Can be Considered the CA-125 and Neutrophil-to-lymphocyte Ratio Values as a Diagnostic Value in Ovarian Endometriosis?

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In Romania it is estimated that there are half a million patients with endometriosis. The main symptoms are pain (70% of patients with chronic pelvic pain have endometriosis) and infertility (50% of infertile patients have endometriosis). It is difficult to make an accurate diagnosis. Numerous studies show a 7-10-year delay in diagnosis in women in developing countries. 47% of patients should be seen by more than 5 physicians over time until the diagnosis is established. The treatment for endometriosis is the surgical procedure and it is most often performed laparoscopically. The present study was carried in the Obstetrics and Gynecology Departments of the Pius Brinzeu Emergency Clinical Hospital Timisoara. We have included in this study patients who were hospitalized between 2013 and 2017. We have 142 patients who qualified for this study. All the patients had made the same medical tests: we collected information about their age, the neutrophil, lymphocyte and CA125 values, the position of the cyst and the cyst dimension. The aim of this study is to find if there is any association between the CA-125 markers (coelomic epithelial antigen) and the neutrophil-to-lymphocyte ratio in patients who were diagnosed with ovarian endometriosis by transvaginal ultrasound. In all cases the patients underwent laparoscopic surgery. After performing a correlation and regression analysis we obtained that we have a positive strong significant association between the CA 125 values and the ratio values ($r=0.94$; $R^2=0.88$; $p<0.001$) . After the surgical excision of endometriosis, CA-125 can be used to monitor the evolution of endometriosis outbreaks, especially when there is a recurring severe pain.

Keywords: ovarian endometriosis, CA125, neutrophil-to-lymphocyte ratio, transvaginal ultrasound, laparoscopy

The growing number of young women at the age of procreation diagnosed with ovarian endometriosis underlines the importance of its in-depth research, involving areas such as gynecology, immunology, pathological anatomy and endocrinology. The classification of endometriosis is based on intraoperative recording and quantification of the lesions, considering the differentiation between deep infiltrating lesions. At present, the revised classification of the American Society for Reproductive Medicine (ASRM) is universally accepted [1-3]. An ovarian endometriosis is a cystic mass that originates from ectopic endometrial tissue in the ovary. Contains a thick, brown, tar-like fluid, which can be called *chocolate cyst*. Endometriomas are often densely adherent to surrounding structures, such as the peritoneum, fallopian tubes, and bowel. Nuclear magnetic resonance imaging has similar sensitivity and specificity to ultrasound diagnosis of deep uterine endometriosis (85 and 88%), vaginal endometriosis (77 and 70%) and colorectal endometriosis (88% and 92%) [4-7]. NICE (National Institute for Health and Care Excellence) Issues Guidelines does not recommend the use of the CA 125 test to diagnose endometriosis because endometriosis may be present despite the normal levels of CA 125. The gold standard for definitive endometriosis diagnosis remains laparoscopy. In comparison with laparoscopy, transvaginal ultrasound was a valuable tool in detection of ovarian endometriosis in our study group. In case of chronic pelvic pain, pelvic ultrasound was the way to detect other causes of pelvic pain, such as adenomyosis. Transvaginal ultrasound has the greatest sensitivity and specificity in identifying ovarian endometriomas. Classical ultrasound findings show an unilocular cyst with homogeneous low-level echogenicity (ground glass echogenicity) of the cyst fluid and poor blood flow. The levels of CA-125 in the serum can be elevated in endometriosis. However, measurement of serum level of CA-125 is not considered to be a diagnostic tool.

Experimental part

Material and method

For this study we took in observation the patients hospitalized in the Obstetrics and Gynecology Departments

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of the Pius Brinzeu Emergency Clinical Hospital Timi°oara between 2013 and 2017 who were diagnosed with ovarian endometriosis by transvaginal ultrasound and underwent laparoscopic surgery. We have 142 female who qualified for this study; all the patients had made the same medical tests. The aim of this study is to find if there is any association between the CA-125 markers and the neutrophil-to-lymphocyte ratio. The database has made using Microsoft Excel program. For the statistical analysis we used the SPSS software and for the graphics and tables we used the Microsoft Excel program.

