Comparison of Sassone Scoring and Adnex Model in Differentiating Benign and Malignant Ovarian Neoplasm in a University Hospital

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ABSTRACT

Background Ovarian cancer is the second most common gynecologic cancer worldwide and are usually diagnosed in advanced stages where prognosis is very poor. Ultrasound has been widely used to screen and differentiate benign and malignant ovarian neoplasm. There are several ultrasound scoring system designed to aid in the diagnosis, however, there is still no standard method accepted for screening of ovarian cancer.

Objective To compare the accuracy of SASSONE Scoring and ADNEX Model in differentiating benign and malignant ovarian neoplasm in the University of Santo Tomas Hospital.

Methodology Sixty-eight women who presented with an ovarian neoplasm by history and physical examination were recruited from January to October 2017. Ultrasound was requested to further characterize the mass.

Sassone scoring and ADNEX Model were applied and computed based on the sonologic findings to differentiate whether the ovarian neoplasm was benign or malignant. The gold standard was the histopathologic examination of the mass after surgery.

Results There was no significant difference in the accuracy of Sassone Scoring and ADNEX model in pre-operatively differentiating benign and malignant ovarian neoplasm with 88% and 89% accuracy rate, respectively. Sassone scoring has a sensitivity of 62.5% and specificity of 91.67% while ADNEX has a sensitivity and specificity of 37.5% and 96.67%, respectively.

Conclusion There is no significant difference in using SASSONE and ADNEX model in differentiating benign and malignant ovarian neoplasm prior to surgery. Both may be used as an ultrasound scoring system for predicting ovarian malignancy. However, in cases of suspicious tumors, ADNEX model is more useful in discriminating the type and stage of malignancy.

Keywords ovarian cancer, adnexa, screening, ultrasound

INTRODUCTION

Ovarian Cancer is the second most common gynecologic cancer worldwide and the sixth most common cancer in women (3) with approximately 255,000 new cases diagnosed each year (5). It has

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the highest mortality rate among gynecologic cancers with a general survival rate of less than 50% (8). Most cases are seen in pre-menopausal and post-menopausal women who often remain asymptomatic in their early phase of the disease because of the anatomic location of the ovaries, deep in the pelvis. Thus, most cases are diagnosed at an advanced stage when prognosis is very poor already (4). The presenting signs and symptoms are also vague like bloating, pelvic or abdominal pain, poor appetite and urinary urgency which may be confused with other gastrointestinal and urologic diseases that can present similarly hence the late consult, diagnosis and management.

Ovarian cancer is a heterogeneous disease and composed of different types of tumors derived from various cell lines with diverse behaviors and clinicopathologic characteristics (4). There are three main types which are responsible for almost all malignant tumors: surface epithelial-stromal tumors (90-95%), sex cord-stromal tumors (5-10%) and germ cell tumors (5-10%) (4).

At present, there is no universal protocol for differentiating benign and malignant ovarian masses. Several studies have attempted to use imaging, cytology and tumor markers but no standard method was accepted for pre-operative screening of ovarian cancer (10).

Ultrasound is the most practical modality for assessment of ovarian tumors. It is non-invasive, readily available, cost-effective and can provide a detailed information in evaluating the characteristic and malignant potential of an ovarian mass. It has an 82% sensitivity and specificity in identifying benign and malignant tumors (8).

Ultrasound correlates the images morphologically with macroscopic pathologic features of tumors such as solid component, thick septations, multiple loculations, and papillary projections (8). Inter-observer difference and extreme variability of macroscopic characteristics of ovarian tumor make an accurate diagnosis difficult by ultrasound alone. Therefore, to offset these limitations, use of ultrasound scoring system was encouraged (8). To aid in the diagnosis as well as to differentiate between benign and malignant ovarian masses. Some of these scoring systems are the SASSONE Scoring and the ADNEX Model where the latter, aside from sonologic findings will be derived from clinical predictors such as age, serum CA-125 level and type of hospital where gynecologic oncology referral is available.

