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MYOINVASIVE PATTERNS OF ENDOMETROID ENDOMETRIAL CARCINOMA & ITS PATHOLOGIC SIGNIFICANT

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ABSTRACT

Introduction: Total abdominal hysterectomy with bilateral salpingo-oophorectomy is still the gold standard for treating endometrioid endometrial cancer, however lymphadenectomy (pelvic and/or para-aortic, systematic or selective) is debatable. This research aims to ascertain whether or not the MELF pattern of myometrial invasion is linked to an uptick in the occurrence of lymph node metastasis and, as a result, could be considered as an additional risk factor for endometrioid endometrial carcinomas that have progressed to stage D. **Method:** Cross sectional study of 68 females with endometrial carcinoma, the data collected from teaching laboratory in medical city, from 2020 to 2022. All cases take age of them and percentage of Myo invasion, lymph vascular involvement, lymph node metastasis, LUS invasion, cervical invasion and grades of tumor also we study the pattern of invasion**. Results:** [58.82%] of patients diagnosed as diffuse pattern of invasion, [22.06%] of patients diagnosed as MELF and [19.12%] of them diagnosed as pushing. There is significant association between Pattern of invasion and LVI, Lymph Node Metastasis, LUS invasion and grade of tumor. **Conclusion:** Most pattern of invasive of endometrium carcinoma is diffuse pattern, MELF Pattern of invasion are present with lymph node involvement, positive Lymph Node Metastasis, positive LUS invasion. Most of diffuse and MELF Pattern of invasion are on grade II.

KEYWORDS: Myoinvasive patterns, endometroid endometrial cancer, pathologic significant.

INTRODUCTION

Total abdominal hysterectomy with bilateral salpingo-oophorectomy is still the gold standard for treating endometrioid endometrial cancer, however there is some debate regarding when and if lymphadenectomy (pelvic and/or para-aortic, systematic or selective) is necessary.[1,2] Patients with stage IA [formerly International Federation of Gynecology and Obstetrics (FIGO) 1B] endometrial carcinomas, grades 1 or 2, have been the subject of a number of studies that have focused on the benefits of lymphadenectomy. Women who participated in studies including lymphadenectomy did not fare better in terms of survival compared to women who did not undergo the procedure.[3–5] Further, the likelihood of pelvic recurrences among this group of patients is observed to range from 0% to 2%, hence they are deemed to be at low risk for having positive lymph nodes.[6] Lymphadenectomy in stage IA endometrial cancer should only be done in patients with adenosquamous, serous, or clear cell carcinoma, and grade 3 tumours of any histological type, according to the guidelines of several investigators.[7] When lymphvascular tumour emboli or deep myometrial invasion are seen in the hysterectomy specimen, further pelvic radiotherapy is recommended for the patient.[8] Recently, the term "MELF" has been adopted to denote a specific form of myometrial invasion.[9] Lymph node metastases that resemble histiocytes have been associated to the microcystic, elongated, and fragmented (MELF) pattern of myometrial invasion in a limited number of patients.[10] This research aimed to identify new risk factors for endometrioid endometrial carcinomas at the advanced stage of stage d by analysing whether the MELF pattern of myometrial invasion is linked to a higher incidence of lymph node metastasis.

METHOD

Cross sectional study of 68 females with endometrial carcinoma, the data collected from teaching laboratory in medical city, from 2020 to 2022. All cases take age of them and percentage of Myo invasion, lymph vascular involvement, lymph node metastasis, LUS invasion, cervical invasion and grades of tumor also we study the pattern of invasion. SPSS 22 was used for statistical analysis, and the results were presented in terms of percentages and frequencies for categorical data and means, medians, and standard deviations for continuous data. Chi-square analysis was done to determine the degree of correlation between the variables. We accept as significant a p-value of less than or equal to 0.05.

