

Characteristics of Suspected Malignant Ovarian Tumor Patients Who Performed Surgery at Tertiary Referral Hospital

Brahmana Askandar Tjokropawiro^{1*}, Nila Krisna Sari¹, Indra Yuliati¹, Lies Mardiyana²

¹Department of Obstetrics and Gynecology, Faculty of Medicine-Dr. Soetomo Teaching Hospital, Universitas Airlangga, Surabaya 60131, Indonesia

²Department Radiology, Faculty of Medicine-Dr. Soetomo Teaching Hospital, Universitas Airlangga, Surabaya 60131, Indonesia

Article History:

Submitted: 27.02.2020

Revised: 07.04.2020

Accepted: 11.05.2020

ABSTRACT

Ovarian cancer is often called as the silent killer because the symptoms appear when the stage is advanced. This study aimed to compare the identification of malignant ovarian tumor by RMI examination and abdominal pelvic CT scan to pathology examination as gold standard. This was a cross-sectional study. The data were obtained through medical records of a suspected malignant ovarian tumor patients who performed surgery at Dr. Soetomo General Hospital, Surabaya from January 2017 to December 2018. Among 64 patients, there were 56% of patients aged 41-60 years, 53% had a normal BMI, 56% multipara, and 56% not yet menopause. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CA-125 diagnostic test were 80.85%, 17.65%, 73.1%, and 25%, respectively. RMI examination had a sensitivity of 82.98% and a specificity of 41.18%. Whereas, abdominal CT scan had a sensitivity of 87.23% and a

specificity of 47.1%. Examination of RMI combined with abdominal pelvic CT scan had a sensitivity and specificity of 100% and 40%, respectively. RMI examination combined with abdominal pelvic CT scan gave better results in diagnosing ovarian malignancies.

Keywords: Ovarian tumors, RMI, CT scan of the abdomen

Correspondance:

Brahmana Askandar Tjokropawiro

Department of Obstetrics and Gynecology, Faculty of Medicine-Dr. Soetomo Teaching Hospital, Universitas Airlangga, Surabaya 60131, Indonesia

Email: brahmanaaskandar@gmail.com

DOI: [10.31838/srp.2020.5.27](https://doi.org/10.31838/srp.2020.5.27)

@Advanced Scientific Research. All rights reserved

INTRODUCTION

Ovarian cancer is ranked as the tenth leading cause of death in women due to cancer at all ages in Indonesia (1,2). The number of new patients of ovarian cancer in 2014-2015 in Dr. Soetomo Hospital, Surabaya, East Java was on rising and was the second largest number of visits after cervical cancer (3). Ovarian cancer is often called the silent killer because the symptoms appear when the stage is advanced. Previous study reported that stage of the disease is a prognostic factor that mostly influences 3-years survival rate of epithelial ovarian cancer patients (4). The survival rate of women with early-stage ovarian cancer is around 70-90%, much higher than the advanced stage which only has survival rate of 20-30%. Because of these large differences in survival rate, many studies have focused on finding the best method for early detection of ovarian cancer because late diagnosis correlates with late treatment and worsens prognosis (5,6). Also, other studies recommended the examination of CD133, CD44, and ALDH1A1 in determining life expectancy with attention to other clinicopathological risk factors (7).

The characteristics of ovarian tumors are important to know, in addition to assessing risk factors, early detection, because it can also be used as a basis for management to prevent progression to ovarian cancer. Knowing and evaluating the malignancy characteristics of ovarian tumors is very important before surgery and is associated with a 5-year survival rate in these patients (6).

Ultrasound and pelvic abdominal CT scan are radiological examinations that can be performed to evaluate ovarian tumors. Ultrasound is the most universally accepted first-line imaging tool for the evaluation of gynecological tumors that are non-invasive, inexpensive, and without radiation.

Whereas, abdominal CT scan can provide information for planning surgery and determine the resectability of surgery but has a weakness in diagnosing tumors that resemble

ovarian malignancies so that tumors which are benign are diagnosed as malignant ovarian tumors. This study aimed to compare the identification of malignant ovarian tumor by RMI examination and abdominal pelvic CT scan to pathology examination as gold standard.