SASSONE Scoring, devised by AM Sassone, is a scoring system that uses traditional gray scale ultrasound to characterize ovarian lesion and composed of four variables such as inner wall structure, wall thickness, septum and echogenicity. Each variable has a corresponding value and a total score of > 9 suggest malignancy.

Assessment of Different NEoplasias in the AdneXa (ADNEX) Model is a scoring program generated by the International Ovarian Tumor Analysis (IOTA) group. It can be downloaded through the internet (www. iotagroup.org) as a computer or mobile phone application. It contains three clinical and six ultrasound predictors: age, serum CA-125 level, type of center (oncology center vs other hospitals), maximum diameter of lesion, proportion of solid tissue, more than 10 cysts locules, number of papillary projections, acoustic shadows and ascites. Once all parameters are assessed, the application will compute for chances of having a benign tumor, risk of malignancy, risk of metastatic cancer to the adnexa, risk stage II-IV ovarian cancer, risk stage I ovarian cancer, risk of having a borderline tumor. It is the first risk model created that can differentiate between benign and four subgroups of malignant adnexal tumors (8). Information of the specific type of adnexal pathology pre-operatively has better patient triage and makes it feasible to optimize treatment (2).

The objective of this study is to determine the diagnostic accuracy of the SASSONE scoring and the ADNEX model in terms of their sensitivity, specificity, positive and negative likelihood ratios, positive and negative predictive values in differentiating benign and malignant ovarian neoplasm.

METHODS

This prospective cohort study included all women with a consideration of an ovarian neoplasm by history and physical examination seen at the University of Santo Tomas Hospital, from January to October 2017.

The study was approved by the Institutional Review Board. Exclusion criteria included those patients with previous history of ovarian malignancy. A minimum of 68 subjects was required for this study based on a level of significance of 5%, a prevalence of 32.14%, sensitivity of 94% with a half-width of the confidence

interval of 0.10. The values for the prevalence of malignant ovarian mass and sensitivity were based from the study by Shende et al., 2016 (1). A written informed consent was obtained from all subjects.

Each patient underwent ultrasound to characterize the ovarian neoplasm: (transvaginal ultrasound for subjects with previous sexual contact, transrectal ultrasound for patients with no history of sexual contact, transabdominal ultrasound if applicable for patients with huge ovarian neoplasm). SASSONE Scoring (Table 1) and ADNEX model (Table 2) were applied and computed based on the sonographic descriptions. However, serum CA-125 was excluded as part of the parameters of ADNEX Model due to the expenses it entails to the investigator and subjects. This parameter will only decrease the distinction between stage II-IV invasive tumors but the application could still differentiate the ovarian mass as benign or malignant. Sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of the SASSONE Scoring and the ADNEX Model in discriminating benign and malignant neoplasm were computed.

The gold standard for the diagnosis was the histopathologic examination of the specimen obtained from laparotomy of the adnexal mass. Borderline tumors were categorized as malignant.

Descriptive statistics were used to summarize the general and clinical characteristics of the subjects. Frequency and proportion were used for nominal variables, median and range for ordinal variables, and mean and standard deviation for interval/ratio variables.

All valid data was included in the analysis. Missing variables were neither replaced nor estimated. Null hypothesis was rejected at 0.05 ⍰-level of significance. STATA 15.0 was used for data analysis.

RESULTS

The study included 68 women with ovarian neoplasms. The mean age of the women was 38.06 ± 12.57 years and their BMI was 25 kg/m2 (Table 3). Majority were nulligravid (52%) and nulliparous (57%), with only 19% using contraceptives (OCP/injectables). The three most common

Table 1. Sassone Scoring: A total score of ≥ 9 suggest malignancy.

