Research Article

Morphological Index of Sassone for Predicting Serous Type of Epithelial Ovarium Cancer

Indeks Morfologi Sassone untuk Memprediksi Kanker Ovarium Epitelial Tipe Serous

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Abstract

Objective: To obtain whether there was a correlation between the Sassone morphological index and CA 125 tumour markers for suspecting epithelial ovarian cancer with serous types.

Methods: This research was analysis correlation and diagnostic test using cross-sectional design. This study was conducted in Dr. Zainoel Abidin Hospital, from November 2018 until April 2019.

Results: There were 30 samples of patients with suspected malignant ovarian tumours. The Mann-Whitney test has been performed and the results show no relationship between the Sassone morphological index and epithelial ovarian cancer with serous type (p-value 0.627) and there was no correlation between CA 125 tumour marker and epithelial ovarian cancer with serous types (p-value 0.251). The diagnostic test was performed to examine the sensitivity and specificity for the Sassone morphological index in epithelial ovarian cancer with serous type, resulting in 60% and 28%, respectively. In this study, the sensitivity and specificity for CA 125 tumour marker in epithelial ovarian cancer with serous type were 80% and 40%, respectively.

Conclusions: There was no correlation between the Sassone morphological index and CA 125 tumour marker for suspecting epithelial ovarian cancer with serous types.

Keywords: CA 125 tumour marker, epithelial ovarian cancer with serous types, morphological index of Sassone.

Abstrak

Tujuan: *Untuk mengetahui adakah korelasi antara indeks morfologi Sassone dan penanda tumor CA 125 dalam memprediksi kanker ovarium epitelial tipe serous.*

Metode: *Penelitian ini menggunakan rancangan potong lintang dengan melakukan uji korelasi dan diagnostik. Penelitian dilakukandi RSUD Dr. Zainoel abidin, dalam kurun waktu November 2018 sampai dengan April 2019.*

Hasil: *Selama penelitian didapatkan 30 sampel penderita tumor ovarium suspek ganas. Dilakukan analisis dengan uji Mann-Whitney, didapatkan tidak terdapat hubungan antara indeks morfologi Sassone terhadap kanker ovarium epitelial tipe serous (p-value 0,627) dan tidak terdapat hubungan antara penanda tumor CA 125 terhadap kanker ovarium epitelial tipe serous (p-value 0,251). Kemudian dilakukan uji diagnostik dimana didapatkan nilai sensitivitas, spesifisitas dari indeks morfologi Sassone pada kanker ovarium epitelial tipe serous adalah 60% dan 28%. Sedangkan nilai sensitivitas dan spesifisitas penada tumor CA 125 pada kanker ovarium epitelial tipe serous pada penelitian ini didapatkan 80% dan 40%.*

Kesimpulan: *Tidak ada hubungan antara indeks morfologi Sassone dan penanda tumor CA 125 dalam memprediksi kanker ovarium epitelial tipe serous.*

Kata kunci: *indeks morfologi Sassone, kanker ovarium epitelial tipe serous, penanda tumor CA 125.*

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INTRODUCTION

Ovarian cancer cases tend to increase in developing countries with cases of more than 20% of all genital cancers in women.[1,2] In the last two decades, cancer cases in these women have continued to increase with the most cases being epithelial type, while the type of germinal is mostly found in women especially in a child or adolescent age. In women aged over 45 years will increase the risk of getting this cancer.[3]

Indonesia as a developing country, cases of ovarian tumours tend to increase every year. Based on national cancer registration data in 2012 it was found that ovarian cancer was in the second rank (23.43%) after cervical cancer (63.39%).[4] Other data obtained from the Jakarta Cancer Registry stated that the incidence rate of ovarian cancer is 4.27 cases per 100,000 population and rank third after breast cancer and cervical cancer.[5]

The biggest challenge of ovarian cancer due to the difficulty of examinations to detect because in the early stages there are no symptoms and symptoms are found when experiencing metastases.[6] The life expectancy of the patients who suffer from ovarian cancer will be higher if ovarian cancer is found as early as possible at an early stage, this will impact on decreased morbidity and mortality in patients with ovarian cancer. Like other cancers, there is an increase in populations migrate from low-risk countries to higher risk countries, indicating a possible role for food and environmental factors.[7]

CA 125 is a glycoprotein used for screening epithelial ovarian cancer. If the CA value is more than 35 U / mL, it is likely to suffer from epithelial malignant ovarian tumour. But CA 125 is not specifically for malignat ovarian tumour with epithelial type and tend to rise on the other conditions such as endometriosis, other malignancies (breast, lung, colon and endometrial cancers), PID and peritonitis.[1]