RESULTS

In current study, 68 patients with endometrial carcinoma, mean age of patients are 60 ± 9 years. [55.9 %] of patients have more than 50% Myo invasion, [69.1%] of patients have lymph vascular involvement, [33.8%] of patients have positive lymph node metastasis, [67.6%] of patients have LUS invasion, [20.6%] of patients have cervical invasion, [67.6%] of patients classified grade II diagnosis. As show in table 1.

Table 1: Distribution of patients according to variables.

Variables		Frequency	Percentage
Myoinvasion	***<50%***	30	44.1
	>50%	38	55.9
Lymph vascular involvement	***Not identified***	21	30.9
	Present	47	69.1
Lymph node	***free***	20	29.4
Metastatic	***Not submitted***	25	36.8
	positive	23	33.8
LUS invasion	***Free***	22	32.4
	Present	46	67.6
Cervical invasion	***Free***	54	79.4
	Present	14	20.6
Grade	***I***	14	20.6
	II	46	67.6
	III	8	11.8

As show in fig 1; [58.82%] of patients diagnosed as diffuse pattern of invasion, [22.06%] of patients diagnosed as MELF and [19.12%] of them diagnosed as pushing.

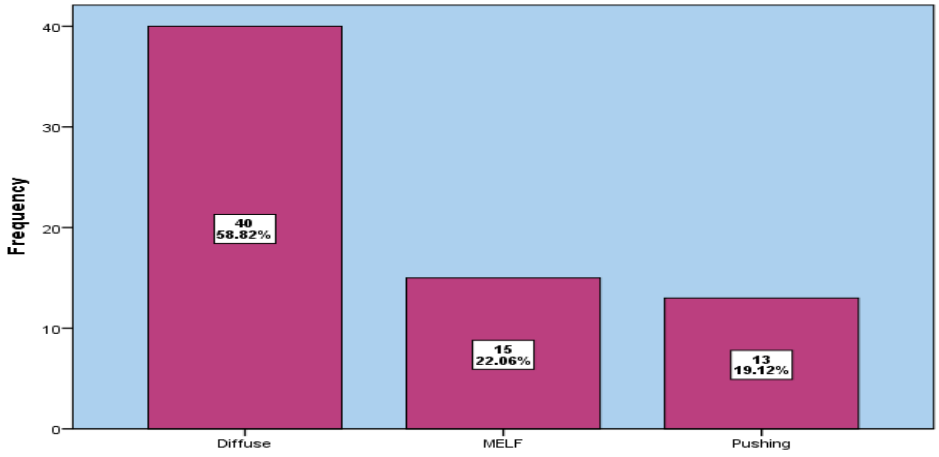


Fig 1: distribution of patients according to pattern of invasion.

There is significant association between Pattern of invasion and LVI, [100%] of patients classified as MELF Pattern of Myo invasion are present with lymph vascular involvement, and [75.2%] of patients classified as diffuse Pattern of Myo invasion are present with lymph vascular involvement.

There is significant association between Pattern of invasion and Lymph Node Metastasis, [73.3%] of patients classified as MELF Pattern of invasion are positive Lymph Node Metastasis, and [30%] of patients classified as diffuse Pattern of invasion are positive Lymph Node Metastasis.

There is significant association between Pattern of invasion and **LUS invasion**, [100%] of patients classified as MELF Pattern of invasion are positive **LUS invasion**, and [67.5%] of patients classified as diffuse Pattern of invasion are positive **LUS invasion**.

