Journal of
Women's Health and Gynecology

Research Article Open Access

Therapeutic Decision on Adnexal Masses: A Performance Protocol Based on HE4 Tumor Marker (Human Epididymis Protein 4), GI-RADS (Gynecology Imaging Reporting and Data System) and Hormonal Status

María de Matías Martínez[1*], María Dolores Martín de los Ríos[2], Ana Belén Cuesta Cuesta[2], Sara Bartolomé[3] and Eduardo Daniel Abreu Griego[2] and María del Rosario Noguero Meseguer[4]

[1]Associate Head of Gynecology. Rey Juan Carlos University Hospital, Móstoles, Madrid. Rey Juan Carlos University, Móstoles, Madrid, Spain

[2]Rey Juan Carlos University, Móstoles, Madrid, Spain

[3]Sotillos Hospital Universitario Rey Juan Carlos, Móstoles, Madrid, Spain

[4]Chief of Obstetrics and Gynecology. Rey Juan Carlos University Hospital, Rey Juan Carlos University, Móstoles, Madrid, Spain

***Corresponding author:** María de Matías Martínez, Associate Head of Gynecology. Rey Juan Carlos University Hospital, Móstoles, Madrid. Rey Juan Carlos University, Móstoles, Madrid, Spain, Tel: +34636057452, E-mail: mariadematias@gmail.com

Received Date: October 03, 2021 **Accepted Date:** November 03, 2021 **Published Date:** November 05, 2021

Citation: María de Matías Martínez (2021) Therapeutic Decision on Adnexal Masses: A Performance Protocol Based on HE4 Tumor Marker (Human Epididymis Protein 4), GI-RADS (Gynecology Imaging Reporting and Data System) and Hormonal Status. J Womens Health Gyn 8: 1-11.

Abstract

Adnexal masses are a relatively frequent problem in gynecological examination but most of them are benign process. Our study aimed to evaluate the diagnosis protocol following the detection of adnexal masses according to hormonal state, HE4 and Gynecologic Imaging Report and Data System (GI-RADS) which avoid unnecessary surgeries. The retrospective cohort study was carried out from July 2015 to June 2017, with patients treated at Hospital Universitario Rey Juan Carlos. Serum testing with tumor markers were requested for all patients based on the finding of an adnexal mass in a high-resolution ultrasound based on the GI-RADS classification. One hundred fifty-four patients were studied, 33.1% (51 cases) of which underwent surgical intervention. Of all patients who underwent surgical intervention,17 (33.3%) were diagnosed with a malignant ovarian neoplasm. The results showed a global sensitivity of 88.2% with a specificity of 83.9%, but in pre-menopausal women the sensitivity and specificity were 100% and 85.4% respectively. The sensitivity and specificity of biomarker HE-4 was 70,6% and 92 % respectively. We conclude that a protocol based on the GI-RADS classification system would be a useful and practical tool for following up and treatment of adnexal masses, avoiding unnecessary surgeries.

Keywords: Ovarian neoplasms Cancer; Biomarker HE4; Ultrasonographic imaging GI-RADS

Introduction

Ovarian cancer is the seventh most common cancer in women with approximately 200,000 new cases diagnosed each year. In developed countries it is the leading cause of death from gynecological tumors. [1] In Spain, ovarian cancer is the second most common gynecologic malignancy, with 3,300 new cases per year and an annual incidence of 9.9 cases per 100,000 inhabitants [2]

Ovarian cancer is a very serious disease due to its insidious onset and growth characteristics. Early stages are usually asymptomatic and the first symptoms are usually nonspecific and appear in advanced stages.

Adnexal image findings are very common in gynecology outpatients visits with a prevalence rate of 3,3 to 18% [3]. In spite of most of them prove to be benign [4] and most women with adnexal mass undergo surgery because of the lack of specificity of the ultrasonographic images and the overestimate risk of malignancy. So, the use of a standardized terminology for description of ultrasound scan is necessary. In 2011, in an attempt to improve communication between sonographers and clinicians, a prospective multicenter study described and analyzed the GI-RADS [5] classification (Gynecologic Imaging Report and Data System), a system equivalent to the BI-RADS system for the breast and which provides an estimated risk of malignancy for each category, therefore, standardizing the management of patients with the same risk of malignancy. When used by expert sonographers, it has shown a sensitivity of 99% and a specificity of 86%.

