Original Article

SENSITIVITY AND SPESIFICITY VALUE OF PLATELETS, MALIGNANCY RATIO INDEX AND BOTH COMBINED IN DIAGNOSING OVARIAN CANCER AT GENERAL HOSPITAL HAJI ADAM MALIK MEDAN FROM 2016-2018

YOVITA V.[1], TALA MRZ[2], DINA S.[3], LUMBANRAJA S. N.[4], LUBIS D. L.[2], ADELLA C. A.[3]

[1]Department of Obstetric and Gynaecology, Medical Faculty, Universitas Sumatera Utara, General Hospital of H. Adam Malik, [2]Urogynecology Division, Department of Obstetric and Gynaecology, Medical Faculty, Universitas Sumatera Utara, General Hospital of H. Adam Malik, [3]Oncology Gynecology Division, Department of Obstetric and Gynaecology, Medical Faculty, Universitas Sumatera Utara, General Hospital of H. Adam Malik, [4]Feto Maternal Division, Department of Obstetrics and Gynaecology, Medical Faculty, Universitas Sumatera Utara, General Hospital of H. Adam Malik
Email: rhiza_tala@yahoo.com

ABSTRACT

Objective: This research aimed to analyze sensitivity and specificity values of platelets, RMI and both combined as ovarian cancer diagnostic modality in Haji Adam Malik Hospital in 2016-2018.

Methods: This is analytic research with *a diagnostic test* design on 204 patients who had been diagnosed with ovarian cancer and patients with ovary benign tumors which have been examined the value of full blood and the malignancy ratio index and ovarian mass that has been proven by the results of anatomic pathology at General Hospital Haji Adam Malik Medan in 2016-2018. The data is tabulated into 2x2 table and then calculated for each sensitivity, specificity, positive predictive value and negative predictive value.

Result: By using platelet cut-off value>450000 per mm^3 in diagnosing ovarian cancer with sensitivity 55.44% and specificity 83.65% were obtained. IRK has a sensitivity 83.16% and specificity 76.92%. Platelet and IRK values provided the highest diagnostic value (specificity) compared to when they were each single which was 97.11% while the combination of platelet and IRK values had a sensitivity of 49.50%.

Conclusion: Platelet and IRK values gives the highest diagnostic value (specificity) compared to when both are used, namely 97.11%.

Keywords: Sensitivity, Specificity, Platelets, Malignancy Ratio Index

INTRODUCTION

Around 192,000 new cases of ovarian cancer are found per year worldwide [1]. According to data from Ministry of Health taken from the Global Cancer Observatory-International Agency for Research on Cancer (GLOBOCAN-IARC) in 2012, the incidence of ovarian cancer is 6% and ovarian cancer is one of the 10 most cancer in Indonesia from 2010–2013 [2].

Significant platelet involvement in cancer growth and metastasis is a longstanding concept. This very large level of platelet production has the potential to increase through thrombocytosis as much as 20 times in response to various tumor and systemic gene factors. Correlations between high platelet counts and shorter survival rates are often found in lung, colon, breast, pancreatic, kidney, and gynecological cancers [3].

A several-fold increase in patient platelet count is a common finding in cancer. High preoperative platelet count is associated with early relapse of non-advanced epithelial ovarian cancer and colorectal cancer. Platelets affect the angiogenic and immunological processes in cancer, and protect tumor cells directly. Platelet proteomic analysis has identified several potential marker tumors. Among them are angiogenic factors that have been shown to be inherited by platelets and sent to the endothelial wall of tumors in early-stage tumors. Detection of platelet-derived growth factor, platelet factor 4 (PF-4) and platelet endothelial cell growth factor is recommended for the diagnosis of several cancers [4, 5].

The malignancy ratio index (IRK) is a formula used to see whether a mass in a pelvic is a malignancy or a benign pelvic mass. IRK is determined by considering age, menopausal status and the amount of Ca.125. By using the IRK 200 cut off value the sensitivity becomes 85% and specificity becomes 97%.

MATERIALS AND METHODS

This research is an analytical study with a diagnostic test design on 204 patients who have been diagnosed with ovarian cancer and patients with ovaries benign tumors which have been examined their complete blood values and malignancy ratio index and also ovarian mass which has been proven by the results of anatomic pathology at Haji Adam Malik Hospital Medan in 2016-2018.

The sample selected must meet the inclusion criteria, namely all medical records of patients who have a mass in the ovary, medical records that have blood test results in the form of platelet values and records of malignant ratio indexes; and exclusion criteria, namely incomplete medical records, diseases that increase platelet values, for example inflammatory bowel disease, acute bleeding, iron deficiency anemia, post-splenectomy and other cancers that occur together, and the presence of other gynecological cancers.

