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CORRELATION BETWEEN TUMOR SIZE AND LYMPHATIC SPREAD IN CASES OF TYPE I ENDOMETRIAL CARCINOMA

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Abstract:

Background and objectives: *In the whole world, one of the most spreading malignancy is the cancer of endometrial. This is the cancer of the genital tract in the females. The most commonly used path for spreading malignancy is the lymphatic spread. Nodes of pelvic lymph is primarily involved in it. Recently, the suggestion was that one of the risk factors for metastases of LN is the size of tumor. The purpose of the following study was to discuss the relation of size of tumor and pelvic LN metastasis in different patients. The patients experiencing careful arranging for type-1 endometrial adenocarcinoma, so as to get ready for legitimate careful methodology.*

Patients and Method: *The experiment was done on 29 people who are the patient of endometrial adenocarcinoma with type -1 in a tertiary care setup in lahore . By gathering the information from the Ultrasound, TS was calculated. This is called the largest three categories of tumor. Pathologically, tumor size was re-surveyed. To survey the connection of LN metastasis and Tumor size was the important result. The mutual relationship between tumor size and different factors for example stage, involvement of lympho-vascular space and grade, were additionally considered as optional results.*

Results: *With the help of ultrasound and other examinations of pathological, the relationship of different sizes of tumors and LN metastasis were discussed. In between the measurement of tumor sizes by ultrasound and different investigations pathologically, different agreements were there. Tumor size which is measured by ultrasounds is factually important discriminator related to metastasis of LN. The value of this is 4.5cm. The tumor size calculated by pathological information is also factually discriminator related to metastasis of LN. The value of this is 5cm.*

Conclusion: *In reports of endometrial adenocarcinoma with type-1, the comparison of tumor sizes obtained from ultrasound and investigations by pathological information was reviewed. These two methods are good for anticipating metastasis of LN with values of 4.5 and 5cm separately. The survey done with the help of ultrasound is much reliable and utilize while planning level of surgery.*

Keywords: *Endometrial cancer, Tumor size, Pelvic lymph nodes, Endometrioid adenocarcinoma, Lymphadenectomy*

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INTRODUCTION:

Globally, one of the most scattering malignancy is the disease of cancer of endometrial. This is the cancer of the genital zone in the ladies. In females, the most common reason for the death is this disease which a type of cancer. From the recent three decades, the following point is more considerable. The main reason of this disease is cancer of breast and lungs in women. This disease is the commonly occurred disease in women at fourth number 2. Mostly, this is happened in aged women who are greater than 50 years, the mean age of patients is 63 years. There are different factors of risks associated with it. There is a chance of a large amount of oestrogen in the people who have endometrial cancer. Those people show a profile of clinical indicating high value of BMI. The main cause of this disease is the increased fatness of body. The other reason of this is Glycaemic load. Some researches show that there are also some other reasons of this disease such as attained height in adults but this is limited. There is also a risk of occurring of infertility and nulliparity by this disease. In the risk of infertility, the major part is PCOS 3, 4. Various other related risk factors include the sooner occurring of menstruation, hypertension, tamoxifen and late menopause. Additionally, there are very rare case of occurring of this disease with type-2 of lynch syndrome 3. On the basis of the histopathology, cancer of endometrial is further divided into 2 groups.

Group 1: typical patients of endometroid and somehow related to oestrogen and lower level of adenocarcinomas. This can be diagnosed at an initial level and can be treated.

Group 2: endometrial disease independent of hormones and at considerable level of adenocarcinomas, serous, carcinosarcomas, and cell carcinomas.

At different chromosomal location, there are p53 mutations. There is also a relation of early spread and prognosis. The commonly occurred path for spreading disease is lymphatic spread and it is occurred three times more than the occurring of spread of blood. Malignant cells are allowed to pass through the parametrium, ovaries and vagina. Generally, this kind of diseases related to cancer includes the nodes of pelvic lymph, internal and external iliac, obturator and common iliac 5. On the basis of the biological specifications of the cancer, the patients are further divided into two sub-categories. Both groups have the disease at a high level. At that stage, surgery is essential. The people who have the disease at initial level, can be treated by the invasive approach. Endometrial carcinoma has a large number of risks related to the recurrence of the disease. These factors include extrauterine and uterine factors. Grade, histologic type, vascular invasion, cervical involvement and myometrial invasion's depth are the factors involved in the uterine group.