VARIABLES				
INNER WALL STRACUTURE (mm)	**WALL THICKNESS (mm)**	**SEPTA (mm)**	**ECHOGENICITY**	**POINTS**
Smooth	Thin </= 3mm	No septa	Sonolucent	1
Irregular </- 3mm	Thick > 3mm	Thin </= 3mm	Low echogenicity	2
Papillarities >3mm	Not applicable mostly solid	Thick >3 mm	Low echogenicity with echogenic core	3
Not applicable mostly solid	-	-	Mixed echogenicity	4
-	-	-	High echogenicity	5

Table 2. ADNEX Model

IOTA – ADNEX Model (PARAMETERS)
1. Age of the patient at examination (years)
2. Oncology center (referral center for gyne-oncology)
3. Maximal diameter of the lesion (mm)
4. Maximal diameter of the largest solid part (mm)
5. More than 10 locules?
6. Number of papillations (papillary projections)
7. Acoustic shadow present?
8. Ascites (fluid outside pelvis) present?
9. Serum CA-125 U/ml (may be optional but will decrease the discrimination between stage II-IV invasive tumors and the other malignancy subtypes.)

Table 3. Demographic and clinical profile of the women with ovarian neoplasm seen at University of Santo Tomas Hospital (n= 68)

	Frequency (%); Mean ± SD;
Age (years)	38.06 ± 12.57
Height (cm)	153.91 ± 2.69
Weight (kg)	59.6 ± 7.07
BMI (kg/m^2)	25.12 ± 3.01
Gravidity	
Nulligravida	36 (52.94)
Primigravida	7 (10.29)
Multigravida	25 (36.76)
Parity	
Nulliparous	39 (57.35)
Primiparous	8 (11.76)
Multiparous	21 (30.88)
Use of OCP/Injectables	13 (19.12)
Presenting signs and symptoms*	
Abdominal pain	28 (41.18)
Irregular menses	16 (23.53)
Abdominal mass	10 (14.71)
Abdominal enlargement	5 (7.35)
Previous ultrasound/ incidental finding of ovarian cyst on ultrasound	12 (17.64)
Dysmenorrhea	2 (2.94)
Others	3 (4.41)
Dysuria	1 (33.33)
Recurrent pregnancy loss	1 (33.33)
Urinary frequency	1 (33.33)
Menstrual status	
Menstruating	53 (77.94)
Peri-menopause	4 (5.88)
Menopause	11 (16.18)
Personal history of cancer	1 (1.47)
Family history of cancer	13 (19.12)

* - Multiple responses

presenting complaints were abdominal pain (41%), irregular menses (23%), and abdominal mass (14%).

Comparing those who were benign versus malignant on histopathology, we found that the benign group was significantly younger (36.8 versus 47.5 years, p = 0.023), and consequently had a higher proportion of menstruating patients (83% versus 37.5%, p = 0.003) (Table 4).

The study assessed the diagnostic accuracy of SASSONE score in relation to the histopathologic results (Table 7) and found it to have an overall accuracy of 88% (95% CI 78.1-94.8%). It has a high negative predictive value: that is, patients who are classified as benign by the SASSONE score (less than 9) has a 94.82% probability of having benign histopathology. Similarly, it was highly specific: where among those who have truly benign histopathologic results, there is a 91.67% probability that their test will turn benign by SASSONE as well. Sensitivity and positive predictive values were equivocal, with point estimates and confidence intervals approaching 50%. Patients who were malignant by SASSONE is 7.5 times more likely to have a malignant neoplasm on histopathology as compared to patients with benign histopathology (Table 5).

In comparison, the ADNEX model (Table 7) has a slightly higher overall accuracy compared to SASSONE score at 89% (95% CI 79.9-95.8%). It also has a higher specificity of 96% (95% CI 88.5-99.6%), albeit a lower sensitivity at 37% (95% CI 8.52-75.51%). Similar to SASSONE, ADNEX had good specificity and NPV. It had high negative predictive value: that is, patients who are classified as benign by the ADNEX score has a 92.06% probability of having benign histopathology. It was also highly specific: where among those who have truly benign histopathologic results, there is a 96.67% probability that their test will turn benign by ADNEX as well. Sensitivity and positive predictive values were non-conclusive, with point estimates and confidence intervals approaching 50%. Patients who were malignant by ADNEX were 11.25 times more likely to have a malignant neoplasm on histopathology compared to patients with benign histopathology (Table 6).

