

Original Research Article

Discrepancy in grade between preoperative biopsy and final specimen in stage I carcinoma endometrium: an institutional review

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ABSTRACT

Background: Most endometrioid endometrial cancer are well differentiated (Grade I). Grade of the tumor is an important predictor of nodal metastasis and the discordance in histological grade of endometrial cancers between diagnostic biopsy and definitive surgery specimen was analyzed in our Institute.

Methods: Around 221 patients diagnosed with carcinoma endometrium between 2006 and 2014 were taken into study. Histologic differentiation of the tumour between diagnostic biopsy and definitive surgery were analysed. All demographic data, tumor factors, follow up and recurrence were recorded.

Results: Of the 221 patients taken into consideration for analysis, median age of presentation was 57 years with range between 38-77 years. The overall median body mass index was 27.70kg/m². 66 % of patients had comorbid illness, with 33% having both diabetes and hypertension. Open staging was performed in 150 patients and laparoscopic staging in 71 patients. Mean duration of surgery was 3.06 hrs in laparoscopic staging and 2.74hrs in open staging. The median tumour size was 4cm. The median number of nodes dissected were 13. Discordance in the grade of tumour between diagnostic biopsy and surgical biopsy were 58.8% of grade 1 tumour, 16.2% of grade 2 tumours and 18.9% of grade 3 tumours.

Conclusions: Discrepancies in correlation of the grade of tumour in diagnostic biopsy and tissue obtained at surgery supports the need for surgical staging in all patients.

Keywords: Carcinoma endometrium, Endometrial biopsy, Grade

INTRODUCTION

Endometrial carcinoma is a heterogeneous spectrum of disease with majority presenting in stage I. Endometrial adenocarcinoma ranks third among gynecological malignancies in our part of country, after cervix and ovarian cancer based on the MMTR database, the incidence of endometrial adenocarcinoma is about 2.45% of all cancers in women.¹

This is in contrast to the US population where it ranks first among the gynecological malignancies is the fourth most common cancer in females after breast, lung and colorectal cancers.²

Most patients present with an early-stage disease, and the overall survival for stage I is around 85-91%, and patients with advanced disease and unfavorable pathological characteristics have a guarded prognosis.^{3,4} The significant prognostic factors are histological type and grade of the tumor, depth of myometrial invasion, lympho-vascular invasion, and lymph node status.⁵

The most frequent histological type of endometrial cancer (80-85%) has a glandular growth pattern that shows a strong similarity with normal endometrial glands, and hence called endometrioid endometrial cancer.⁶ Endometrioid endometrial cancer is graded based on FIGO grading criteria, which depends on the percentage

of solid growth and nuclear atypia.⁴ Grade 1 tumors have 5% or less; grade 2 have 6% to 50; grade 3 have more than 50% of a non-squamous or non-morular solid growth pattern. A higher degree of nuclear atypia (on comparison with the architectural grade) escalates the grade 1 or grade 2 tumor to next higher grade.

In 1983, Bokhman reported endometrial cancer as two different types based on his observations of both clinical and pathological factors.⁷ Type I patients frequently have superficially invasive well differentiated (low-grade endometrioid) tumors and a good prognosis, while type II patients have deep invasive high grade non endometrioid tumors with a more aggressive progression. This has been attributed to endometrial hyperplasia in type I tumors that would delay myometrial invasion.

Most endometrioid endometrial cancer (80%) are well differentiated (grade 1) or intermediate grade tumors. Endometrioid type tumors usually develop in an estrogen rich environment, are found to occur in a milieu of endometrial hyperplasia and can be predated by atypical endometrial hyperplasia. Non endometrioid cancers, is many a times preceded by endometrial intraepithelial carcinoma (EIC) and seen in a background of atrophic endometrium.^{6,8}

METHODS

Retrospective analysis of all the patients with stage I carcinoma endometrium treated at our institution between January 2006 and December 2014.

All patients had a biopsy done by pipelle biopsy or dilatation and curettage to establish a histological diagnosis. In patients whom the diagnosis was not established, intra-operative frozen section study was used and then surgical staging was done.