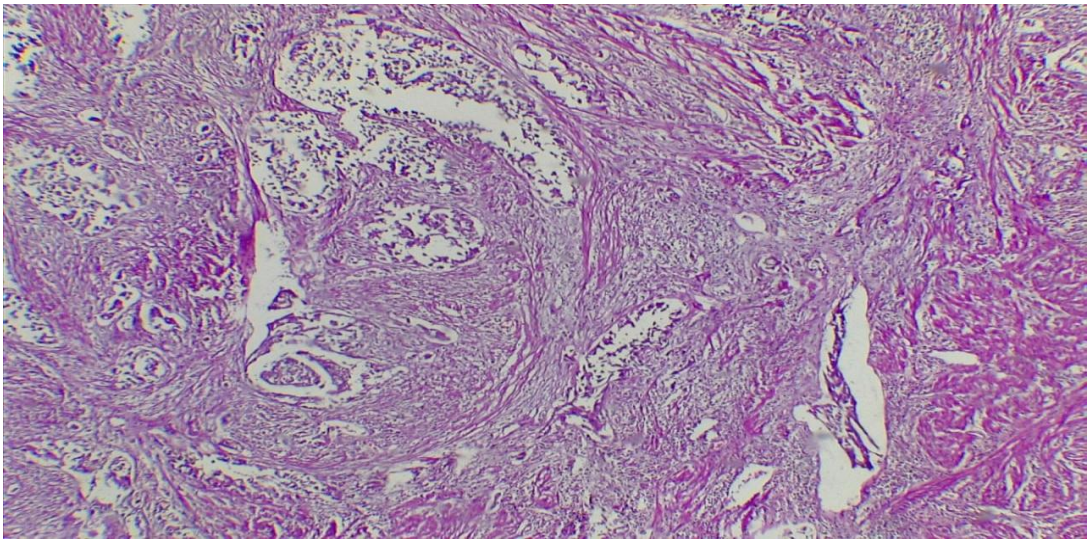
There is significant association between Pattern of invasion and **grade**, [72.5%] of patients classified as diffuse Pattern of invasion are on grade II, and [20 %] of patients classified as diffuse Pattern of invasion are positive grade I, while [7.5%] of them classified as diffuse Pattern of invasion are positive grade III.

No significant association between Pattern of invasion and (Percentage of invasion, cervical invasion).

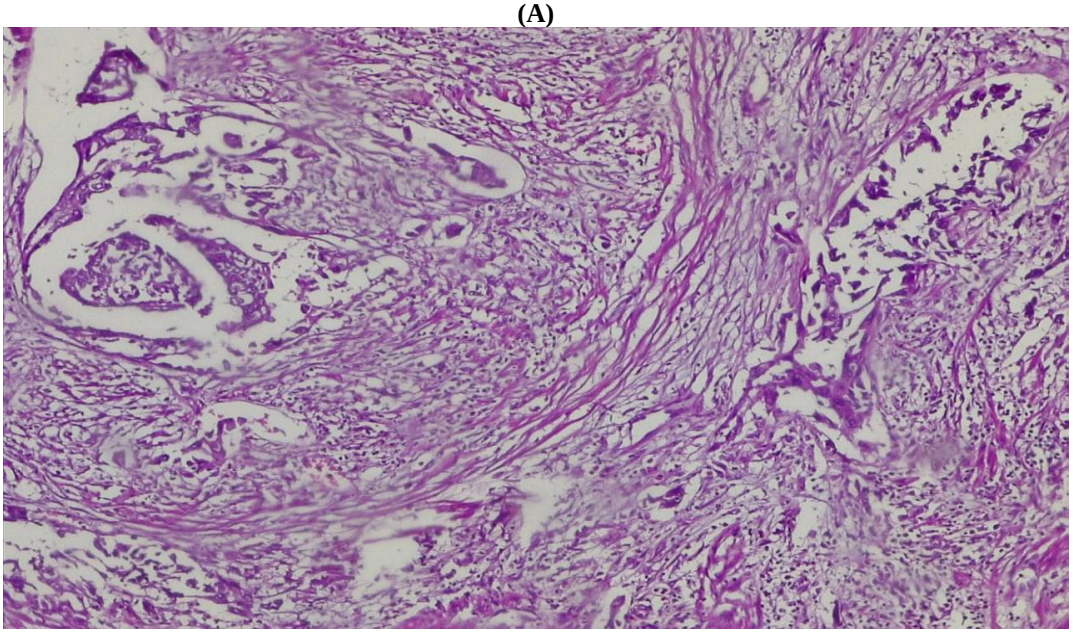
Table 2: Association between Pattern of invasion and variables include in this study.