Malignant cases in the study by histopathology were compared using SASSONE Scoring and ADNEX model. SASSONE Scoring was more sensitive in screening of ovarian lesions but ADNEX Model was more specific as to what type of ovarian malignancy (Table 8).

DISCUSSION

Ovarian neoplasm represents a common problem in clinical practice. About 10% of women will undergo exploratory laparotomy for evaluation of ovarian tumors during their lifetime10. Early identification of ovarian malignancies and referral to gynecologic oncologist can improve patient's prognosis.

This study compared the accuracy of SASSONE scoring and ADNEX model in differentiating benign and malignant neoplasm. Since there is no standard protocol yet for screening of ovarian malignancies. Histopathologic diagnosis of the ovarian mass during surgery remains to be the gold standard.

Table 4. Comparison of patients with malignant versus benign histopathology (n= 68)

	Malignant via histopathologic results (n=8)	Benign via histopathologic results (n=60)	P-value
	Frequency (%); Mean ± SD		
Age (years)	47.5 ± 14.08	36.8 ± 11.93	**0.023**‡
Height (cm)	155.63 ± 1.77	153.68 ± 2.72	0.054‡
Weight (kg)	62.88 ± 5.38	59.17 ± 7.18	0.165‡
BMI (kg/m^2)	25.75 ± 2.19	25.03 ± 3.11	0.531‡
Gravidity			0.188$
Nulligravida	2 (25)	34 (56.67)	
Primigravida	1 (12.5)	6 (10)	
Multigravida	5 (62.5)	20 (33.33)	
Parity			0.079$
Nulliparous	3 (37.5)	36 (60)	
Primiparous	3 (37.5)	5 (8.33)	
Multiparous	2 (25)	19 (31.67)	
Use of OCP/Injectables	2 (25)	11 (18.33)	0.643$
Presenting signs and symptoms*			
Abdominal pain	1 (12.5)	27 (45)	0.128$
Irregular menses	14 (23.33)	2 (25)	1.000$
Abdominal mass	2 (25)	8 (13.33)	0.334$
Abdominal enlargement	2 (25)	3 (5)	0.102$
Previous ultrasound of ovarian cyst	1 (12.5)	11 (18.33)	1.000$
Dysmenorrhea			
Others	0	2 (3.33)	1.000$
Dysuria			
Recurrent pregnancy loss	1 (12.5)	2 (3.33)	0.317$
Urinary frequency	1 (100)	0	
	0	1 (50)	
	0	1 (50)	
Menstrual status			
Menstruating	3 (37.5)	50 (83.33)	0.003$
Peri-menopause	0	4 (6.67)	
Menopause	5 (62.5)	6 (10)	
Personal history of cancer	0	1 (1.67)	1.000$
Family history of cancer	2 (25)	11 (18.33)	0.643$

* - Multiple responses, Statistical tests used: ‡ - Independent sample t test; $ - Fisher's exact test

Table 5. Comparison between Sassone Scoring and histopathology (n= 68)

	Malignant via histopathologic results	Benign via histopathologic results	Total
	Frequency (%)		
Malignant as assessed by SASSONE score	5 (7.35)	5 (7.35)	10 (14.71)
Benign as assessed by SASSONE score	3 (4.41)	55 (80.88)	58 (85.29)
Total	8 (11.76)	60 (88.24)	68 (100)

Our analysis showed that there is no significant difference in distinguishing benign from malignant neoplasm sonographically, between Sassone Scoring and ADNEX Model, their accuracy rate are 88% and 89% respectively.