In addition, there are several tumor markers and indexes that attempt to estimate a risk of malignancy for each adnexal mass, but none of them is sufficiently sensitive or specific. In 2008, HE4 (human epididymis protein 4) emerged as a new marker, appearing to provide increased specificity over Ca125 (carbohydrate antigen 125), a tumor marker previously used widely at the time. At present, only 25% of ovarian cancers are diagnosed at an early stage [2].

There is a lack of information on conservative management of adnexal masses in current literature.

The purpose of this study was to evaluate the use of GI-RADS in women with an adnexal mass to identify patients with low risk of malignancy who may undergo conservative management, though non-surgical treatment which avoids surgical complications.

Our study suggests the use of the GI-RADS system as a common ultrasound language, which improves diagnostic capacity for clinical decision-making in patients with ovarian masses.

Therefore, more studies are needed to help improve the detection of ovarian cancer, increasing the likelihood that a tool will be available for screening in the future.

Material and Methods

A retrospective cohort study was carried out from July 2015 to June 2017. This protocol was approved by the ethics committee of the hospital.

Patients

The study population comprised women who presented to the gynecology clinic of our hospital with findings of an adnexal mass, leading to diagnostic testing with tumor markers (HE4 measured using the COBAS E411 platform manufactured by ROCHE, with positivity indicated by values above 130 pmol/L)).

Additionally, we used transvaginal, transabdominal or transrectal high-resolution ultrasound scans obtained with the VOLUSON (model E6), ultrasound system to classify the adnexal mass according to the GI-RADS system. Ultrasound scan were performed by expert ultrasound examiners, all of whom are gynecologists with more than 10 years of experience.

Management protocol for adnexal masses at Hospital Universitario Rey Juan Carlos

In 2012, a review of the most relevant articles on the management of adnexal masses and the latest protocols of scientific societies was made, due to the lack of a clear definition in this regard. After several consensus sessions, a protocol of action was elaborated by the gynecology team of the hospital, taking into account the principle of "right care" [6], that is, choosing a standard of care that brings to the patients more benefits than unwanted effects, and in this way decreasing any form of overdiagnosis and overtreatment.

One of the methods that is incorporated into the protocol is the GI-RADS that was endorsed by SEGO (Spanish Society of Obstetrics and Gynecology) [7].

An adnexal mass was cataloged with a GI-RADS based on the presence of 5 signs of malignancy: thick papillary pro-

jections larger than 3 mm, septations thicker than 2 mm, solid areas, ascites and vascularization as evidenced on Doppler sonography.

Clinical outcomes

After a complete clinical history was obtained during the outpatient visit, an ultrasound scan was performed, an adnexal mass was cataloged with a GI-RADS score. Patients were considered to be postmenopausal if they reported absence of menstruation for a whole year (amenorrhea for at least 12 consecutive months).

According to their risk of malignancy, theses masses were classified with the following categories GI-RADS 1 (estimated probability 0%), GI-RADS 2 (estimated probability <1%), GI-RADS 3 (estimated probability 1-4%), GI-RADS 4 (estimated probability 5- 20%) and GI-RADS 5 (estimated probability >20%), and followed-up as shown in Table 1.

As show in Table 1, the management for adnexal mass is different according to hormonal status, and so due to fertility compromise, which leads to a more aggressive management in postmenopausal women.

Table 1. Management protocol for adnexal masses according to GI-RADS classification and hormonal status.

All women classified with GI-RADS 5 score must undergo a surgical intervention and only the GI-RADS 4 cases with small size and in pre-menopausal women a follow up could be permitted. Also, we indicated surgical removal of an adnexal mass if patient had symptoms like pain, or if pelvic mass presented with hight risk of torsion or rupture. If a positive tumor marker was found in an adnexal masses classified GI-RADS 3 or 4 we contraindicated conservative management.

Pathology results

The surgical samples were studied by pathologist team at the hospital and the diagnosis was reflected in a pathology report.