Variables			**Pattern of Invasion**		
		Diffuse	**MELF**	**Pushing**	**P-value**
Percentage	***<50%***	17	5	8	
Of invasion		42.5%	33.3%	61.5%	
	≥ 50%	23	10	5	0.3
		57.5%	66.7%	38.5%	
	Total	40	15	13	
		100.0%	100.0%	100.0%	
	Not identified	11	0	10	
		27.5%	0.0%	76.9%	
LVI	***Present***	29	15	3	**0.0001**
		72.5%	100.0%	23.1%	
	Total	40	15	13	
		100.0%	100.0%	100.0%	
Lymph node	***free***	15	1	4	
Metastasis		37.5%	6.7%	30.8%	
	Not submitted	13	3	9	
		32.5%	20.0%	69.2%	**0.0001**
	positive	12	11	0	
		30.0%	73.3%	0.0%	
	Total	40	15	13	
		100.0%	100.0%	100.0%	
	Free	13	0	9	
LUS invasion		32.5%	0.0%	69.2%	
	Present	27	15	4	**0.0001**
		67.5%	100.0%	30.8%	
	Total	40	15	13	
		100.0%	100.0%	100.0%	
	Free	31	10	13	
Cervical		77.5%	66.7%	100.0%	
Invasion	***Present***	9	5	0	0.08
		22.5%	33.3%	0.0%	
	Total	40	15	13	
		100.0%	100.0%	100.0%	
	I	8	0	6	
		20.0%	0.0%	46.2%	
Grades	***II***	29	10	7	
		72.5%	66.7%	53.8%	**0.003**
	III	3	5	0	
		7.5%	33.3%	0.0%	
	Total	40	15	13	
		100.0%	100.0%	100.0%	

P-value ≤ 0.05 (significant).



(A)



(B)

Fig. 2: (A and B) MELF pattern ofmyoinvasion of endometroid endometrial carcinoma. H&E staining (10 and 40) PF.

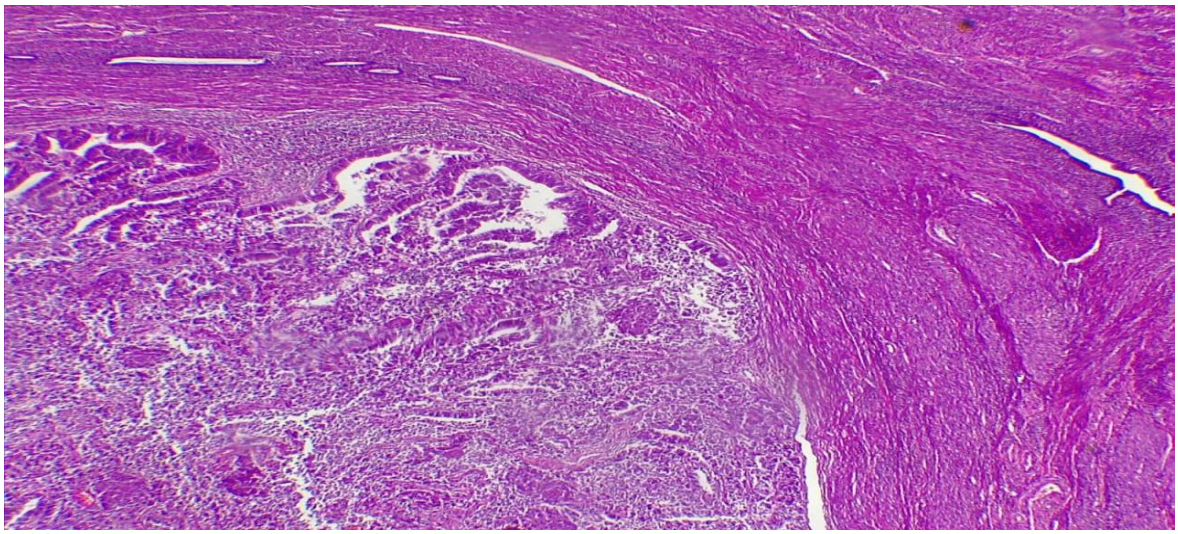


Fig. 3: Pushing pattern of myoinvasion in endometroid endometrial carcinoma. H&E staining (10 PF).