Results and discussions

In this study we have 142 female with the age between 20 and 45 years. Beside the age we have collected information about some medical tests such as: the neutrophil, lymphocyte and CA125 values, the cyst position and the cyst dimension.

Laparoscopy remains the only way to diagnose endometriosis with certainty. In terms of laboratory there is currently no test available to certify the diagnosis of endometriosis. CA125 - coelomic epithelial antigen - has been highlighted as significantly increased in patients with moderate / severe endometriosis[8-10].

In the first part of our analysis we made some descriptive statistics for the numerical data and frequencies tables and graphics for the ordinal and qualitative variables (Table 1-3, fig. 1,2).

We calculated a ratio between the neutrophil and lymphocyte values and we compared this values with the CA 125 values because the aim of this study is to find if there is any association between the CA-125 and the ratio

Variables → / Descriptive statistics ↓	*Age*	*Neutrophils*	*Lymphocytes*	*Ratio*	*CA125*
Mean	32.53	24.41	9.17	6.18	80.26
Standard Error	0.59	2.52	1.15	0.98	4.05
Median	31.5	4.84	2.4	1.98	76.25
Mode	35	4.62	1.79	1.54	51.5
Standard Deviation	7.07	30.05	13.72	11.72	48.23
Sample Variance	49.98	902.95	188.12	137.40	2326.48
Kurtosis	-1.08	-0.84	0.84	4.43	2.52
Skewness	0.16	0.95	1.59	2.50	0.95
Range	25	92.65	46.38	42.26	290.1
Minimum	20	0.45	0.32	0.8	0.9
Maximum	45	93.1	46.7	43.06	291
Sum	4619	3466.84	1301.7	877.38	11397.1
Count	142	142	142	142	142

Table 1
THE DESCRIPTIVE STATISTICS FOR THE NUMERICAL DATA CONTAINED IN OUR STUDY.

Cyst Dimension	Number of patients	%
Above 4 cm	7	4.93%
Between 4 and 6	8	5.63%
Between 6 and 8	91	64.08%
Between 8 and 10	25	17.61%
Over 10 cm	11	7.75%
Total	142	100.00%

Table 2
THE FREQUENCY TABLE FOR THE CYST DIMENSION

Table 3
THE FREQUENCY TABLE FOR THE CYST POSITION

Cyst Position	Number of patients	%
Bilateral	9	6.34%
Left	82	57.75%
Right	51	35.92%
Total	142	100%