Table 1: Management protocol for adnexal masses according to GI-RADS classification and hormonal status

Ultrasound image	Size (cm)	Follow-up	Surgery (cm)
GI-RADS1			
Normal	-	No	No
GI-RADS2			
Functional	> 5	6w/3m/6m/1y	According to symptoms
GI-RADS3			
Premenopausal			
• Teratoma	3-4		>4
• Endometrioma	3-5	6w/3m/6m/1y	>5
• Simple cyst	>3		>10
Postmenopausal			
• Teratoma	<3		>3
• Endometrioma	<3	6w/3m/6m/1y	>3
• Simple cyst	>2.2		>10
GI-RADS4			
1-2 findings suggestive of malignancy	<3 premenopausal	6w/3m/6m/1y	>3
GI-RADS5			
>3 findings suggestive of malignancy			All cyst

Statistical Analysis

Categorical variables were compared using the chi-square test and quantitative variables (tumor volumes) were compared using the Mann–Whitney U-test. We calculated the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) of the GI-RADS system for identifying adnexal masses at high risk of malignancy, considering GI-RADS 2 and 3 as low risk and GI-RADS 4 and 5 as high risk. The gold standard was histologic diagnosis (benign or malignant) or spontaneous resolution of the cyst during follow-up (benign).

Categorical variables are expressed as rates and measurable variables are expressed as mean (standard deviation) or median (interquartile range).

We calculated the ROC curves: The optimal cutoff point was estimated by the point that maximizes the sum of specificity and sensitivity. All statistical analyses were performed with the use of SPSS software (version 17.0), and all reported probability values were 2-sided. We assumed significance at the 5% level ($P<0.05$).

Results

Patients

A total of 154 women were studied, with a mean (SD) age of 44.3 (14.3), 25.3% of whom had reached menopause status.

GI-RADS

The results of pelvic ultrasononography are described in Table 2 which reveals that half of the cases were classified as GI-RADS 3, the most frequent mass being endometrioma. 24% of the cases presented risk or high risk of malignancy (GI-RADS 4 and GI-RADS 5).

Solid areas (12.3%), thick septations (11.7%) and vascularization as evidenced on

Doppler sonography (13%) were the most frequent malignancy findings.

TABLE 2. Sonographic characteristics

Clinical Outcomes

Of the 154 patients included in our study, one did not undergo follow-up.

The monitoring and therapeutic approach according to the protocol is showed in Figure 1. After the first phase of the follow up study of the adnexal mass, the decision to perform surgery without further testing was taken in 3.9% of the cases. On the first follow-up visit, 14.9% had no pathological images on ultrasound, falling to 9.6% after 6 months.

Twenty-four patients with stable ultrasound images (first and second follow-up visit) underwent surgical treatment. Adnexal masses were removed for different causes: persistent masses changed classification from GI-RADS 2 to 3 or because of associated symptoms such as pain, sensation of weightiness. Surgery was performed in 33.1% of the adnexal masses studied. In 2 patients, the GI-RADS did not correctly discriminate between benignity and malignancy, since the adnexal image was characterized as GI- RADS 2 (being a sarcoma) and GI-RADS 3 (in the case of a serous ovarian carcinoma) and the patients were operated after 6 and 3 months respectively.

Figure 1. Monitoring and therapeutic decision of adnexal masses according to protocol.

The non-operated patients (66.9%) were younger women with a median age of 40, a circumstance that reflects a more conservative therapeutic decision due to unfulfilled reproductive wishes. The majority of these patients had a non-suspicious ultrasound image of malignancy, most frequently classified as GI-RADS 3.

With the disappearance of 21.3% of the adnexal masses during the first two follow-up visit (22 and 11 patients respectively), unnecessary surgeries were avoided.

Pathology Result

Out of 51 patients undergoing surgery, 33.3% presented with ovarian cancer; from whom 88.2% were older women with a score of 4-5 in GI-RADS index. The median time from diagnosis of surgery was 9 months for benign masses and 1.5 months for malignant masses. Five patients with confirmed malignancy (2 cases of ovary, 2 borderline, 1 sarcoma) underwent surgery after 6 months of follow-up.