All patients who were eligible for the study had undergone total hysterectomy with bilateral salpingo-oophorectomy, peritoneal wash cytology, pelvic lymph nodal dissection. Sampling or dissection of paraaortic nodes was only done in patients with suspicious nodal disease.

Subject eligibility

All the clinically stage I carcinoma endometrium patients treated in Cancer institute, Chennai from January 2006 to December 2014

Inclusion criteria

- All age group,
- Patients who are primarily treated in our institute,
- Patients who have undergone laparoscopic/open surgery.

Exclusion criteria

- Patients who have undergone surgery elsewhere,
- Patients who have high risk histology-clear cell, serous papillary cancer.

Authors have recorded parameters including age of patient, parity, BMI, mode of tissue diagnosis, mean operation time, postoperative adjuvant treatment, blood loss, intraoperative and postoperative complications, postoperative hospitalization, International Federation of Gynecology and Obstetrics (FIGO) surgical stage, histologic type, grade of tumor, number of lymph nodes harvested, size of tumor, recurrence and duration of follow up. Pearson's Chi-square test by cross table and independent sample T-test were used for analysis.

RESULTS

We had around 221 patients with postoperative stage I carcinoma endometrium after excluding tumors with clear-cell and serous-papillary histology. We grouped our cases based on the FIGO 2009 system of staging and risk stratification based on ESMO 2011 guidelines. (Table 1). 136 of the patients were in low risk category i.e.: Stage IA grade I and II, 65 were in intermediate risk group, of which, 21 were in low intermediate group and 44 in high intermediate risk group.

Table 1: Risk stratification of study population.

	No. of patients
Low Risk - Stage IA, Gr I, II	136
Low Intermediate - Stage IA, Gr III	21
High Intermediate - Stage IB, Gr I, II	44
High Risk	20

Age

Of the 221 patients taken into consideration for analysis, 121 (55%) were in their 6th decade of life. Median age of presentation was 57 years with range between 38-77 years, with 87%, (192) patients were above the age of 50 years.

BMI and comorbid illness

The overall median body mass index was 27.70kg/m², in range of 17.5-43.80kg/m². 69.2% of the patients were in overweight/obese range. In node positive patients the median BMI was 25.50. 66 % of patients had comorbid illness, with 33% having both diabetes and hypertension.

Type of surgery

Open staging was performed in 150 (68%) patients and laparoscopic staging in 71 patients (32%). Mean duration of surgery in laparoscopic surgery was 3.06hrs and open staging was 2.74hrs.

Size of tumor

The median size of the tumor in our analysis was 4cm with range of 0.5-8cm.

Nodal yield

The median number of nodes dissected were 13, over a range of 5-25 nodes. >92% of patients had the required minimum of 6 nodes sampled.

Grade of tumor

Pre-operative grade of tumor determined from biopsy had showed grade II to be commonest in 129 patients (58%). 17 patients in our analysis did not have preoperative confirmatory biopsy and were identified on hysterectomy specimen

There was change in postoperative grade in 17 patients (26.1%). In pre-operative grade I tumors there was escalation to higher grade in 58.8% patients, In Grade II tumors there was escalation to post-operative grade III in 16.2%. Pre-operative grade III tumors were downgraded in 18.9% patients (Table 2, Figure 1). Change between pre and post-operative grade showed a statistically significant difference on analysis.

Table 2: Percentage changes in grade of tumor.

		Postop grade			Total	% change
		1	2	3		
Preop grade	0	0	14	3	17	
	1	7	10	0	17	58.8%
	2	0	108	21	129	16.2%
	3	0	11	47	58	18.9%
Total		7	143	71	221	

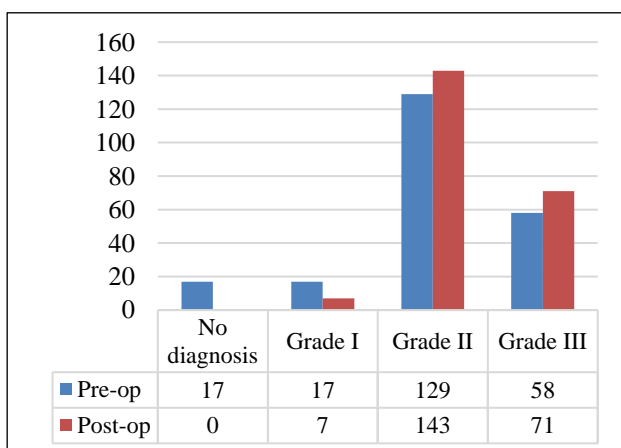


Figure 1: Pre-op vs post-op change in tumor grade.