Sassone Scoring had a 91.67 % specificity and 62.5% sensitivity. This scoring system takes into consideration the inner wall structure, wall thickness, septa and echogenicity of the mass. It is a more useful tool in screening ovarian lesions due to its

Table 6. Comparison between ADNEX Model and histopathology (n=68)

	Malignant via histopathologic results	Benign via histopathologic results	Total
	Frequency (%)		
Malignant as assessed by ADNEX Model	3 (4.41)	2 (2.94)	5 (7.35)
Benign as assessed by ADNEX Model	5 (7.35)	58 (85.29)	63 (92.65)
Total	8 (11.76)	60 (88.24)	68 (100)

Table 7: Statistical comparison between the two scoring systems

Statistical Parameter	Sassone Scoring system (%)	ADNEX Model (%)
Sensitivity	62.5% (24.5% – 91.5%)	37.5% (8.52 – 75.51)
Specificity	91.67% (81.6% – 97.2%)	96.67% (88.5% – 99.6%)
Positive Predictive Value	50% (27% – 73%)	60% (22.7% – 88.5%)
Negative Predictive Value	94.83% (88.2% – 97.8%)	92.06% (87.1% – 95.2%)
Positive Likelihood Ratio	7.5 (2.77 – 20.31)	11.25 (2.2 – 57.42)
Negative Likelihood Ratio	0.41 (0.17 – 1.0)	0.65 (0.38 – 1.11)
Accuracy	88.24% (78.1% – 94.8%)	89.71% (79.9% – 95.8%)
P value	0.727*	0.453*

**McNemar's test*

Table 8. Comparison of SASSONE Scoring and ADNEX model in malignant ovarian neoplasm by histopathology

Case	SASSONE Scoring	ADNEX Model
1 Adenocarcinoma with clear cell and signet ring feature, bilateral ovaries	9 (Malignant)	Risk of Malignancy 37.8% Chance of Benign Tumor 62.2% Risk of Borderline Tumor 16.6% Risk of stage I Ovarian cancer 10.3% Risk of stage II-IV Ovarian cancer 8.9% Risk of Metastatic cancer to the Adnexa 2.0%
2 Borderline Mucinous tumor	7 (Benign)	Risk of Malignancy 10.4% Chance of Benign Tumor 89.6% Risk of Borderline Tumor 5.2% Risk of stage I Ovarian cancer 3.7% Risk of stage II-IV Ovarian cancer 0.9% Risk of Metastatic cancer to the Adnexa 0.5%
3 Papillary Serous Carcinoma of the ovary, stage III	13 (Malignant)	Risk of Malignancy 79.1% Chance of Benign Tumor 20.9% Risk of Borderline Tumor 2.4% Risk of stage I Ovarian cancer 12.4% Risk of stage II-IV Ovarian cancer 50.6% Risk of Metastatic cancer to the Adnexa 13.7%
4 Borderline Serous Tumor	8 (Benign)	Risk of Malignancy 38.1% Chance of Benign Tumor 61.9% Risk of Borderline Tumor 27.2.6% Risk of stage I Ovarian cancer 5.4% Risk of stage II-IV Ovarian cancer 4.4% Risk of Metastatic cancer to the Adnexa 1.0%
5 Clear cell carcinoma of the left ovary Stage IC1	14 (Malignant)	Risk of Malignancy 75.5% Chance of Benign Tumor 24.5% Risk of Borderline Tumor 63.2% Risk of stage I Ovarian cancer 8.1% Risk of stage II-IV Ovarian cancer 3.0% Risk of Metastatic cancer to the Adnexa 1.2%

Table 8. Continued...

