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## Original Research Article

# Re-staging surgery in endometrial cancer: an audit on its value

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## ABSTRACT

**Background:** Incomplete surgical staging in carcinoma endometrium is not an uncommon entity in developing world. Proper surgical staging has got a role in prognostication and planning adjuvant treatment. So, an audit was done to assess the extent of upstaging in women with endometrial cancers who were referred to index centre from outside hospitals with incomplete surgical staging.

**Methods:** It is a retrospective study. The demographic, clinical and treatment details of women with complete data having at-least one follow up after completion surgery were analyzed. Patients who had any other anticancer treatment elsewhere were excluded. The extent of upstaging was studied based on International federation of gynecology and obstetrics (FIGO) 2008 staging.

**Results:** A total of 88 patients of endometrial cancer were evaluated retrospectively, of which 10 had completion surgery. 10% of the patients were upstaged according to the FIGO stage (one from IA to IB), while one patient upstaged from IIIA to IVB after slide review by index centre. According to FIGO Grade, 40% patient upgraded (one upgraded from I to II, three from II to III) while one downgraded from II to I. Recurrence rate was 40%.

**Conclusions:** Upstaging is seen in 10% of patient after completion surgery, which requires the necessity of evaluation by gynecologic oncologist selectively. However, larger and multi-centric studies needed to draw definite conclusion. There is a significant discordance in grade and histology after the review at index centre.

**Keywords:** Endometrial carcinoma, Upstaging, Restaging surgery, Completion surgery

## INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy in the developed world with incidence of 1.28% annually making it third most common gynecologic malignancy after cervix and ovary.<sup>1,2</sup> Out of all hysterectomies done for benign conditions 0.3-3% have endometrial malignancy on final histopathology.<sup>3</sup> Endometrial cancer is classically thought to spread in a stepwise manner with invasion into the myometrium followed by metastasis to the regional lymph nodes and ultimately systemic spread.<sup>4</sup> The most important prognostic factors for endometrial cancer is the disease stage and the lymph nodes metastasis.<sup>5</sup> There is a disagreement regarding lymph node dissection in the

management of low risk disease. Agar et al, advocated a single procedure including lymphadenectomy also to reduce that morbidity.<sup>6</sup> The potential benefits of lymph node dissection must be weighed against the intra-operative and post-operative risks.

Helpman et al reported the results of 1329 consecutive patients during 10-year period. Of 255 patients whose biopsies were grade I (G I) adenocarcinoma, 45 (18%) were upgraded to grade II (G II) on final pathology, 6 (2%) were upgraded to grade III (G III) and 5 (2%) were final changed to non-endometrioid high-grade histology, in grade II, 10% tumors (12/125) while grade III, 24% had change in histopathology from endometrioid to non-endometrioid, in this study outside hospitals slides were not

reviewed at index centre.<sup>7</sup> Though recommended as a part of the surgical staging, Positive peritoneal cytology is not included in staging of endometrial carcinoma.<sup>8</sup> Pooled analysis of 926 patients of PORTEC 1 and two trials showed that lymphovascular space invasion is the most important predictor of recurrence (pelvic and distant) and overall survival while stage I tumors have low lymphovascular space invasion.<sup>9</sup>

There have been studies regarding nodal metastasis in both low and high-risk endometrial cancer but there is scarce data on upstaging. So, the current study was aimed to study upstaging and lymph node positivity.

## METHODS

This was retrospective observational study done at a tertiary cancer care centre in South India, on women who underwent completion surgery for endometrial cancer from January 2015 to March 2018. Institutional review board approval was taken at the onset of the study. Completion surgery is done in patients of endometrial cancers who underwent incomplete primary surgery from outside hospitals and were referred there. Inclusion criteria were women who underwent completion surgery during study period and had completed at least one follow-up after completion treatment. Exclusion criteria were women who had history of radiation or chemotherapy treatment elsewhere before completion surgery.

The demographic, clinical and treatment details of all the subjects were collected from the medical record department. All patients initial histopathology was reviewed by onco-pathologists at the index centre. Then the upstaging and lymph node positivity of endometrial cancer was done by International federation of gynecology and obstetrics (FIGO) classification of cancer endometrium 2008 along with baseline Computed tomography (CT) scan and histopathology.

### Statistical analysis

Data was entered in Microsoft excel sheet. Descriptive and inferential statistics was used to analyze the data. The data were expressed in terms of number and percentages. The statistical analysis was done using IBM Statistical package for social sciences (SPSS) version 23 statistics software.

## RESULTS

Database of 88 patients were studied during the study period which met inclusion and exclusion criteria, out of which ten patients had indication and underwent completion surgery. Patients who underwent completion surgery, majority were in the age group of 51-60 years (50%). 20% had diabetes mellitus and 30% had hypertension as co-morbidity.