METHODS

This was a cross-sectional study. The data were obtained through medical records of the suspected malignant ovarian tumor patients who performed surgery at Dr. Soetomo General Hospital, Surabaya from January 2017 to December 2018, which had not previously been operated on, was not a case of tumor evaluation (restaging), had never received chemotherapy and before the operation were performed pelvic abdominal CT scan with contrast.

The suspected malignant ovarian tumors patients underwent an ultrasound examination and CA-125 examination to then calculate the RMI value. Patients with an RMI value >200 or with RMI value <200 but from an ultrasound result suspected malignancy were then referred to the oncology outpatient clinic, and pelvic abdominal CT scan was planned. To assess the accuracy of the RMI and CA-125 diagnostic test, the CA-125 and RMI results were compared to the pathology results, which is a gold standard examination.

RESULTS

Based on data from the medical record in 2017-2018 obtained most of suspected malignant ovarian tumor patients who underwent surgery at Dr. Soetomo General Hospital is aged between 41-60 years. The most patients were multipara by 56%. It is found 56% of suspected malignant ovarian tumor patients who have not yet menopause and 44% who have menopause. Most of patient on average complained of an enlarged abdomen and

palpable lumps. When anamnesis was performed on the first examination at the Gynecology outpatient clinic and Oncology outpatient clinic Dr. Soetomo General Hospital, most symptoms appear <3 months as much as 61%. Most patients have to wait for surgery about 1-3 months.

Table 1: Cross tabulation between CA-125 serum level and pathology results

CA-125 serum level	Pathology result		Total
	Malignant tumor	Benign Tumor	
>35	38	14	52
<35	9	3	12
Total	47	17	64

Sensitivity : 80.85%

Specificity : 17.65%

Positive predictive value (PPV) : 73.1%

Negative predictive value (NPV) : 25%

The pathology results of surgery showed that 75% of epithelial tumors were dominated by mucinous subtypes. Table 1 shows comparison results between CA-125 diagnostic test and pathology results. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CA-125 diagnostic test was 80.85%, 17.65%, 73.1%, and 25%, respectively. While in Table 2, the RMI had 82.98% sensitive, 41.18% specific. The PPV and NPV was 79.59% and 46.67%, respectively.

Table 2: Cross tabulation between RMI result and pathology results

RMI	Pathology result		Total
	Malignant tumor	Benign Tumor	
>200	39	10	49
<200	8	7	15
Total	47	17	64

Sensitivity : 82.98%

Specificity : 41.18%

Positive predictive value (PPV) : 79.59%

Negative predictive value (NPV) : 46.67%

Table 3: Cross tabulation between CT scan result and pathology results

CT Scan	Pathology result		Total
	Malignant tumor	Benign Tumor	
Malignant	41	9	50
Benign	6	8	15
Total	47	17	64

Sensitivity : 87.23%

Specificity : 47.1%

Positive predictive value (PPV) : 82%

Negative predictive value (NPV) : 57.14%

Table 4: Cross tabulation between RMI complemented

RMI	CT Scan	by CT scan result with pathology results		Total
		Pathology result		
		Malignant tumor	Benign Tumor	
>200	Malignant	32	6	38
<200	Benign	0	4	4
Total		32	10	42

Sensitivity : 100%

Specificity : 40%

Positive predictive value (PPV) : 84.21%

Negative predictive value (NPV) : 100%

All patients with suspected malignant ovarian tumor who came to the gynecology outpatient clinic or oncology outpatient clinic had a pelvic abdominal CT scan performed. Table 3 presents result of CT scan compared to pathology examination. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CT scan was 87.23%, 47.1%, 82%, and 57.14%, respectively. Table 4 displays combination RMI and CT scan compared to pathology examination. RMI examination with pelvic abdominal CT scan had a sensitivity of 100% and a specificity of 40%, a positive predictive value (PPV) of 84.21% and a negative predictive value (NPV) of 100%.

DISCUSSION

Most patients with suspected malignant ovarian tumors who performed surgery were proven to be malignant according to the pathologic results. RMI examination combined with abdominal pelvic CT scan gave better results in diagnosing ovarian malignancies compared to only using an RMI examination or abdominal pelvic CT scan alone.