Table 2: Sonographic characteristics

Sonographic characteristics	**N (%)**
Size**	Size**
GI-RADS	
- 2	38 (24.7)
- 3	79 (51.3)
- 4	25 (16.2)
- 5	12 (7.8)
Diferents GI-RADS 3	
- Endometrioma	36 (45.6)
- Teratoma	14 (17.7)
- Simple cyst	29 (36.7)
Malignancy findings	
- Solid areas	19 (12.3)
- Ascites	5 (3.2)
- Tinck septations	18 (11.7)
- Thinck papillary projections	11 (7.1)
- Vascularization on color or power Doppler	20 (13)
Sonographic changes	
- 1st follow-up (6 weeks-3 months) o Persistence	120 (81.9)
o Spontaneus resolution	22 (14.8)
o Change in adnexal mass	4 (2.7)
- 2nd follow-up (6 months)	
o Persistence	77 (67.8)
o Spontaneus resolution	11 (9.6)
o Change in adnexal mass	25 (21.7)

** Data expressed in cms as median values (interquartile range, RIQ)

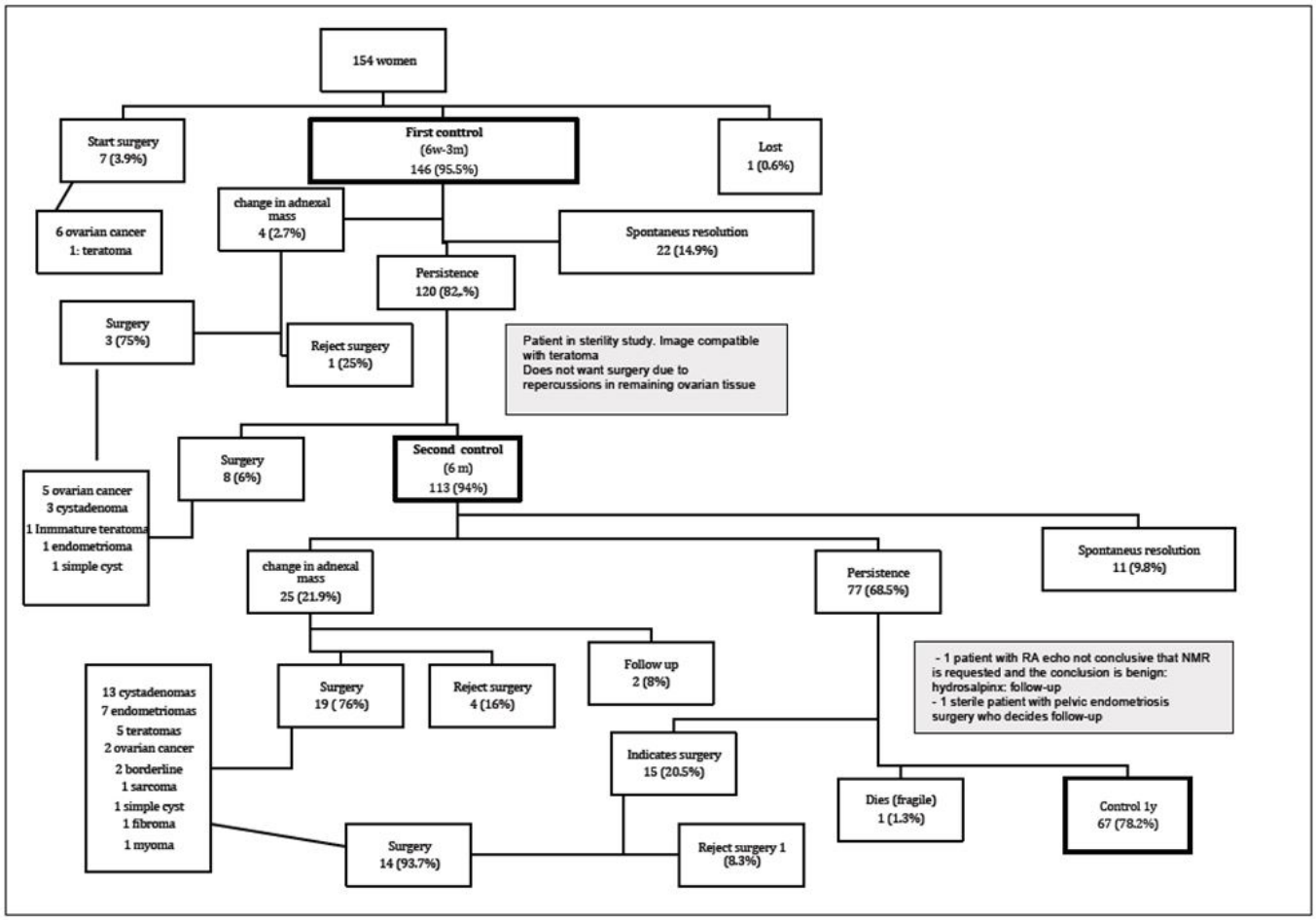

Figure 1: Monitoring and therapeutic decision of adnexal masses according

The case with the greatest delay in the diagnosis (22 months after the first ultrasound scan) was an endometrial sarcoma, a histological finding that was reached after the indicated surgery due to a discrepancy between radiological tests (MRI and CT), which were inconclusive.

Table 3 shows the histologic results of the surgeries performed

Table 3. Histologic results

The tumor marker HE4 was positive in 13 patients (8.4%), Ca125 was positive in 16 (15.5%) and Ca 19.9 in 31 (20.7%). The remaining markers (CEA, BHCG and AFP) were positive in only 3, 1 and 4 cases respectively. From 13 patients with positiveHE4, 4 did not undergo surgical intervention, one due to comorbidity (fragility), despite a high suspicion of malignancy. The other 3 patients did not develop cancer during 6-month follow-up.

All the patients operated on with elevation of the HE4 tumor marker (9 women), had a diagnosis of cancer except for one case of cystadenoma; a false-positive result was obtained in a patient with chronic renal failure and high creatinine levels (Cr: 5.97 mg/dl). Out of 17 malignant neoplasms, 8 patients (47.1%) had positive HE4.