Average hospital stay was about  $7\pm 1.7$  days and mean interval between completion surgery and adjuvant treatment was  $31.33\pm 8.41$  days while mean Interval

between first surgery and adjuvant treatment  $100.6\pm 22.95$  days. Complications included myocardial infarction (grade IVA), burst abdomen (grade IIIB) and lymph edema (grade I), one each.<sup>10</sup> Nine patients required radiotherapy of which eight received while only one out of four who required adjuvant chemotherapy received (64% of required treatment actually received).

**Table 1: Socio-demographic and clinical profile of patients who underwent completion surgery (n=10).**

Characteristic	Number	
Age (in years)	41-50	2 (20%)
	51-60	5 (50%)
	61-70	3 (30%)
Comorbidity	Diabetes mellitus	2 (20%)
	Hypertension	3 (30%)
	None	5 (50%)
Average hospital stay	$7\pm 1.7$ days	
Mean interval between completion surgery and adjuvant treatment	$31.33\pm 8.41$ days	
Interval between first surgery and adjuvant treatment	$100.6\pm 22.95$ days	
Median follow up period	13.5 months (4.6-35.9 months)	
Complication (morbidity grade)	Myocardial infarction	1 (grade 4a)
	Burst abdomen	1 (grade iiib)
	Lymph edema	1 (grade i)
Adjuvant radiotherapy	Requirement-9	Received -8
Adjuvant chemotherapy	Requirement-4	Received -1

According to FIGO stage- one patient (endometroid carcinoma) upstaged from IA to IB while one (malignant mixed mullerian tumor (MMMT)) from IIIA to IVB upstaged during slide review, while according to FIGO grade, one patient (endometroid carcinoma) upgraded from I to II, three patients (2 endometroid carcinoma and 1 serous adenocarcinoma) from II to III and one patient (endometroid carcinoma) from II to I.

Out of the 10 patients who underwent completion surgery, 9 patients had agreement on tissue type of histopathology report from outside and the index centre except for the one where histopathology report from outside reported endometroid carcinoma found to be serous adenocarcinoma at the index centre.

Four out of ten patients had recurrence, 3 had distant recurrences (two inguinal lymph node involvement and one vertebral metastasis), while one patient had local vaginal vault recurrence. Three patients received adjuvant radiation while one received adjuvant chemotherapy.

**Table 2: Upstaging and upgrading according to FIGO stage (2014) and FIGO grade.**

Histopathology	Histopathology	FIGO stage		FIGO grade		Adjuvant
Outside centre	Index centre	Outside centre	Index centre	Outside centre	Index centre	Received
Endometrioid carcinoma	Endometrioid carcinoma	IA	IA	I	I	FU
Endometrioid carcinoma	Endometrioid carcinoma	IA	IB	I	II	RT
Endometrioid carcinoma	Endometrioid carcinoma	IB	IB	II	I	RT
Endometrioid carcinoma	Endometrioid carcinoma	IB	IB	II	II	RT
Endometrioid carcinoma	Endometrioid carcinoma	IB	IB	II	III	RT
Endometrioid carcinoma	Endometrioid carcinoma	IB	IB	II	III	RT
Endometrioid carcinoma	Serous Adenocarcinoma	IB	IB	II	III	RT
Clear cell carcinoma	Clear cell carcinoma	IB	IB	III	III	RT
Serous adenocarcinoma	Serous adenocarcinoma	IB	IB	III	III	RT
Malignant mixed mullerian tumor	Malignant mixed mullerian tumor	IIIA	IVB	III	III	CT

RT=Radiotherapy; FU=Follow Up; CT=Chemotherapy.

**Table 3: Follow up and recurrence among patients.**

Histopathology	Site of recurrence	Interval between initial surgery and adjuvant (weeks)	Adjuvant RT received	Adjuvant CT received	DFI (Months)	Palliation
MMMT	Vaginal vault	>12	No	Yes	14	RT
Serous carcinoma	Inguinal lymph node	>12	Yes	No	6	CT
Adenocarcinoma	Vertebral metastasis	10	Yes	No	7	RT
Serous adenocarcinoma	Inguinal lymph node	>12	Yes	No	8	Opted out

MMMT-Malignant Mullerian Mixed Tumour, DFI-Disease Free, RT=Radiotherapy; CT=Chemotherapy.

## DISCUSSION

Incomplete surgical staging in case of endometrial cancers is not a rare entity. It may be due to improper evaluation in preoperative period, lack of precise frozen section or pathology reporting due to less trained pathologist in low middle income countries like India.<sup>11</sup> Other reasons may be inadequate evaluation of abnormal uterine bleeding in post-menopausal age group and unfortunately malignant final histopathology in patients operated for benign conditions. For better management of patients we have to choose in between restaging with lymphadenectomy or may be omentectomy, follow up with no adjuvant treatment in selected group of patients, adjuvant radiations or chemotherapy or both.