It was found that as many as 75 percent of cases of serous ovarian epithelial cancer had an increase in CA 125 tumour markers with an average value of 156 U / ml. [8] Also found 80% of CA 125 tumour markers rose in these cancer patients, with a sensitivity of 50% in the early stages and 90% and advanced stages. [2] Examination of CA 125 tumour markers in postmenopausal women has a PPV of 98% and NPV of 72%, whereas in premenopausal women have a PPV of 49%.[9]

The value of tumour markers and ultrasonography for screening epithelial ovarian cancer remain unclear. Transabdominal ultrasound screening results increase, but specificity has a limitation.[10] Ultrasonography is an indicator to predict malignancy that can be seen from irregular thickening of the cystic wall or septa (> 3 mm), the presence of vegetation or papillary features, the presence of greater cystic mass of 10 cm, and the presence of solid components.[11]

Ultrasonography is one of the most important tools in examining and assessing adnexal disorders. Suspicion of malignancy in patients with ovarian tumours if fluid is found in the abdominal cavity and nodules in the peritoneum on abdominal or vaginal ultrasound examination. Doppler ultrasound examination can be used to look for neovascular in dense masses and areas of cystic mass. In a meta-analysis of 46 studies (5,159 patients) a combination of morphology and Doppler ultrasound could increase sensitivity and specificity.[12]

Ultrasonography is a modality examination for ovarian tumours to identify the nature of tumours before surgery using a morphological assessment system, which links morphological images and macroscopic pathological characteristics of ovarian tumours.[13]

Table 1. Morphology Index of Sassone[14]

Inner wall structure	Wall thickness	Septa	Echogenicity
Smooth	Thin, ≤ 3 mm	None	Sonolucent
Irregularities ≤ 3 mm	Thick, > 3 mm	Sonolucent	Poor echogenicity
Papillarities > 3 mm	Not applicable, usually dense	Not thick, ≤ 3 mm	Poor echogenicity, with echogenic score
Not applicable, mostly solid		Thick, > 3 mm	Blended echogenicity
			Elevated echogenicity

One of the morphological index assessment to determine the nature of ovarian tumours is the morphological index of Sassone, with assessing the inner wall structure, septa, wall thickness and echogenicity of a tumour (Table 1.).[14]

Limitations of examining tumour marker of CA 125 in several peripheral areas in Aceh, the authors try to use other tests to find ovarian cancer quickly. For this reason, the authors use ultrasonography modalities, which can be found in peripheral areas in Aceh, by calculating the morphological index of Sassone in the study.

The purposed of this research was to find out whether there was a correlation between the morphological index of Sassone and tumour markers of CA 125 in predicting serous type of epithelial ovarian cancer. It is expected that the results of the study can be used in areas that do not have any CA 125 tumour markers, if the study found that the morphological index of Sassone has a higher sensitivity and specificity than CA 125 tumour markers.

METHODS

This research was cross-sectional study by conducting analysis correlation and diagnostic tests. This study was conducted at Dr. Zainoel Abidin Hospital (RSUDZA), from November 2018 to April 2019. All samples were suspected to be malignant ovarian tumours were included in the inclusion criteria such as new patients, patients had never undergone surgery, patients had never undergone neoadjuvant chemotherapy, patients who would undergo surgery at RSUDZA, and patients with tumour ovary suspected malignant. The exclusion criteria were patients with residual ovarian cancer, patients who have had surgery in other hospitals with open and closed cases, and patients with ovarian cancer who were metastasized from other places. Then all pastients who came to the emergency department/ obstetrics and obstetric diseases were performed examination of CA 125 tumour markers of morphology index of Sassone in the Radiology department, then surgery was performed and the results of the surgery were sent to the Pathology Anatomical department to confirm serous type of epithelial ovarian cancer.

RESULTS

This study involved 30 samples that suffered from the suspected malignant ovarian tumour. Based on table 2, there were 5 samples (16.7%) with histopathological results of the serous type of epithelial ovarian cancer, while the remaining 83.3% with non-serious type of epithelial ovarian cancer. Furthermore, it could be known that 20 samples (66.7%) with a morphological index of Sassone were greater than 9, while the remaining 33.3% with the morphological index of Sassone below 9. Table 2, also showed that 11 samples (36.7%) with CA 125 tumour marker value were greater than 35, while the remaining of 63.3% with CA 125 tumour marker value were under 35. From 30 research samples were known that 15 samples (50%) of them were greater than 45 years old, while the rest of 50% were under 45 years old.