Most patients aged between 41-60 years. This is not much different from the study at Bandar Lampung, Indonesia which found that most ovarian cancer patients in 2015-2016 aged >36 years old were 85%. This is also consistent with the results of study in Makassar, Indonesia which found that distribution of ovarian cancer patients was mostly found in the age group of 41-50 years old which was 62.7% (8).

Most patients were multipara. This is in accordance with previous study which stated that most ovarian cancer patients had given birth or had children ≥ 1 . This is not in accordance with the theory of various studies show that women with high parity have a lower risk of ovarian cancer than women who do not have children. There are many factors that can be the cause. This can occur because of the recurrent ovulation process in women who have never given birth that causes chronic irritation of the ovaries (9). Another study stated that parity is not a risk factor for ovarian cancer (8). The most patients with suspected malignant ovarian tumor who performed surgery had normal BMI of 53%. The same thing was found in five of the nine case-control studies in hospitals that found no association between BMI and ovarian cancer cases (10,11).

A half of suspected malignant ovarian tumor patients who have not yet menopause were found. This is not much different from other studies which found that most ovarian cancer patients in 2015-2016 aged >36 years old were 85%. According to the American Cancer Society, most cases of ovarian cancer are found in women >63 years old or older. According to the hypothesis of gonadotropin stimulation, in

premenopausal women, the pituitary-ovarian axis is controlled by a feedback mechanism to keep the menstrual cycle going. In postmenopausal women, the feedback mechanism does not occur so that the production of gonadotropins by the pituitary gland will continue to increase which will further increase the degradation of the basement membrane and transformation of ovarian surface epithelial cells into pre neoplastic lesions (12).

Most of patients on average complained of an enlarged abdomen and palpable lumps. When anamnesis was performed on the first examination at the Gynaecology outpatient clinic and Oncology outpatient clinic of Dr. Soetomo General Hospital, most symptoms appeared <3 months as much as 61%. This shows that the patients have sufficient awareness to immediately go to a health facility. As soon as ovarian cancer is diagnosed, then surgery can be done immediately. Women with ovarian cancer who undergo optimal cytoreduction surgery (no macroscopic residual mass is obtained after surgery) have a 2-fold cure rate (30-40%) compared to non-optimal surgery (15-20%). A significant factor related to optimal cytoreduction surgery is the size of the tumor mass volume during surgery, so the time interval for diagnosis greatly influences the optimal success of cytoreduction surgery (13).

The pathology results in this study were dominated by mucinous subtypes. These results are also different with other study that serous subtypes were the most numerous, followed by the mucinous subtype (14). From the findings during surgery, the most ovarian cancer was found in stage I which was 41%, followed by stage III as much as 32%. This can happen because many patients with suspected malignant ovarian tumors immediately checked themselves into a health facility within <3 months from the symptoms appeared, so ovarian cancer could be detected immediately, and surgery at an early stage could be performed.

Most ovarian tumor patients treated at Dr. Soetomo General Hospital are referrals from outside hospitals diagnosed with suspicious malignant ovarian tumors based on the discovery of high CA-125 serum level or from ultrasound or abdominal CT scan results with suspected malignancy. RMI is the scoring system that most commonly used in Dr. Soetomo General Hospitals to assess an ovarian tumor malignancy. RMI is preferred because it is very simple, easy to remember, so its use is easily applied in daily clinical practice compared to other scoring systems. Examination of CA-125 serum level can also be easily carried out in Dr. Soetomo General Hospital. Several studies stated that CA-125 is a potential tumor marker for ovarian cancer screening (15,16). The CA-125 level is also related with serum matrix metalloprotein- 9 level (MMP) (17). As a single modality, CA-125 has a sensitivity of 50-79% and a specificity of 96-99%. The CA-125 examination of sensitivity figure was not much different from previous study, but the specificity was low (18).

RMI is statistically effective for distinguishing whether a ovarian tumor is benign or malignant. Specificity figures in this study were obtained which are not much different from previous study which stated the use of RMI with a cut-off level of 200 had a sensitivity of 85% and a specificity of 97% (19).