Data collection was carried out by the researchers themselves by examining the patient's medical record in the Haji Adam Malik General Hospital Medan medical record section. Patient medical records that match the inclusion and exclusion criteria were sampled and the data was entered into a computer for data analysis. Then the data is tabulated into a 2x2 table to calculate the values of sensitivity, specificity, positive predictive value and negative predictive value.

RESULTS

Characteristics of research sample
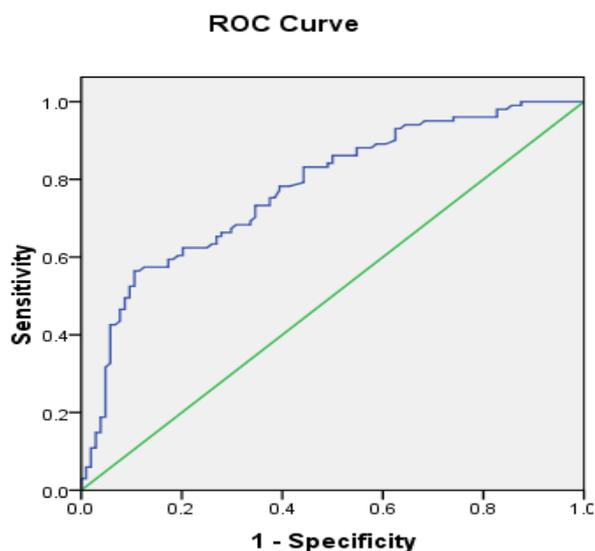
Table 1: Characteristics of research subjects by age and parity

Characteristics	Research subjects	
	Ovarian cancer	Benign tumor
Age (years old)		
<20	2	4
20-35	12	39
36-50	41	39
>50	46	22
Parity		
Nulipara	25	33
Primipara	21	22
Secundipara	25	26
Multipara	11	6
GrandeMultipara	19	17
Total	101	104

Based on table 1. it can be seen that the characteristics of ovarian cancer patients are more likely above 50 y old followed by age 36-50 y (40.6%) and the lowest with age below 20 y (2%), whereas in the benign tumor patient group are more likely with ages 20-35 y and ages 36-50 y respectively 37.5% and the lowest with ages under 20 y (3.8%). This shows that ovarian cancer patients are more common in the older age group compared to ovarian tumor patients who are more likely to be found at a younger age.

Based on parity, the ovarian cancer group was more prevalent with secundipara and nullipara parity of 24.8% each and the lowest with multipara parity of 18.8%. In the ovarian tumor group more with nullipara parity that is equal to 31.7% followed by secundipara parity of 25% and the lowest with multipara parity of 5.8%.

Diagnostic tests are performed to see the strength of platelet diagnostic value as a screening tool for ovarian cancer, with ROC curve analysis, sensitivity and specificity values.

ROC/AUC analysis calculation to determine platelet cut-off values

Fig. 1: Area under the curve platelet values in detecting ovarian cancer
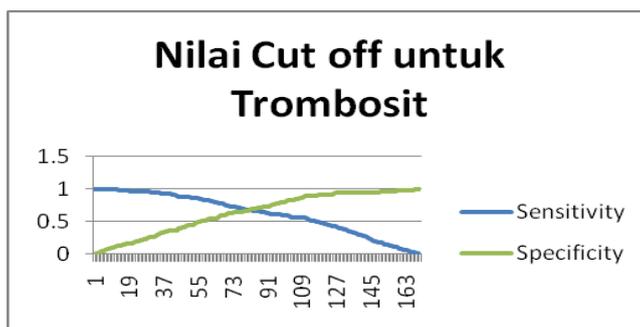

Fig. 2: Optimal cut-off sensitivity and specificity of platelet values in detecting ovarian cancer

From the ROC curve the Area Under the Curve (AUC) of 0.776 was obtained.(fig. 1) This shows from the group of research subjects the value of platelets can diagnose ovarian cancer by 77.6%. From the sensitivity and specificity values, the platelet count of 450000 is cut off to get a sensitivity of 56.4% and a specificity of 89.4% (fig. 2).

Characteristics of research subjects based on platelet values

By using a cut-off value of>450000 per mm³ in diagnosing ovarian cancer, a sensitivity of 55.44% and specificity of 83.65% were obtained. This means that platelet values can filter 55.44% of ovarian

cancer patients from total ovarian cancer patients and platelet values can diagnose 83.65% of patients who do not have ovarian cancer from total patients who really do not have ovarian cancer (table 2).

ROC/AUC analysis calculation for determining IRK cut off value

From the ROC curve, it obtained an AUC of 0.86. (fig. 3) This shows from the group of research subjects the value of IRK can diagnose ovarian cancer by 86%. From the sensitivity and specificity values, the IRK value of 202.35 becomes cut off to get a sensitivity of 83.2% and a specificity of 76.9% (fig. 4).