In case of Ca125, only 4 cancer histological had got this tumor marker positive, in 12 cases the result was a false positive

Statistical analysis

When comparing the ultrasonographic characteristics, tumor markers and hormonal status among patients with and without surgical intervention, we observed that the patients who underwent surgery were older, postmenopausal, with larger tumor size, greater HE4 positivity and had a higher GI-RADS [4-5] score, these differences being statistically significant ($p < 0.05$). No differences were found in the Ca125 marker.

Table 4. Comparison of study groups: surgical vs no surgical intervention.

Table 5 contains the results obtained by studying the sensitivity (S) for both the GI- RADS classification and tumor markers according to age.

Table 3: Histologic results

Histologic results	**N (%)**
- Simple cyst	2 (3.9)
- Teratoma	6 (11.6)
- Immature teratoma	1(2)
- Endometrioma	8 (15.7)
- Cystadenoma	16 (31,4)
- Carcinoma	12 (23.5)
- Borderline	2 (3.9)
- Dysgerminoma	1 (2)
- Myoma	1(2)
- Fibroma	1(2)
- Sarcoma	1 (2)
Carcinomas:	
- Serous	8 (66.7)
- Endometrioid	3 (25)
- Mucinous	1 (8.3)
Diferentation grade:	
- Grade 1	2 (15.4)
- Grade 2	4 (30.8)
- Grado 3	7 (53.8)

Table 4: Comparison of study groups: surgical vs no surgical intervention

Variable	Surgery N (%)	No surgery N (%)	p
Age*	48.1 (17.1)	41.6 (12.1)	0.017
Menopausal	21 (41.2)	18 (17.5)	0.001
Size(cm)**	5.9 (3.9)	4.2 (1.7)	<0.0001
HE4 negative	42 (82.4)	99 (96.1)	0.010
Ca125	32 (78)	55 (88.7)	0.144
GI-RADS			
- 2	5 (9.8)	33 (32)	<0.0001
- 3	21 (41.2)	58 (56.3)	
- 4	14 (27.5)	11 (10.7)	
- 5	11 (21.6)	1 (1)	

D* Data expressed as mean (SD) ** Data expressed as median (RIQ)

Table 5: Calculation of Sensitivity (S), Specificity (E), VPP and VPN of tumor and ultrasound markers