It was found that the pelvic abdomen CT scan with contrast had a good sensitivity, but low in specificity. This is consistent with earlier study which states that pelvic abdominal CT scans without tools have a sensitivity of 87.1% and a specificity of 22.2% in diagnosing ovarian tumor malignancies (20). CT scan is able to detect masses of size more than 1 cm with a sensitivity of 85-93% and specificity of 91-96%, but the sensitivity drops to 25-50% for detection of mass sizes of less than 1 cm (21). A study conducted regarding the diagnostic value of pelvic abdominal CT scan in 88 patients with suspected malignant ovarian tumor who had a pelvic abdominal CT scan with contrast performed before surgery at Dr. Soetomo General Hospital from January 2017 to December 2018 found that CT scan without tools had a sensitivity of 87.1% and a specificity of 22.2% (20). The low specificity value in this study was contributed by the large false positive value in cases of seromucinous cystadenoma ovary and endometriosis cysts. In this study, CT scans had difficulty in distinguishing malignancies from benign masses in the advanced phase of seromucinous cystadenoma ovary, with mass characters that are usually large >10 cm, attached to the abdominal wall, multiloculated, septae with septae thickness of 2-3 mm thick, containing fluid with a density of water to blood, and in general this tumor was obtained in decades 3 and 4.

Likewise, endometriosis cysts, where lesions with cystic and solid components are found, can be unilateral or bilateral with regular external walls, sometimes with papillary projection, showing contrast enhancements accompanied by ascites and peritoneal implants, so it is very likely to be difficult to distinguish from malignancy (20). Other reports also found (pre)malignant endometrial lesion in the endometrium of women diagnosed with epithelial ovarian cancer (22).

Another study reported the sensitivity and specificity values were higher in CT scan with tools when compared without tools (20). Eighty-eight samples were reviewed by the female organ division of the radiology department Dr. Soetomo General Hospital blindly and used "tools" (primary findings and additional malignancy of modified ovarian tumors) then correlated with his histopathological findings. The Friedman test results obtained that there was no difference between the results of histopathological examination with CT scan results, so CT scan examination is as good as the histopathology results.

CONCLUSION

Most patients with suspected malignant ovarian tumors who performed surgery were proven to be malignant according to the pathologic results. RMI examination that is combined with abdominal pelvic CT scan gives better results in diagnosing ovarian malignancies compared to only using an RMI examination or abdominal pelvic CT scan alone.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J cancer*. 2015