Case	SASSONE Scoring	ADNEX Model
6 High grade carcinoma with focal papillary transitional and glandular features, left ovary	10 (Malignant)	Risk of Malignancy 75.8% Chance of Benign Tumor 24.2% Risk of Borderline Tumor 44.9% Risk of stage I Ovarian cancer 21.1% Risk of stage II-IV Ovarian cancer 8.7% Risk of Metastatic cancer to the Adnexa 1.1%
7 Mucinous cystadenocarcinoma Stage IA, right ovary	9 (Malignant)	Risk of Malignancy 5.0% Chance of Benign Tumor 95.0% Risk of Borderline Tumor 2.7% Risk of stage I Ovarian cancer 1.0% Risk of stage II-IV Ovarian cancer 0.8% Risk of Metastatic cancer to the Adnexa 0.5%
8 High grade papillary serous carcinoma of the ovary, Stage IIIB	8 (Benign)	Risk of Malignancy 9.9% Chance of Benign Tumor 90.1% Risk of Borderline Tumor 4.1% Risk of stage I Ovarian cancer 2.9% Risk of stage II-IV Ovarian cancer 2.0% Risk of Metastatic cancer to the Adnexa 1.0%

high sensitivity. Study done by Vikram Shende et al. which concluded that the sonographic scoring system has a 94% specificity and 88% sensitivity rate1. They had a 88% negative predictive value and 94% positive predictive value in contrast with our findings of negative and positive predictive value of 94.83 % and 50% respectively. The difference was probably due to our small number of malignant cases as compared to benign by histopathology.

The ADNEX Model is the first risk assessing ultrasound scoring system. It distinguishes between benign and four subgroups of malignant adnexal tumors. It consists of three clinical predictors (age, type of center where patient has been referred for ultrasound examination and serum CA-125) and six ultrasound predictors (maximal diameter of the lesion, maximal diameter of the largest solid part, presence of more than 10 locules, number of papillations, presence of acoustic shadow, presence of ascites). Aside from discriminating between benign and malignant neoplasm, it can detect whether the malignancy is primary or metastatic. Such information of the type of adnexal pathology before surgery can improve patient triage and maximize treatment options8. In turn, this may result in reduction of morbidity and lead to enhanced survival from the various types of ovarian malignancy.

The ADNEX model can differentiate well between benign tumors, stage I cancers and advanced stages, advanced primary cancer and secondary metastatic cancers (8). In our study, it has a 96.67% specificity and 37.5% sensitivity. In contrast, the study done by Ben Van Calster showed that ADNEX model has 71.3% specificity and 96.5% sensitivity (8). It has a 60% positive predictive value and 92.06% negative predictive value similar to that of SASSONE scoring.

The type of referral center is one predictor of the ADNEX model based on the perception that patients with masses that look suspicious are more frequently referred to a specialized center for assessment and treatment such as UST Hospital. Based on the study by Van Calster that malignancy rates are higher in specialized center with 22-66% rates as compared to other centers with 0-30% rates (8).

Serum CA-125 is also an important factor for discrimination between stage II-IV and stage I and secondary metastatic cancer. However in our study, it was excluded as part of the parameters. Its utilization will decrease the distinction between stage II-IV invasive tumors but the ADNEX application still differentiated the ovarian masses as benign, borderline and malignant. Though the model seems complicated, it gives a more detailed differentiation of the type of ovarian neoplasm. In our study, the ADNEX model has poor sensitivity that decreases its utility for screening but its high specificity makes it a better tool for predicting ovarian malignancy and better planning options for management.

CONCLUSION

In conclusion, our study showed no significant difference in using SASSONE and ADNEX model to predict benign from malignant ovarian neoplasm.

Both may be used as an ultrasound scoring system to distinguish pre-operatively between benign and malignant ovarian masses. However, in cases of suspicious tumors, ADNEX model is more useful in discriminating the type and stage of malignancy. Knowing the type and stage of ovarian malignancy is useful to both the clinicians and the patient. For the clinicians, early referral of the patient to a gynecologic oncologist aids in early proper staging and intervention. Consequently, this leads to avoidance of unnecessary cost and morbidity on the part of the patient.

CONFLICT OF INTEREST

There were no conflicts of interest involved in the study. The ultrasound were done by the rotating sonographer at the University of Santo Tomas Hospital High Risk Unit. The primary investigator computed the SASSONE and ADNEX model score.

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