Table 2: Characteristics of research subjects based on platelet values

Platelet	Ovarian cancer	Benign tumor	Total
>= 450000	56	17	73
<450000	45	87	132
Total	101	104	205

Sensitivity: 55,44 %, Specificity: 83,65 %, Positive Predictive Value: 76,71%, Negative Predictive Value: 65,90%
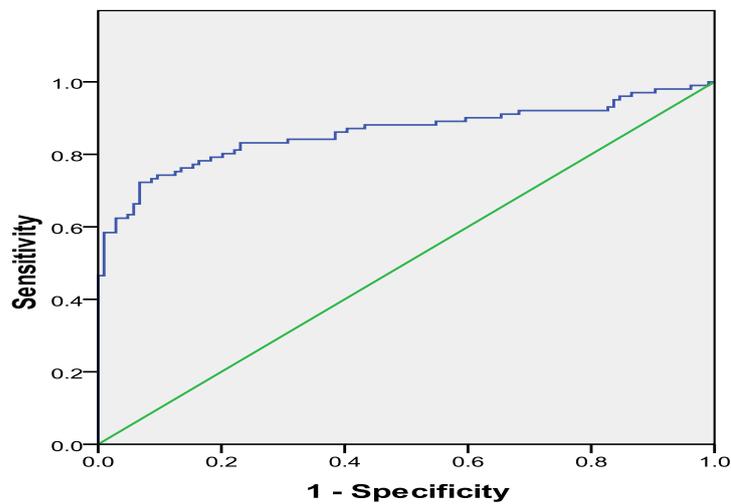

Fig. 3: Area under the curve number of IRK in detecting ovarian cancer
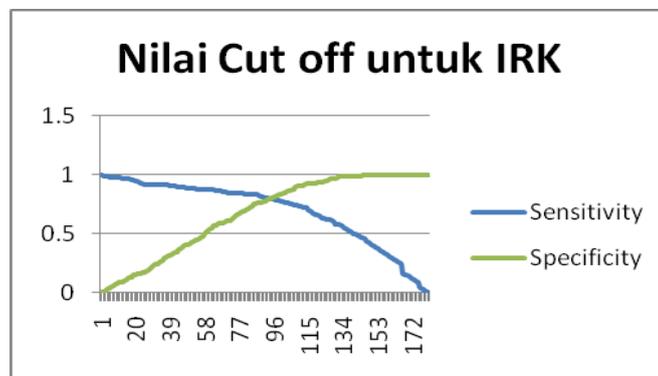

Fig. 4: Optimal cut-off IRK sensitivity and specificity in detecting ovarian cancer

Characteristics of research subjects based on IRK

Table 3 above explains that the ovarian cancer group had IRK cut off>202.35, in contrast to ovarian tumors with an IRK<202.35. IRK has a sensitivity of 83.16% and specificity of 76.92%.

This means that IRK can filter 83.16% of ovarian cancer patients from total ovarian cancer patients and IRK value can diagnose 76.92% of patients who do not have ovarian cancer from the total number of patients who actually do not have ovarian cancer (table 3).

Table 3: Characteristics of research subjects based on IRK

IRK	Ovarian cancer	Benign tumor	Total
>= 202,35	84	24	108
<202,35	17	80	97
Total	101	104	205

Sensitivity: 83.16%, Specificity: 76.92 %, Positive Predictive Value: 77.77%, Negative Predictive Value: 82.47%

Table 4: Table combination of platelet values and IRK

Combination	Platelet value		Total
	Ovarian cancer	Benign tumor	
IRK Malignant	50	3	53
Benign	51	101	152
Total	101	104	205

Sensitivity: 49.50 %, Specificity: 9711%, Positive Predictive Value: 94.33%, Negative Predictive Value: 66.44%

To get the sensitivity and specificity of the combination of the use of platelet and IRK values, a 2x2 table was formed. In this study the researchers assumed if the platelet value>450000 and IRK>202.35 then this is ovarian cancer, conversely if one of the values between platelet values <450000 or IRK value<202.35, this is assumed to be a benign tumor.

Characteristics of research subjects based on a combination of platelet values and IRK

When viewed from the results of the analysis, the combination of platelet values and IRK gives the highest diagnostic value (specificity) compared to when both were single, namely 97.11%. This means that the combination of platelet values and IRK can diagnose 97.11% of patients who do not have ovarian cancer out of the total patients who actually did not have ovarian cancer. While the combination of platelet and IRK values has a sensitivity of 49.50%, meaning that the combination of the two can filter out 49.50% of ovarian cancer patients from total ovarian cancer patients (table 4).