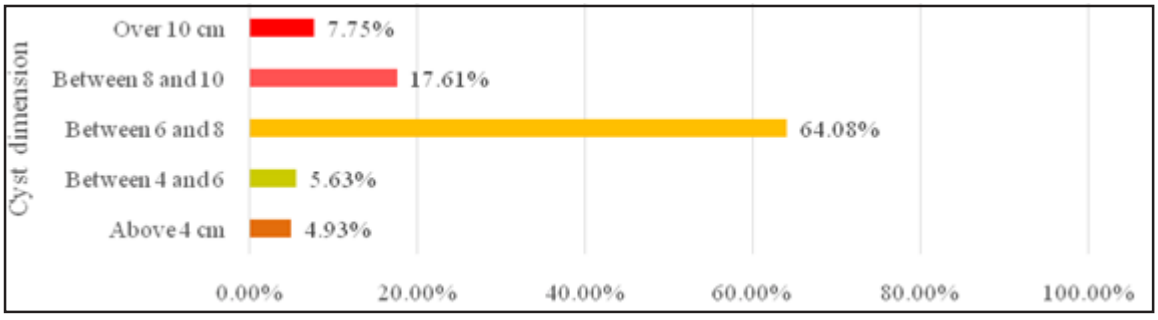

Fig. 1. The distribution for the cyst dimension

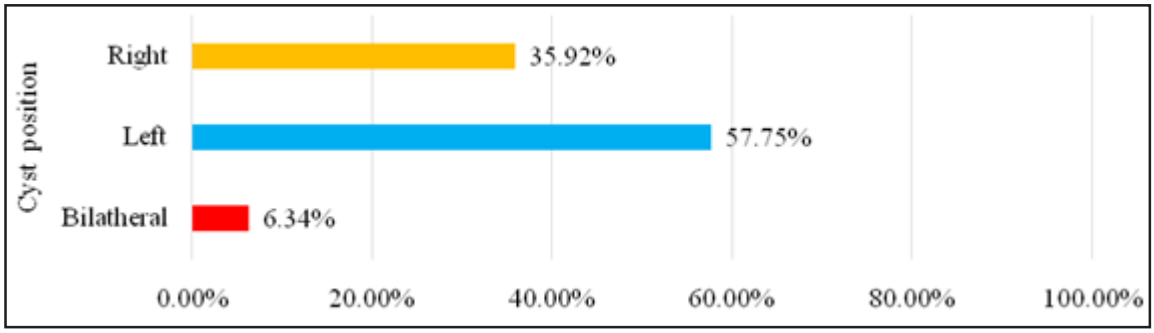

Fig. 2. The distribution for the cyst position

values. In other words we want to see if we can use the CA 125 values as a predictor for the endometrioses dynamics. So, for this we plotted the histograms for the main variables (fig. 3, 4) and we applied a correlation and regression analysis in order to determine the strength and the signification of this association (fig. 5).

Based on the figure 5 we observed that on our data we have to different behaviors. If we consider all the patients we obtain a median positive significant correlation ($r=0.66$, $R^2=0.43$, $p<0.001$), but if we exclude the patients which ratio is above five (only 16 patients out of 142, 11.27%) we obtain a smaller sample ($N1=126$) but a much better association ($r=0.94$, $R^2=0.88$, $p<0.001$), (fig. 6). This exclusion is recommendable because of the ratio dynamics: 88.73% of patients have the ratio values between (0.8; 4.89), the rest 11.27% have the ratio values between (34.98; 43.06) and we have a gap within this interval (5; 34.97) (fig. 3).

Conclusions

There are numerous studies to confirm the sensitivity and specificity of the CA 125 marker in correlation with the lymphocyte / neutrophil ratio in patients with endometriosis diagnosed at different stages and with different localizations [11-16].

Clinical management of endometriosis requires a good understanding of the objectives of surgery because it might reduce ovarian reserve. If surgery can relieve symptoms, then the aim of the complete excision will be the absence of disease recurrence.

After applying the statistical test we can say that the CA 125 values can be considered as a guideline in the management of this disease. A high CA125 values implies as well a high value for neutrophils to the lymphocytes which can conduce as to the hypothesis that we can see a severe form of endometriosis.

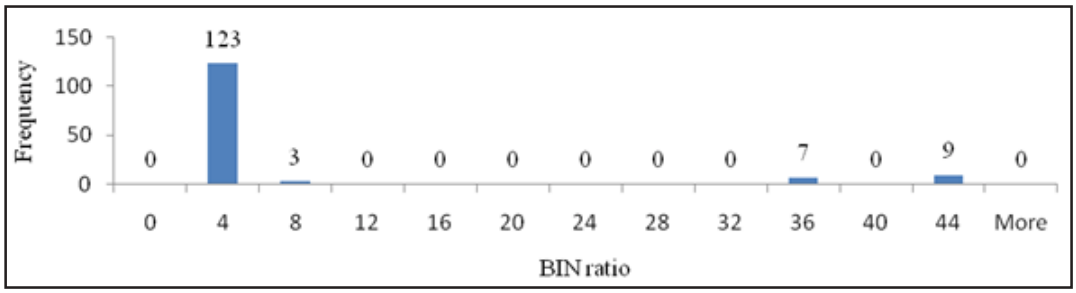

Fig. 3. The histogram for the ratio obtained by dividing the neutrophil to the lymphocyte values

