 (Divisi Onkologi-Ginekologi, Departemen Obstetri dan Ginekologi FK Unud/RSUP Sanglah Denpasar). 2013. 179-85.
9. Sussane J. IOTA Terminology, Simpel Descriptor and Simpel Rules T Van Gorp, et al. HE4 and CA125 as a diagnostic test in ovarian cancer: prospective validation of the Risk of Ovarian Malignancy Algorithm. British Journal of Cancer 2016. p;1-8.
10. Vinicius P, et al. The Contribution and Perspective of Proteomics to uncover ovarian cancer tumor marker. 2018.
11. Yurkovetsky Z, et al. Development of a Multimarker Assay for Early Detection of Ovarian Cancer. Journal of Clinical Oncology The University of Pittsburgh. 2010; 2159-166