While involvement of adnexal, positive cytology of peritoneal, metastasis of intraperitoneal are the factor of extrauterine 7, 8, 9, 10, 11. Different studies by different authors explained the relationship of TS and metastasis of lymph node. The main benefit for utilization of TS depends on the statics for which extra sources are not required. While talking about the other factors for example grade for which there is a need of experiences pathologist. The resources for them is intensive and variable on the basis of different sections.

Objectives:

The main purpose for which the following study is conducted is to review the relationship of sizes of different tumors and metastasis of lymph node in various patients. The patients are under consideration of type-1 surgical treatment of endometrial adenocarcinoma.

Patients and Technique:

The following investigation is an imminent observational examination. From 2nd June 2016 to 1st January 2017, the direction of following study occurred. Permission was taken from the committee of ethics to conduct the examination. The study was according to the principles of the ethical committee. The committee performed experiments on the human beings.

Patient Selection and Procedures:

The selection of various cases was done from the people who are from the Jannah Hospital, Lahore. There number of total patients included was 29. Endometrial adenocarcinoma with type-1 was diagnosed in them. Total hysterectomy was also planned for them. There were also some patients from the type – 2 and type-3 who are not fit for surgical treatment. Some people were also present who have other malignant diseases and requires radiotherapy. Different results were computed from reviewing all the given data and information. Permissions in both oral form and written form were also taken. Tumor size of all the patients was explained with the help of the ultrasound which is 2D greyscale. This is the best definition of the major three directions of tumor.

The experiment of gathering the information from all the ultrasounds was done by a specialist radiologist. This was all done in 10 days. Total groups of the patients are directed to the hysterectomy also related to the bilateral salpingo-oophorectomy. These all paients are then passed though the phase of the evaluation of histopathologic. All the patients are considered in accordance with their investigations obtained from the experiments performed at Jannah Hospital Lahore 16. Patients were categorized on the basis on FIGO which is staging review in 2009. The major dimension of tumors reviewed by pathological observations 17. In the consideration of both +ive and -ive nodes, the study of lymph nodes was done which is not dependent on the number of nodes.

Outcomes:

In the patients of endometrial adenocarcinoma with type-1, to observe the connection of TS and metastasis of LN was the major outcome.

The other results are to investigate the relationship of TS with different factors included grade, involvement of space of lympho- vascular, stage.

Factual method:

For entering the gather information and data to the personal computer, the software used is SPSS. This software is used for analyzing the statistics 18. The version of given software is 21. The entered data is in the form of the numeric values. To reveal the distribution importance in various variables is done by test of normality of Kolmogorov-Smirnov. The adoption of non-parametric statistics is also included 19. Different ranges were set to arrange the data which is not normally distributed. These ranges involved max, min, and median. With the help of total percentage and frequency, the description of variable of Categorical were done.

Bu using the Mann-Whitney U test, two different non-distributed studies were compared 20. To check the relation between variables which are qualitative, the used test named as Chi-square. Correction of Monte Carlo was used where it was required 21. For quantifying the reliability of ultrasounds and sizes of pathological studies, correlation of intra-class was utilized 22, 23. Various type of graphs were used. Different ranges are set for accepting the errors. The range set for alpha error is 5.5% with a degree of 96%. The range set for beta error is 20%.

RESULTS:

By applying the criteria of inclusion, exclusion, different 29 patients were examined who have endometrial adeno-carcinoma of type-1. They all are directed to the hysterectomy. Using the system of CAP, all the patients are also observed histopathologic ally. Firstly, the data was collected and then tabulated and at the end it was analyzed. The characteristics of various patients and tumors are listed in the table 1. 60 years is the average age of the selected patients. The average size of tumor obtained from the ultrasound is up to 3.5cm.