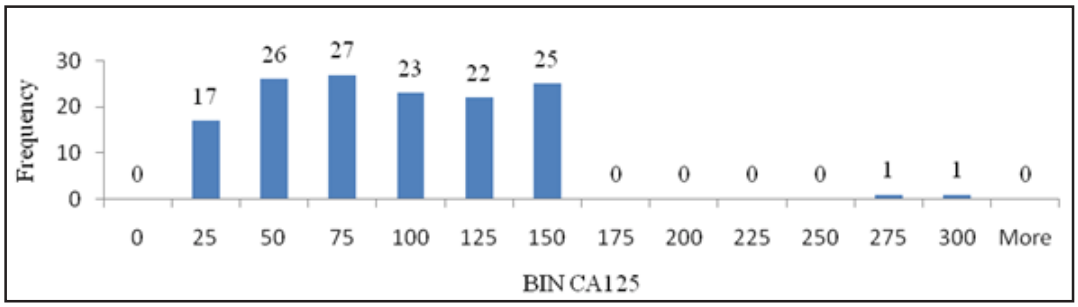

Fig. 4. The histogram for the CA 125 values

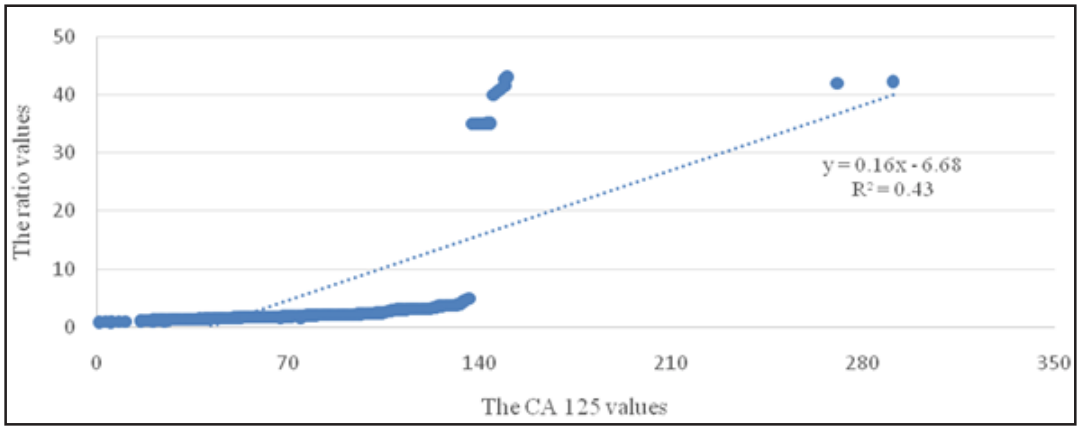

Fig. 5. The association between the CA 125 and the ratio values for the whole sample (N=142)

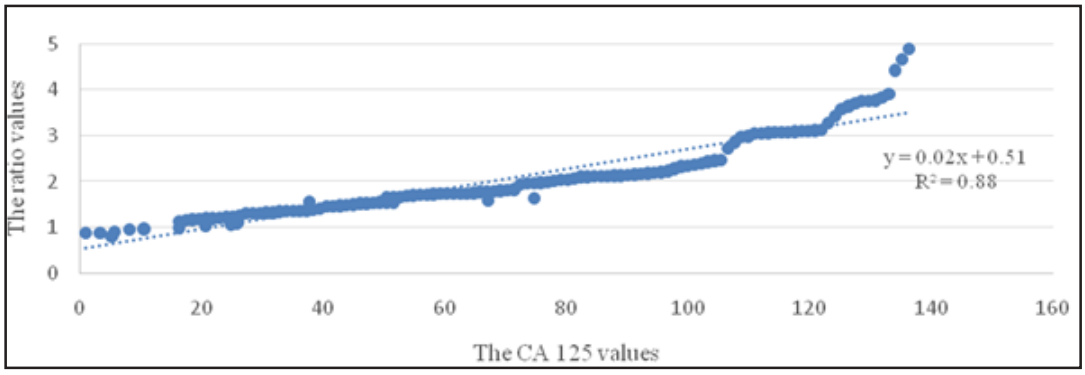

Fig. 6. The association between the CA 125 and the ratio values for the whole sample (N1=126)

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