Based on table 3, it was known that 3 samples (10%) with a morphological index of Sassone were greater than 9 and had histopathological results of serous type of epithelial ovarian cancer, while the remaining of 6.7% with morphology index of Sassone below 9 and had histopathological results of serous type of epithelial ovarian cancer. Table 3, also showed that 4 samples (13.3%) with CA 125 tumour marker values greater than 35 were equal and had histopathological results serous type of epithelial ovarian cancer, while the remaining of 3.3% with CA 125 tumour marker values below 35 and had histopathological results serous type of epithelial ovarian cancer.

Table 2. Characteristics of the Sample Based on Histopathology, Morphological Index of Sassone, CA 125 Tumour Marker and Age Group

Variables	Total (samples)
Histopathology	
Serous type of epithelial cancer	5
Non Serous type of epithelial cancer	25
Morphology index of Sassone	
< 9	10
≥ 9	20
Ca 125 U/ml	
< 35	19
≥ 35	11
Age (y.o)	
< 45	15
≥ 45	15

Table 3. Characteristics of Samples Based on a Morphological Index of Sassone and Tumour Marker of Ca 125 with Serous Type Epithelial Ovarian Cancer

Variable	Serous type of epithelial cancer (samples)
Morphological index of Sassone	
< 9	2
≥ 9	3
Ca 125 U/ml	
< 35	1
≥ 35	4

Table 4, showed comparison of the morphological index of Sassone and Ca 125 tumour markers values in the epithelial ovarian tumour malignant group with serous type and non-serous type, it was showed that the value of CA 125 tumour markers in the epithelial ovarian tumour malignat group with non-serous type was much greater than the epithelial ovarian cancer group with serous type, but statistically the two groups had different CA 125 tumour marker values. This was because the CA 125 tumour marker value in the non serous type of epithelial ovarian cancer had a very large SD value. Furthermore, the Mann-Whitney test results in Table 4, showed that the epithelial ovarian cancer with serous type and non serous type also had the same morphological index of Sassone statistically indicated by the p-value testing greater than 0.05. Both of these comparison results show that the CA 125 tumour marker value and the morphological index of Sassone in this study had not been able to distinguish between epithelial ovarian cancer with serous type and non serous type

Table 4. Comparison of the Morphological Index of Sassone and the Values of CA 125 Tumour Marker between Epithelial Ovarian Cancer with Serous Type and non Serous Type.

Variable	Avarage	SD	*P-value*
Morphological index of Sassone			
Non Serous type of epithelial cancer	10.28	2.11	0.627[a]
Serous type of epithelial cancer	10.60	4.04	
CA 125			
Non Serous type of epithelial cancer	349.25	1132.86	0.251[a]
Serous type of epithelial cancer	165.34	91.48	

Measuring the morphological index of Sassone compared to tumour markers of CA 125 against serous type of epithelial cancer were required special examinations such as sensitivity and specificity analysis, positive and negative likelihood ratio, positive and negative predictive value and accuracy. In the diagnostic test, the morphological index of Sassone was classified into 2 categories: mild if the results of the morphological index of Sassone were below 9, and suspected malignant if the morphological index of Sassone was greater than 9. Tumour markers of CA 125 values were categorized as mild if CA 125 values below 35 and suspects malignant if the CA 125 value was greater than 35.

Diagnostic test results showed that the use of morphological index of Sassone as a predictor of serous type epithelial ovarian cancer would have sensitivity value of 60%, specificity value of 28%, PPV of 14%, NPV of 78%, positive and negative likelihood ratio were 0.83 and 1.42, respectively and accuracy were 33.3%. While the diagnostic test results of CA 125 tumour marker as a predictor serous type of epithelial ovarian cancer had sensitivity value of 80%, specificity value of 40%, PPV of 21%, NPV of 91%, positive and negative likelihood ratio were 1.33 and 0.50, respectively and accuracy was 46.7%.

DISCUSSION

The study involved 30 samples obtained from primary data collected from November 2018 to April 2019. Patient characteristics by age were 15 samples (50%) of which were older than 45 years old with 12 samples having malignant histopathology. Furthermore, as many as 50% under 45 years old in which 4 samples had the results of malignant histopathology. This is consistent with the literature that the age of occurrence of ovarian cancer is most often above the 45 years old with the incidence increasing significantly at the 45-54 years old.[3,15] Even though, statistics on ovarian cancer in 2018 showed a higher incidence in women over 65 compared to women under 65 years old.[16]