Table 1: characteristic features of different patients and tumors

	Number	Percent
Patient age		
- Min-Max	31.0-73.0	
- Mean ± S.D.	56.76 ± 10.93	
- Median	61.0	
Tumor size from ultrasound		
- Min-Max	1.54-9.00	
- Mean ± S.D.	3.333 ± 1.78	
- Median.	3.35	
Tumor size from pathology		
- Min-Max	1.6-11	
- Mean ± S.D.	4.16 ± 3.95	
- Median.	5.0	
Grade of Tumor		
I	9	27.6
II	18	58.6
III	5	13.8
Tumor Stage		
Ia	20	65.5
Ib	7	23.1
IIIa	3	6.9
IIIb	1	4.4

LVSI		
-ve	19	56.5
+ve	11	43.5
LN metastasis		
-ve	25	83.8
+ve	6	15.2

After the evaluation of the patient on the basis of the pathologic, the average calculated size of tumor by this method is 4cm. classification of patients were done as mostly people are categorized as partially differentiated and these are 17 people. 19 patients' cases were called as at the Ia stage. In five cases, positive affection of LN was detected. 19 patients have LVSI.

Table 2 describes the significant relation of affection of LN and tumor size from U/S. This is also related to the metastasis of LN (fig. 1).

Table 2: Relationship between TS and LN metastasis

	LN Metastasis		**Value of p**
	Negative (n=24)	**Positive (n=5)**	
Size (From ultrasound)			
- Min-Max	1.60-6.50	3.650-8.00	Z(MW)=2.656
- Mean ± S.D.	3.41±1.429	5.990±1.46	p=0.0099*
- Median (IQR)	3.40	6.00	
- KS test	D=0.119, p=0.088 NS	D=0.1136 p=0.2300 NS	
Size (From pathology)			
- Min-Max	1.50-8.00	3.60-11.00	Z(MW)=2.605
- Mean ± S.D.	3.52±1.658	6.60±2.245	p=0.0011*
- Median (IQR)	3.75 (2.00-4.75) D=0.154,	5.00	
- KS test	p=0.147 NS	D=0.226 p=0.2200 NS	

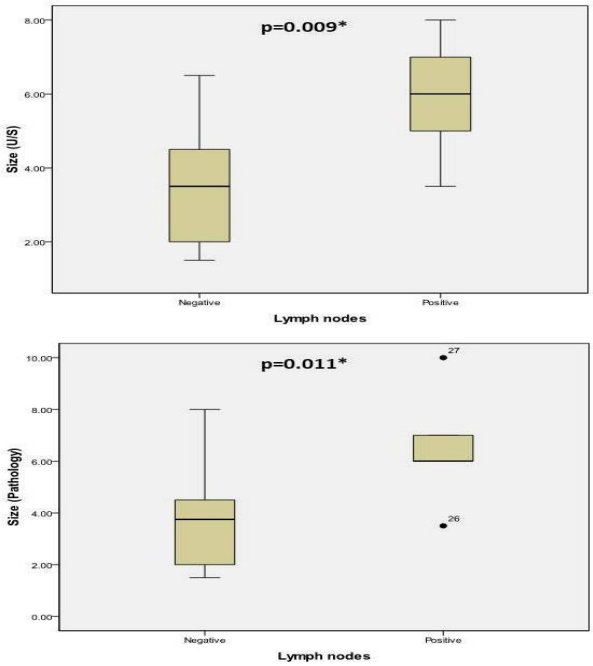

Fig 1: Relationship between TS and LN metastasis

By using two different methods, obtained TS were analyzed. The results indicate that there is an agreement in between TS of U/S and from pathologic information. The value of the intra -class relationship is 0.0976 (fig. 2).