- Mar;136(5):E359-86.
2. Sulistiowati E, Lolong DB, Pangaribuan L. Gambaran Penyebab Kematian Kanker di 15 Kabupaten/kota di Indonesia 2011. *Bul Penelit Sist Kesehat*. 2016;19(2):119–25.
 3. Khotimah FK, Febriani A, Mulawardhana P. Ovarian cancer with pleural and lung metastasis in Dr. Soetomo Hospital, Surabaya, Indonesia, in 2014-2015. *Maj Obstet Dan Ginekol*. 2018;26(1):7–19.
 4. Damayanti IN, Yulianti I, Kusumastuti EH. Three years survival rate of epithelial ovarian cancer patients in Dr. Kariadi Hospital, Semarang, Central Java. *Maj Obstet Dan Ginekol*. 2016;24(3):100–4.
 5. Fleischer AC, Lyschick A, Hirari M, Moore RD, Abramson RG, Fishman DA. Early Detection of Ovarian Cancer with Conventional and Contrast-Enhanced Transvaginal Sonography: Recent Advances and Potential Improvements. Ho C-M, editor. *J Oncol*. 2012;2012:302858.
 6. Song H, Dicks E, Ramus SJ, Tyrer JP, Intermaggio MP, Hayward J, et al. Contribution of Germline Mutations in the RAD51B, RAD51C, and RAD51D Genes to Ovarian Cancer in the Population. *J Clin Oncol Off J Am Soc Clin Oncol*. 2015 Sep;33(26):2901–7.
 7. Pelupessy NU, Andrijono, Sutrisna B, Harahap AR, Kanoko M, Nuranna L, et al. CD133, CD44, and ALDH1A1 as cancer stem cell markers and prognostic factors in epithelial ovarian cancer. *Med J Indones*. 2019;28(1):63–9.
 8. Fachlevy AF, Abdullah Z, Russeng SS. Ovarian Cancer Risk Factors On Wahidin Sudirohusodo Hospital Makassar. *J Sains Teknol*. 2012;2(1).
 9. Simamora RPA, Hanriko R, Sari RDP. Hubungan Usia, Jumlah Paritas, dan Usia Menarche Terhadap Derajat Histopatologi Kanker Ovarium di RSUD Dr. H. Abdul Moeloek Bandar Lampung Tahun 2015-2016. *Med J od Lampung Univ*. 2018;7(2):7–13.
 10. Whittemore AS. Characteristics relating to ovarian cancer risk: implications for prevention and detection. *Gynecol Oncol*. 1994 Dec;55(3 Pt 2):S15-9.
 11. Rodriguez C, Calle EE, Fakhrabadi-Shokoohi D, Jacobs EJ, Thun MJ. Body mass index, height, and the risk of ovarian cancer mortality in a prospective cohort of postmenopausal women. *Cancer Epidemiol Biomarkers Prev a Publ Am Assoc Cancer Res cosponsored by Am Soc Prev Oncol*. 2002 Sep;11(9):822–8.
 12. Rampersad AC, Wang Y, Smith ER, Xu X. Menopause and ovarian cancer risk: mechanisms and experimental support. *Am J Clin Exp Obs Gynecol*. 2015;2(1):14–23.
 13. Gong T-T, Wu Q-J, Vogtmann E, Lin B, Wang Y-L. Age at menarche and risk of ovarian cancer: a meta-analysis of epidemiological studies. *Int J cancer*. 2013 Jun;132(12):2894–900.
 14. Makwana H, Maru A, Lakum N, Agnihotri A, Trivedi N, Joshi J. The relative frequency and histopathological pattern of ovarian masses--11 year study at tertiary care centre. *Int J Med Sci Public Heal*. 2014;3(1):81–5.
 15. Koh SCL, Chan YH, Lutan D, Marpuang J, Ketut S, Budiana NG, et al. Combined panel of serum human tissue kallikreins and CA-125 for the detection of epithelial ovarian cancer. *J Gynecol Oncol*. 2012;23(3):175–81.
 16. Koh SCL, Razvi K, Chan YH, Narasimhan K, Ilancheran A, Low JJ, et al. The association with age, human tissue kallikreins 6 and 10 and hemostatic markers for survival outcome from epithelial ovarian cancer. *Arch Gynecol Obstet*. 2011;284(1):183–90.
 17. Rusda M, Nurvita D, Yaznil MR, Aldiansyah D, Ardiansyah E, Rivany R. The correlation of matrix metalloproteinase-9 serum levels with clinicopathological factor in epithelial type ovarian cancer patients. *G Ital di Ostet e Ginecol*. 2018;40(3):108–12.
 18. Goff BA, Mandel LS, Drescher CW, Urban N, Gough S, Schurman KM, et al. Development of an ovarian cancer symptom index: possibilities for earlier detection. *Cancer*. 2007 Jan;109(2):221–7.
 19. Jacobs I, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. *Br J Obstet Gynaecol*. 1990 Oct;97(10):922–9.
 20. Ramayuda IBG. Nilai Diagnostik CT Scan Abdomen Pada Tumor Ovarium Di RSUD Dr. Soetomo Periode Januari 2017 – Desember 2018. Universitas Airlangga; 2019.
 21. Bennett GL, Slywotzky CM, Giovannello G. Gynecologic causes of acute pelvic pain: spectrum of CT findings. *Radiographics*. 2002;22(4):785–801.
 22. Mingels MJM, Masadah R, Geels YP, Otte-Höller I, De Kievit IM, Van Der Laak JAWM, et al. High prevalence of atypical hyperplasia in the endometrium of patients with epithelial ovarian cancer. *Am J Clin Pathol*. 2014;142(2):213–21.