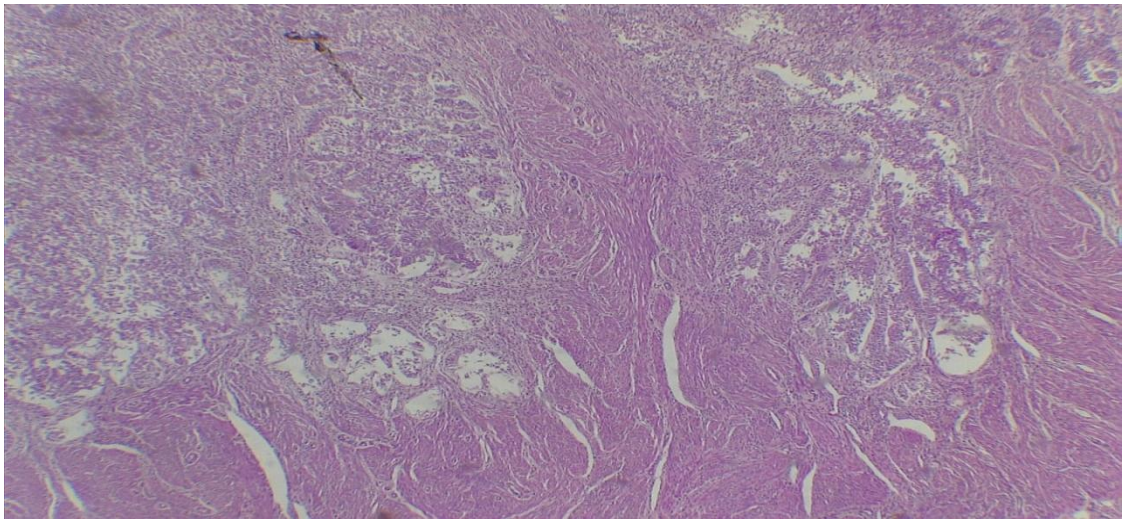


Fig. 4: Diffusely infiltrative pattern of myoinvasion in endometroid endometrial carcinoma. H &E staining (10 PF).

DISCUSSION

Microcysts lined by cells with prominent eosinophilic cytoplasm, elongated structures, and clusters of detached cells associated occasionally with retraction artefact characterise a recently described glandular change of myoinvasive endometrioid carcinoma glands known by the acronym MELF (microcystic, elongated, frag mented).[9] Several investigations have shown that the alterations in MELF may constitute a distinct tumour-stromal reaction, analogous to the epithelial-mesenchymal interactions reported in other cancers, rather than a degenerative process as was previously believed.[11] Several factors have been identified as predictors of lymph node metastases, including tumour size 2cm, myometrial invasion >50%, the MELF pattern of invasion, invasion of the lymphovascular space, involvement of the lower uterine segment, and involvement of the cervical stroma.[12] In current study, 68 patients with endometrial carcinoma, mean age of patients are 60 ± 9 years. [55.9 %] of patients have more than 50% Myo invasion, [69.1%] of patients have lymph vascular involvement, [33.8%] of patients have positive lymph node metastasis, [67.6%] of patients have LUS invasion, [20.6%] of patients have cervical invasion, [67.6%] of patients classified grade II diagnosis, this is similar other study done in USA and Greece (13, 14), stated that there were a total of 304 patients in the study. They were between the ages of 23 and 91, with a median age of 61. The patients were divided as follows: 77 (25.3%) had lymph node metastases with or without extrauterine disease; 19 (6.3%) had extrauterine disease without lymph node metastases; and 208 (68.4%) had neither lymph node metastases nor extrauterine disease. For the 96 people in the study group with advanced disease, tumour sizes ranged from 1.5 cm to 13 cm (mean 5.0 cm +/- 2.7 cm). For the 208 people in the control group who had FIGO stage I/II disease, tumour size ranged from 0.2 to 9 cm (mean 3.5 cm +/- 2.1 cm).