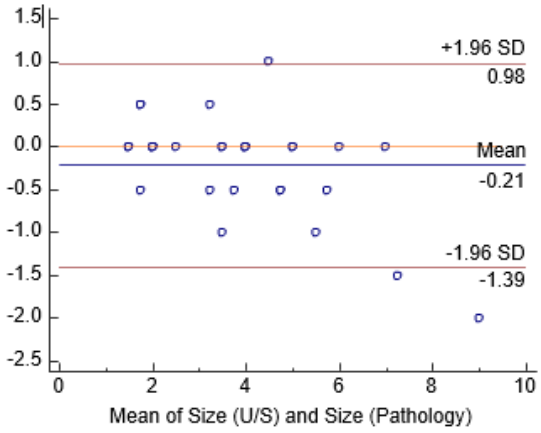

Fig 2: agreement in between TS of U/S and from pathologic information

Diagnostic test for accuracy statistics:

With the region covered by the ROC curve, it was clear that the tumor size measured from the ultrasounds is the important discriminator of metastasis of LN. By using Youden index for the purpose of diagnostic, the value of the level is greater than 4.5 cm. the value of sensitivity and specificity is 80% and 79% respectively. The value of positive predictive is 44% and the value of -ive predictive is 95%.

It was also clear that the tumor size measured from the pathologic information is the imperative discriminator of metastasis of LN with the area covered by the ROC curve. By means of Youden index for the persistence of diagnostic, the value of the level is greater than five cm. While the value of sensitivity and specificity is 80% and 91% respectively. The value of positive predictive is 66% and the value of negative predictive is 95%. Fig. 3 and 4 shows the difference between the two ROC curves.

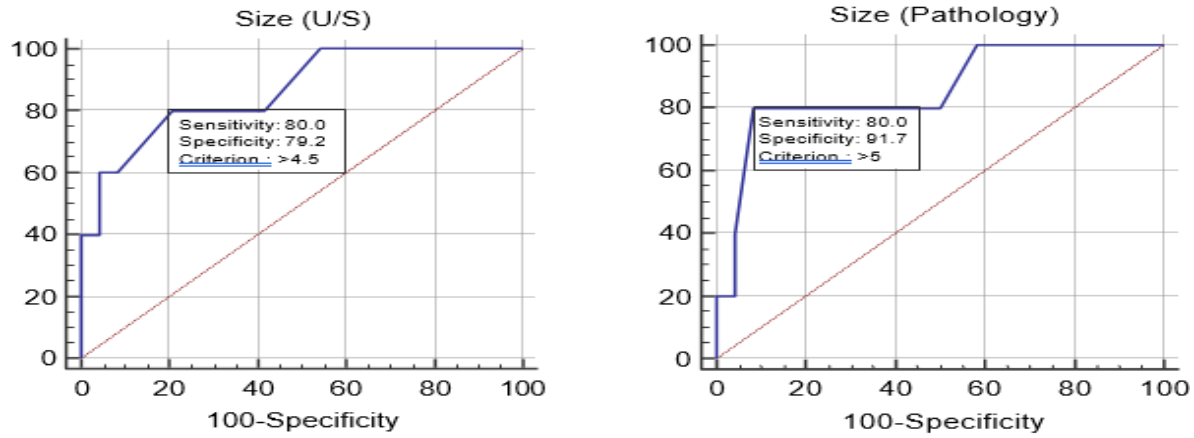

Fig. 3: Detection of LN metastasis by TS calculated from both U/S and pathology

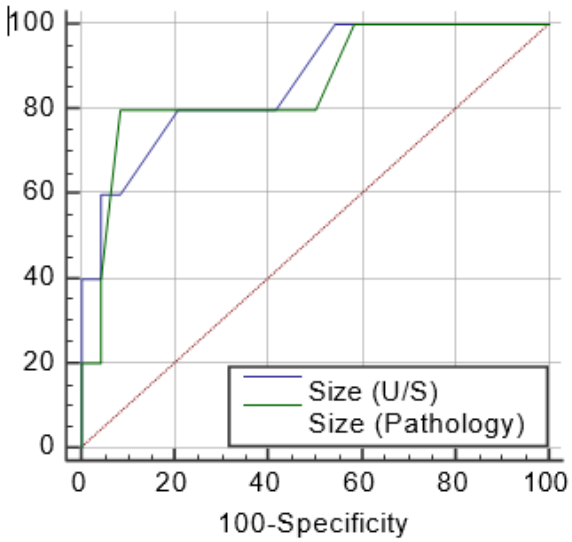

Fig. 4: Comparison of the two ROC curves to detect metastasis of LN from TS obtained from both (U/S) and pathology