Retrospective analysis of 88 patients were done of which, ten patients underwent completion surgery. Upstaging was present in 10% of the patients. The rate of upstaging is low as all the stages are taken into consideration and not only apparently early stages. However there is slightly a higher percentage of upstaging by Thomas et al, which was 25%.<sup>12</sup> Majority of patients (50%) who underwent completion surgery were in the age group of 51-60 years which is in concordance with studied by Thomas et al,

where most of patients fall in range of 31-67 years.<sup>12</sup> This shows that the age group between 51-60 years is prone for endometrial cancer which is also the case in the present study.

In the present study 20% had diabetes mellitus and 30% had hypertension as co-morbidity which are the components of metabolic syndrome. These findings are strengthened by the findings of Thomas et al, where 40% had body mass index (BMI) of more than 30.<sup>12</sup> Complications included myocardial infarction, burst abdomen and lymph edema (one each) in the present study. While in the other study complications included iliac vein injury and bladder injury.<sup>12</sup> The difference might be due to multiple factor like general status of the patient and disease progression.

Out of the ten patients who underwent completion surgery, 90% (9 patients) required radiotherapy after final histopathology reporting, but 8 had indication of adjuvant radiations after slide review, so one patient upgraded in adjuvant radiotherapy group. However adjuvant radiotherapy was received by eight patients (88.89%). Adjuvant chemotherapy was required by 40% of patients after slide review but no change in adjuvant chemotherapy

patients, out of which only 25% (one patient) received it, was due to poor compliance (two patients), and long duration of treatment (one patient) despite having acceptable general condition. However in other study 20% (5 patients) required radiotherapy (vaginal brachytherapy therapy) and 20% (5 patients) were advised both chemotherapy and radiation.<sup>12</sup> This difference would be due to age of the patients, final stage, grade and histopathology while consideration for adjuvant treatment.

In the present study, according to FIGO stage (10%) one (MMMT) from IIIA to IVB) patient upstaged while according to FIGO grade, 40% patient upgraded (one patient upgraded from I to II, three patients from II to III) while 10% downgraded (one patient from II to I). While in study by Zhou et al, showed 34.6% (28/81) of patients had change in tumor grade. 25.9% on slide review showed upgrading as compared from 8.6% were downgraded.<sup>13</sup>

Out of the 10 patients who underwent completion surgery, 8 (80%) patients had agreement on histopathology report from outside and the index centre which is in close concordance with other study that showed 75.3% agreement.<sup>12</sup> In this study one histopathology report from outside reported endometrioid carcinoma and serous adenocarcinoma at the index centre and endometrioid adenocarcinoma from 1A to 1B. In the present study, majority of patient (60%) had endometrioid type of endometrial carcinoma which is the most common type, while other study by Zhou et al (85.2%) and Thomas et al (70%) showed majority of histopathology were endometrioid type.<sup>12,13</sup>

In the present study, recurrence rate is 40%. Four patients had recurrence during median follow up period 13.5 months (4.6-35.9 months), of which the woman with MMT (DFI-14 months) had indication for chemo-radiation but opted out for radiations due to lack of compliance. This may be the cause of local (vaginal cuff) recurrence. Two out of four recurrences had serous histopathology, were advised for chemo-radiation therapy and both took only radiation therapy. They had inguinal lymph node recurrences (distant recurrence). One woman with adenocarcinoma had indication for adjuvant radiation therapy. After 7 months she had vertebral recurrence which might be due to adjuvant radiation only treatment, who does not protect distant recurrences and she expired after palliative radiations. The overall recurrence rate was 2/20 (10%) patients during the study period of 48 months, and two women died of disease progression in a study by Thomas et al.<sup>12</sup> A study by Kaewpangchan et al showed vaginal cuff recurrence was 37.5%, while inguinal lymph node and bone recurrence was 4.8% each.<sup>14</sup> This discordance in recurrence percentage might be due to the fact that patients did not follow the standard treatment during adjuvant period.

## CONCLUSION

Upstaging is seen in 10% of patient after completion surgery in carcinoma endometrium which requires the necessity of evaluation by gynaecologic oncologist selectively. However, larger and multi-centric studies are needed to draw definite conclusion. Before completion staging we have to keep in mind, the performance status of patient and whether we are able to change the adjuvant treatment in the patient without adding much morbidity and significant delay in completion of adjuvant treatment. There was a significant discordance in grade and histology after the review at a tertiary centre which raises the requirement of trained onco-pathologist to review the slides. So, re-surgery has a dubious role for delaying the adjuvant treatment and discourages the patients from taking adjuvant treatment, this should be evaluated in large series.

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