In our study there is significant association between Pattern of invasion and LVI, [100%] of patients classified as MELF Pattern of invasion are present with lymph node involvement, this is similar to other study that stated even though the univariate analysis confirmed what had already been said about tumour size 2cm, myometrial invasion >50%, MELF pattern of invasion, lymphovascular space invasion, lower uterine segment involvement, and cervical stromal involvement as predictors of lymph node metastases, the multivariate analysis found that only the percentage of myometrial invasion, cervical stromal involvement, and lymphovascular space invasion were independently significantly predictive.[14-17]

There is a strong correlation between the type of invasion and the likelihood of lymph node metastasis in the current study, with [73.3%] of patients classified as MELF Pattern of invasion being positive for Lymph Node Metastasis. This finding is consistent with previous research showing that when the MELF pattern of invasion is seen in endometrioid endometrial carcinoma, there is a high likelihood of lymph node metastasis. The high prevalence of concomitant lymph vascular space invasion and, to a lesser extent, the observed fibromyxoid stromal response are likely to blame for this phenomenon in the current investigation. This discovery is similar with the findings of other researchers who have shown that endometrioid endometrial carcinomas with a fibromyxoid stroma or vascular space invasion have a poor prognosis and a significant probability of recurrence.[9,18,19]

Patients with a MELF invasion pattern have a [100%] positive LUS invasion. There is a strong correlation between Pattern of invasion and LUS invasion. On multivariate analysis, patients with endometrioid histology were more likely to have lymph node metastases than those with other grades or histologies of endometrial adenocarcinoma.[17] Closer inspection of our

raw data reveals that of the 77 control patients with verified lower uterine segment involvement, 24 (31%) also had endocervical gland (9/24) or stromal involvement (31/64) whereas only 40 (62.5%) of the study patients with lower uterine segment involvement did. This shows that endocervical involvement is more likely in the presence of lower uterine segment involvement than is advanced disease stage.[20]

Patients with a widespread pattern of invasion (72.5%) are more likely to be diagnosed with a high-grade tumour. This modest pattern of lymph node metastases was initially documented by cKenney et al.[21] According to the authors, the metastatic cells shared morphological traits with cells identified in areas of MELF pattern invasion, even though the primary tumour was a gland-forming adenocarcinoma. Myoinvasive endometrial adenocarcinomas are the most common kind, however this pattern of lymph node metastasis has been observed in a small percentage of cases. Some pelvic and one para-aortic lymph node were found to have gland-forming and dispersed or tiny pseudopapillary metastatic foci in one of our patients. Because grade corresponds with surgical stage and eventually prognosis,[15,22,23] tumour grade is generally provided with staging information in endometrial, endometrioid adenocarcinoma. The influence is greatest for grade 3 tumours. One research found no differences in survival rates between FIGO grades 1 and 2 endometrial cancers,[25] and further studies have combined FIGO grades 1 and 2 tumours as a "low grade" entity to stratify risk with respect to lymph node metastasis.[16,24] In addition, studies.[15,23] have demonstrated that binary grading systems increase both inter- and intraobserver consistency.

CONCLUSION

Most pattern of invasive of endometrium carcinoma is diffuse pattern, MELF Pattern of invasion are present with lymph node involvement, positive Lymph Node Metastasis, positive LUS invasion. Most of diffuse and MELF Pattern of invasion are on grade II.

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