	Sensitivity (95%CI) %	Specificity (95%CI) %	VPP (95%CI) %	VPN (95%CI) %
HE4 GLOBAL ROC 76.6%				
- PC 70	70.6 (46-95.2)	88.3 (82.6-94.1)	42.9 (22.7-63)	96 (92.2-99.8)
- **PC 82**	**70.6 (46-95.2)**	**92 (87.1-96.9)**	**52.2 (29.6-74.8)**	**96.2 (92.5-99.8)**
- PC 100	58.8 (32.5-85.2)	95.6 (91.8-99.4)	62.5 (35.6-89.3)	94,9 (90,9-98,9)
- PC 130	47.1 (20.4-73.7)	96.3 (92.8-99.9)	61.5 (31.2-91.8)	93.6 (89.2-98)
HE4 PREMENOPAUSAL ROC 66.1%				
- PC 70	60 (7,1-100)	82.7 (87.4-98)	27.3 (0-58.1)	98.1 (95-100)
- **PC 82**	**60 (7.1-100)**	**94.5 (89.8-99.2)**	**33.3 (0-69.7)**	**98.1 (95-100)**
- PC 100	40 (0-92,9)	97.3 (93.8-100)	40 (0-92.9)	97.3 (93.8-100)
- PC 130	40 (0-92,9)	98.2 (95.2-100)	50 (0-100)	97.3 (93.8-100)
HE4 POSMENOPAUSAL ROC 77.2%				
- PC 70	75 (46.3-100)	70.4 (51.3-89.5)	52.9 (26.3-79.6)	86.4 (69.7-100)
- **PC 82**	**75 (46.3- 100)**	**81.5 (65-98)**	**64.3 (35,6-93)**	**88 (73.3-100)**
- PC 100	66.7 (35.8-97.5)	88.9 (75.2-100)	72.7 (41.9-100)	85.7 (71-100)
- PC 130	50 (17.5-82.5)	88.9 (75.2-100)	66.7 (30.3-100)	80 (64-96)
Ca125	26.7 (0.9-52.4)	84.1 (75.9-92.3)	22.2 (0.2-44.2)	87.1 (79.3-94.8)
GIRADS - Global	88.2 (70-100)	83.9 (22.4-90.4)	40,5 (23.4-57.7)	98.3 (95.5-100)
- Premen	100 (90-100)	85.4 (78.4-92.5)	23,8 (3.2-44.4)	100 (99.5-100)
- Posmen	83.3 (58.1-100)	77.8 (60.2-95.3)	62.5 (35.6-89.3)	91.3 (77.6-100)

We obtained a global sensitivity of 88,2% with a specificity (SP) of 83,9%, but in pre- menopausal women the S and SP were 100% and 85,4% respectively. In postmenopausal women we obtained worse results with a S of 83,3% and SP of 77,8%. The sensitivity and specificity of biomarker HE-4 was 70,6% and 92 % respectively. The overall sensitivity obtained for HE4 was 58.8% and for Ca 125 was 26,7%.

Different cut-off points (CP) were calculated for HE4, with the level of 82 pmol/L being the most optimal. When analyzing the HE4 marker according to hormonal status, this tumor marker exhibited better performance in postmenopausal women, although the most appropriate cut-off point was the same for both subgroups. On the other hand, in the study of GI-RADS, we observed a difference of sensitivity according to hormonal state, which raises to 100% in premenopausal women.

Table 5 Calculation of Sensitivity (S), Specificity (E), VPP and VPN of tumor and ultrasound markers.

Discussion

Adnexal masses are found very often in routine gynecology practice. Correct handling of this entity supported by a protocol is highly important.

Our study analyzes the results obtained by applying the adnexal mass protocol in our hospital. This protocol is based on the GI-RADS method, hormonal status and the result in HE4 tumor-marker assay. We have not found any similar protocols in the literature. Based on our results, standardized management of adnexal masses based on the GI- RADS method (Figure 1) is found to be a valid approach.