DISCUSSION

The results of this study found that characteristics of ovarian cancer patients were more common in the older age group that is>50 y compared to ovarian tumor patients who were more likely to be found at a younger age ie 20-50 y. Based on parity, there were more ovarian cancer groups with scaffold and nullipara parity of 24.8% each and in ovarian tumor group more with nullipara parity with 31.7%.

Risk factors for ovarian cancer vary from hereditary factors, gene mutations, hormonal, age to lifestyle [6,7]. As reported by Hunn J, Rodriguez GC (2012) mentions that the risk factors for epithelial ovarian cancer include older women, nulliparous and infertility [6].

From the measurement of platelet levels found 56 patients with ovarian cancer with platelet values>450000, while patients with benign ovarian tumors found 17 patients with platelet values >450000. This indicates that trombocytosis is more common in ovarian cancer. Thrombocyte Sensitivity as a diagnostic modality for ovarian cancer is 55.44%, while the specificity is 83.65% with a cuttoff value of 450000.

From the results of this study it was found that most ovarian cancer groups had IRK>202.35, in contrast to ovarian tumors which mostly had IRK<202.35. IRK sensitivity as a diagnostic modality for ovarian cancer is 83.16%, while the specificity is 76.92%.

In this study when combining the value of thrombosis and IRK obtained a sensitivity of 49.50% and specificity of 97.11%. This shows that when platelet values are combined with IRK, it can increase specificity in predicting malignant masses in preoperative ovaries.

Thrombocytosis is a frequent complication of ovarian cancer and is associated with a poor prognosis, indicating the importance of platelets in the pathology of ovarian cancer. There is a strong dynamic interaction between ovarian cancer cells and platelets

in-vitro. This interaction involves platelet adhesion, platelet activation and degranulation and a resultant pro-survival and proangiogenic signal for ovarian cancer cells that potentially promotes ovarian cancer cell metastasis [8].

Crasta et al. found that patients with preoperative thrombocytosis were found to have lower hemoglobin (p<0.0002), advanced stage (p<0.05), and high grade tumor (p<0.02). Zeimet et al. studied 130 women with epithelial ovarian tumors and found that thrombocytosis was associated with advanced disease, high serum Ca-125 levels, ascites, and greater likelihood of suboptimal cytoreduction. Menczer et al. conducted the same retrospective study in a cohort of seventy patients with invasive epithelial ovarian carcinoma and reported a higher incidence of thrombocytosis in women with advanced disease and a significantly shorter survival period. Other studies have also found that thrombocytosis is significantly correlated with advanced stages and higher epithelial ovarian tumors, lymph node metastases, greater ascites volume, and less optimal tumor cytoreduction with disease-free survival and shorter overall survival [9].

Ovarian cancer with thrombocytosis is associated with suboptimal tumor resection, and elevated levels of Ca-125. Activation of platelets induced ovarian cancer is mediated by adenosine 59-diphosphate which is released from tumor cells and can be blocked by adenosine 59-diphosphate receptors (P2Y12 and P2Y1). Some research also shows that tumor cells can cause secretions of solid granules containing adenine nucleotides through the Fcg platelet IIa receptor. Platelet activation by tumors throughout the metastatic cascade phase leads to the release of factors derived from platelets stored in granules leading to inflammatory, proliferative, and proangiogenic platelet activity to encourage tumor growth, tissue invasion, and metastasis [9].

Increased production of thrombopoetic cytokines by tumors and host tissues is a major cause for paraneoplastic thrombocytosis. Specifically, this process is mediated by increased synthesis of liver thrombopoetin in response to excessive interleukin-6, thereby increasing platelet counts, which in turn increases tumor growth.

CONCLUSION

Characteristics of ovarian cancer patients more with age above 50 y with nullipara parity. The sensitivity of platelet value as a diagnostic modality for ovarian cancer was 55.44%, while the specificity was 83.65% with a cut-off value of 450000. IRK sensitivity as a diagnostic modality for ovarian cancer was 83.16%, while the specificity was 76.92% with a cut-off value 202.35. The combination of platelet values and IRK diagnostic modality has a sensitivity of 49.50% and a specificity of 97.11%. The combination between platelet and IRK values gives the highest diagnostic value (specificity) compared to when both are used, namely 97.11%.

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realization of this research. In addition, the researcher also thanked all the staff involved and the research samples who participated in this research. The combination of platelet values>450000 and IRK>202.35 can be used as a diagnostic modality for ovarian cancer. It is necessary to conduct a study of the combination of platelet and IRK values as a modalistic diagnosis of ovarian cancer with a prospective research design in order to get better sensitivity and specificity.

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declare none

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