Post-operative complication

Around 48 patients had no post-operative complication, 9 had wound infection in immediate post-operative period.

1 patient developed lymph cyst managed with aspiration, 1 developed lymphedema, both occurring with open staging. 1 patient had ureteric injury following laparoscopic staging and had postoperative uretero-vaginal fistula and required re-exploration and ureteric reimplantation.

There were 2 deaths in the study population (n-65), during the follow up period one was due to pre-existing carcinoma breast and other due to recurrence of endometrial cancer. The median overall survival was 85.5 months in the study population. In patients without pelvic nodal metastasis median overall survival was 88.6 months compared to 77.1 months in patients with positive pelvic nodal metastasis.

DISCUSSION

Endometrial cancer, with an increasing incidence, happens to be the most common cancer of genital tract in women in developed countries, with increasing incidence in our country. Due to the limitations of clinical assessment of carcinoma endometrium, FIGO switched from clinical staging published in 1977 to surgical staging back in 1988, following results of GOG 33 study.⁴ The study GOG 33, also showed grade of tumor, depth of myometrial invasion, and lympho-vascular space invasion as factors predicting increased risk of nodal metastasis.⁴

In our review grade I tumors were upgraded in 58.8%, this finding could be due to the number of grade I tumors in our analysis. In review analysis by Obermaier of well differentiated endometrial adenocarcinoma, it was upgraded in 20.4% of cases.⁹

Pipelle biopsy (endometrial aspiration biopsy) has a sensitivity of 99.6% in diagnosing endometrial cancer. DandC has similar sensitivity; it serves as the procedure for diagnosis when pipelle biopsy is not possible or is unsatisfactory.¹⁰ After diagnosing endometrial cancer, preoperative evaluation of the extent of the disease is very crucial to plan the surgery. Patients have a 15% to 20% risk of having lymph nodal metastasis when the endometrial cancer is high grade.⁴ Therefore, the capacity to grade the tumor precisely on the diagnostic biopsy is very crucial, be it either a pipelle biopsy or by dilatation and curettage.

Dilatation and curettage indicates the final FIGO grade more precisely than a pipelle biopsy. Leitao et al, in his analysis reported, 8.7% up gradation of tumor on hysterectomy, when the diagnosis was by dilatation and curettage, in contrast to 17.4% when diagnosed by pipelle biopsy.¹¹ Obermaier in his review reported Grade 1 tumors on dilatation and curettage showed 20% up gradation to grade 2 and 2-3% up gradation to grade 3 tumors on final pathology. He also reported 4% down gradation of tumors at final pathology.⁹ In short, pre-operative Grade 1 carcinoma endometrium correlates

with final pathology on hysterectomy specimen in 80-85% cases.

Frumovitz in his review of 153 patients with grade 1 or 2 carcinoma endometrium comparing pre-operative grade of tumor and final pathology.¹² There was 32% (49 patients) discrepancy amidst preoperative and final biopsy. Thirty-seven (27%) of the patients had their tumor upgraded or had high risk histology other than endometrioid carcinoma. He concluded that a significant number of patients will have an advanced disease which cannot be reliably predicted using prognostic factors and should not be relied upon for staging.

CONCLUSION

The following restrictions with our study must be acknowledged. First, this was a retrospective study involving limited number of patients, and only restricted interpretation can be derived from our data. The discordance rates in grade of tumour tissue obtained at diagnostic biopsy and from the definitive surgery, implies the need for surgical staging in all patients with carcinoma endometrium.

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