In most ovarian cancers, suspicion of malignancy came from the findings of the first and/or second ultrasound assessment, with diagnosis taking place later in the case of more rare tumors such as the borderline subtype or uterine sarcoma. In these cases, particularly sarcoma, early detection is very difficult. Two of the cases of carcinoma (serous and endometrioid) in which surgery was performed 6 months after the first ultrasound

scan were initially cataloged as GI-RADS 3 and 4, respectively, and the tumor markers were negative. These two are exceptional cases in which standardization fails to detect malignancy.

In 33 patients, the adnexal mass observed in the first ultrasound scan disappeared during follow-up. Thus, the watchful waiting approach indicated in our protocol has an obvious benefit, avoiding the risks derived from overtreatment which involve surgery and its subsequent effects on fertility and risk of menopause.

Most of the cancers that underwent surgery after 6 months were re-classified with a higher GI-RADS score due to the increased complexity evidenced in adnexal image.

Our results reflect an overall GI-RADS sensitivity of 88.2% (100% in premenopausal women) and a specificity of 83.9%. Reviewing the most updated scientific literature there are only two studies that analyze the diagnostic capacity of the GI-RADS method in the adnexal masses, that of Amor, *et al.* [5] (which reflects a sensitivity of 99.1% and a specificity of 85.7%) and the article by Zhan [8] (sensitivity 96.4% and specificity 84.3%). Both articles conclude that GI-RADS classification performed well in the diagnosis of malignant adnexal masses.

Within the variables included in our protocol, GI-RADS classification was the most decisive for management adnexal mass. The differences found between our results and those appearing in the literature are likely due to the experience of the sonographer performing the characterization. This is considered the main limiting factor of our study.

Although the HE4 marker is a tool that supports diagnosis, in our experience it is less useful for therapy. We obtained a 47.1% sensitivity and a specificity of 96.3%. The most important advantage of this marker is that it is not altered in physiological situations such as the menstrual period. However, special care must be taken when interpreting this value in patients with renal failure. The study by Escudero et al. (9) found that greater levels than 1.3 mg/dL in serum creatinine increased the HE4 concentration. This could explain our false positive of HE4 in a patient with renal insufficiency and creatinine above 5mg/dl who was awaiting kidney transplantation.

Another factor that requires a detailed analysis is the decision of which is the most discriminating point or cut-off value (CP) of the HE4 marker. The CP 150 pmol/L established in 2008 and used in our study showed low figures of sensitivity and specificity. In an attempt to find the most optimal cut-off point and analyzing the s of 150, 130, 100, 82 and 70 pmol/L, the best CP was 82 pmol/L (70.6% sensitivity and 92% specificity). In the study published by Moore et al. (10), they used a CP of 70 pmol/L, a value that caused a loss of specificity which was 88.3%. In our patients, CP 130 was used to improve our diagnostic ability, which has been modified to 100 pmol/L.

On the other hand, the sensitivity of HE4 found in posmenopausal patients was higher (75% sensitivity 81.5% specificity) thus making this a better diagnosis tool in this group.

There are many diagnostic algorithms in the scientific literature (ROMA, CPH-I, RMI, IOTA), though none of them have demonstrated superiority for the management of adnexal masses and have complex scoring systesm. In the study by Adriana Yoshida [11], the author uses the ROMA (Risk of Ovarian Malignancy Algorihm) and the CPH- I (Copenhagen Index) with a sensitivity of 70%, which are lower than ours. The algorithm developed by Sarikapan Wilailak [12] produced the same conclusions as in our study, we observed that HE4 is a better predictor of malignancy than Ca125. In our analysis, the Ca125 marker does not provide additional information as a 26.7% sensitivity was very low, and specificity was 84.1%. The Sarikapan algorithm established a malignancy risk score based on HE4, hormonal status and ultrasound findings (with five features analyzed: multiloculated, solid nodule, bilaterally, ascites and peritoneal metastases). This algorithm had proved superior to the RMI (Risk of Malignancy Index) and ROMA since it obtains better results in sensitivity (77.2%) but not in specificity (86%), similar to our results. In the original study by Timmerman, *et al.* [13] with the "simple ultrasound-based rules" used in IOTA study, the authors obtained a sensitivity of 93% and a specificity of 90%. However, in order to correctly perform this ultrasound analysis, a specific outpatient visit is needed in order to collect all the items; this method is not reproducible within our "all-in-one" clinical-radiology outpatient system. The GI-RADS reporting system is easier to implement than the IOTA program in a first medical visit by general practitioners.