Based on this research, only 5 samples (16.67%) from 30 ovarian cancer patients were included in epithelial malignant ovarian tumour

with serous type, the remaining 25 samples (83.33%) included in epithelial malignant ovarian tumour with non-serous type. This differs from the literature which found that the incidence rate of epithelial malignant ovarian tumour with serous type was 60%.[17,18] The registration data of cancer centres in North America in 2016, the classification of ovarian cancer was serous 52%, endometrioid 10%, mucinous and clear cells were 6%.[19]

The CA 125 tumour marker was the primary examination of ovarian cancer and fallopian tube, epithelial ovarian cancer when the value is greater than 35 U / mL.[1,20] Increased concentration tumour markers of CA 125 found in 75% of women with serous type of epithelial ovarian cancer, mentioned that increased concentrations occur in women with ovarian serous type of epithelial cancer followed by endometrioid and clear cell types.[8,21,22]

It is not suitable with the results of this study in which the CA 125 value only increased in 4 samples (13.3%) with histopathological results serous type of epithelial ovarian cancer from a total of 30 samples (p-value 0.251). So from the study, it was found that there was no correlation between increasing the value of CA 125 tumour marker and epithelial ovarian cancer with serous type.

Characteristics of benign or malignant ovaries could be confirmed by ultrasonography as the main imaging modality. The ultrasound morphology correlated with the macroscopic pathological picture of ovarian mass, with the highest scoring score on PID, corpus luteum cysts and the lowest score on serous ovarian cystadenoma.[23] In this study, the ultrasound examination used the morphology index of Sassone, which assessed the inside of wall structure, wall dense, septum and resonance. From the assessment conducted only 3 samples (10%) with a serous type of epithelial ovarian cancer with a morphological index of Sassone greater than 9 (p-value 0.623). It can be stated that there is no relationship between Sassone morphological index and epithelial ovarian cancer with serous type.

In this study, the morphology index of Sassone was greater than 9 are 3 samples that were diagnosed with a serous type of epithelial ovarian cancer, with sensitivity value 60%, specificity 28%, PPV 14%, NPV 78%, positive and negative likelihood ratio were 0.83 and 1.42, respectively and accuracy was 33 %. With positive and negative likelihood ratio values were below 10 and above 0.1, respectively. These results stated that the morphological index of Sassone had a poor diagnostic value. This was different from the study that had been done by Desai et al, who obtained a higher sensitivity value of 81.8% and the specificity value of the index was 92.3% in the Sassone morphological index in patients with malignant ovarian masses.[24] The study that has been done, found sensitivity, specificity values, PPV, NPV, and accuracy are 89.5%, 78.4%, 68%, 93.5% and 82.1%.[25] From the study who obtained the sensitivity value was 91.7% and the specificity value was 77.7 % in the Sassone morphological index in women with an adnexal mass.[26]

Mentions that patients with malignant ovarian masses of serous type, the sensitivity value of CA 125 84% compared to mucinous, endometrioid, clear cell and undifferentiated types were 66.7%, 80%, 33.7% and 95%.[27] Whereas in the study it was found that CA 125 value was greater than 35 U / mL were 4 samples that were diagnosed with serous type of epithelial ovarian cancer, with a sensitivity value 80%, specificity 40%, PPV 21%, NPV 91%, positive and negative likelihood ratio were 1.33 and 0.50, respectively and accuracy was 46.7%. With positive and negative likelihood ratio values were below 10 and above 0.1, respectively. It was indicated that the morphological index of Sassone had a poor diagnostic value.

The two statistical studies that previously done were comparative analysis of CA 125 tumour marker values and morphological index of Sassone between serous type and non-serous of epithelial ovarian malignant tumour, and diagnostic test such as sensitivity and specificity, PPV, NPV, positive and negative likelihood ratio and accuracy indicate that CA 125 values and the morphological index of Sassone in the study could not be used as good predictors of serous type of epithelial ovarian cancer. It also could be concluded that the use of the morphological index of Sassone had not been proven to be statistically better than the tumour marker of CA 125 as a predictor of serous type epithelial ovarian cancer. The results of the two tests showed that the use of curves of the receiver operating characteristic to determine the cut-off point of each CA 125

predictor variable and the morphological index of Sassone for the serous type of epithelial ovarian cancer could not be performed because it would give biased results. One reason why the results were not good was that the number of the samples from serous type of epithelial ovarian cancer was very small. Increasing the number of the sample from epithelial ovarian cancer with serous type will make the result better.

CONCLUSION

There was no correlation between the morphological index of Sassone and epithelial ovarian cancer with serous type, p-value 0.627. The CA 125 tumour markers were not related to the epithelial ovarian malignat tumour with serous type, p-value 0.251.

SUGGESTION

For further study, we need a larger sample to suspect a serous type of epithelial ovarian cancer for diagnostic the disease quickly and accurately.

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