DISCUSSION:

Pelvic lymphadenectomy during careful arranging for endometrial disease is as yet a questionable issue. Recent recommendations have limited lymphadenectomy to middle of the road high hazard malignancies; those with over half myometrial attack, levels specialists or assessing the conceivable term of medical procedure. The present examination is the first that uses U/S in evaluation of TS so as to relate it to LN metastasis. Not just that, we likewise identified an understanding between the two strategies in estimating TS, and in this manner, could be utilized for forecast of pelvic LN metastasis, however with an alternate cut off qualities. Thirty-four cases were essential taken a crack at the present examination, 5 cases were barred; two were arrange IV, two others had just absolute hysterectomy with reciprocal salpingo-oophorectomy without lymphadenectomy because of dreary heftiness and employable trouble. What's more, the last one - 82 years-kicked the bucket because of heart failure earlier booking for laparotomy.

Our outcomes demonstrated that TS can be used to confirm the nearness of pelvic LN metastasis, with cut off estimation of 4.5 cm for estimating TS by U/S, and of 5 cm for estimating TS by net pathology.

In 2010, ESMO rules have distributed that TS and area are to be considered in evaluation of endometrial malignancy, in spite of the fact that excluded from the FIGO staging.(1) The equivalent was distributed by the NCCN rules, 2013, they expressed that patients with arrange I endometrial disease and who are totally carefully organized are stratified by unfavorable hazard factors (for example age, positive lympho-vascular space attack, tumor size, and lower uterine fragment involvement.(29) No extra contemplations were distributed in the rules of ESMO-ESGO-ESTRO Accord Gathering on Endometrial Malignant growth in 2016.(12) and the later NCCN rules in 2017.(30)

In a past report in 1991, Lurain et al announced diminishing in the danger of lymph hub metastases and an expansion of endurance in tumors <2 cm. (31) In later investigations, other (higher) slice off qualities were accounted for to anticipate LN metastasis. One hundred forty-seven instances of endometrial carcinoma were examined by Berretta et al, they have discovered that a checked connection existed between tumor biggest breadth and nodal metastases. The normal element of tumor with nodal metastases was 6.3 cm (±3.1) and the middle was 6.5 cm. The connection coefficient was 0.03. (7) This slice off worth was near the one assessed by pathology in the present investigation (5 cm). Senol et al, have expressed that tumor measurement was seen as indicator for repeat with higher qualities than by and large accepted. (32) Likewise, Mahdi et al, announced that TS was an autonomous indicator of LN metastasis and sickness specific endurance in patients with endometrioid endometrial carcinoma terribly confined to the uterus (organize I). Tumor (5 cm) was an indicator of illness specific endurance yet no distinction in result was noted among tumor and tumor. (27)

CONCLUSION:

In the patients of the endometrial adenocarcinoma of type-1, the comparison of the survey for calculating

the tumor size from ultrasound and the review of tumor size from pathologic information is the conclusion of the article. These two methods are flexible for anticipation of the metastasis of LN with a range of 4.5 cm and 5.1 cm separately. By reviewing the literature, it is observed that the method of calculating tumor size from ultrasounds is more in use and much utilized while planning the level of treatment of surgery. This is also useful when there is pelvic lymphadenectomy required.

The limitation of the purposed examination is the minimum number of the patients selected. The suggestion for the future scope is to perform the same experiment at a large level with a lot of patients to observe. The results will be more accurate. Another recommendation for the study is to review the calculation of tumor size by a smaller volume of tumor in the place of using larger diameters.

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