Moore, *et al.* [14] compared RMI and ROMA concluding that ROMA is a better diagnostic algorithm because, although both have a specificity of 75%, the sensitivity of ROMA was significantly better than that of the RMI (94.3% to 84.6%), a conclusion we cannot reach in this study because of the use of ultrasound, resonance and TC scan imaging, which are hardly comparable.

According to Frederick R. Ueland [15] their results with OVA1 revealed a sensitivity of 94% but an unacceptable low specificity of 54%.

There were some limitations in our study: namely being a retrospective study with a small cohort from only one hospital, doctors who do ultrasound are experts with years of experience.

As a conclusion, the protocol of action used in our study, based on the GI-RADS method, hormonal status and HE4, facilitates the indication of successful therapeutic measures without overdiagnosing or overtreating patients with benign or functional masses.

References

1. Siegel RL, Miller KD, Jemal A (2018) Cancer statistics, 2018. CA: A Cancer J Clin 68: 7–30.

2. del Campo JM (2020) Cáncer de ovario – SEOM.

3. Solnik MJ, Alexander C (2012) Ovarian incidentaloma. Best Practice & Research Clinical Endocrinology & Metabolism 26: 105–16.

4. Froyman W, Landolfo C, De Cock B, Wynants L, Sladkevicius P, et al. (2019) Risk of complications in patients with conservatively managed ovarian tumours (IOTA5): a 2-year interim analysis of a multicentre, prospective, cohort study. The Lancet Oncology 20: 448–58.

5. Amor F, Alcázar JL, Vaccaro H, León M, Iturra A (2011) GI-RADS reporting system for ultrasound evaluation of adnexal masses in clinical practice: a prospective multicenter study. Ultrasound Obstet Gynecol 38: 450–5.

6. Kleinert S, Horton R (2017) From universal health coverage to right care for health. The Lancet 390: 101–2.

7. Diagnostic evaluation of adnexal masses Healthcare protocols of the Spanish Society of Gynecology and Obstetrics 2016.

8. Zhang T, Li F, Liu J, Zhang S (2017) Diagnostic performance of the Gynecology Imaging Reporting and Data System for malignant adnexal masses. Int J Gynaecol Obstet 137: 325-31.

9. Escudero JM, Auge JM, Filella X, Torne A, Pahisa J, et al. (2011) Comparison of Serum Human Epididymis Protein 4 with Cancer Antigen 125 as a Tumor Marker in Patients with Malignant and Nonmalignant Diseases. Clinical Chemistry 57: 1534–44.

10. Moore RG, Brown AK, Miller MC, Skates S, Allard WJ, et al. (2008) The use of multiple novel tumor biomarkers for the detection of ovarian carcinoma in patients with a pelvic mass. Gynecologic Oncology 108: 402–8.

11. Yoshida A, Derchain SF, Pitta DR, De Angelo Andrade LAL, Sarian LO (2016) Comparing the Copenhagen Index (CPH-I) and Risk of Ovarian Malignancy Algorithm (ROMA): Two equivalent ways to differentiate malignant from benign ovarian tumors before surgery? Gynecologic Oncology 140: 481–5.

12. Wilailak S, Chan KK, Chen C-A, Nam J-H, Ochiai K, Aw T-C, et al. Distinguishing benign from malignant pelvic mass utilizing an algorithm with HE4, menopausal status, and ultrasound findings. J Gynecol Oncol. 2015;26(1):46.

13. Timmerman D, Testa AC, Bourne T, Ameye L, Jurkovic D, Van Holsbeke C, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. Ultrasound Obstet Gynecol 31: 681–90.

14. Moore RG, Jabre-Raughley M, Brown AK, Robison KM, Miller MC, et al. (2010) Comparison of a novel multiple marker assay vs the Risk of Malignancy Index for the prediction of epithelial ovarian cancer in patients with a pelvic mass. Ame J Obstetrics Gynecol 203: 228.e1-228.e6.

15. Ueland F (2017) A Perspective on Ovarian Cancer Biomarkers: Past, Present and Yet- To-Come. Diagnostics 7: 14.