ORIGINAL ARTICLE1

Trends of Endometrial Cancer in Central India: An Institutional Review

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ABSTRACT

AIM: To study the demographics, staging, treatment details, and outcomes of operable endometrial cancers.

METHOD: All operable endometrial cancers treated between January 2013 and February 2017 were included in the study. The details regarding demographics, staging, surgical procedure, pathological staging, adjuvant treatment, and outcomes were extracted from the case records.

RESULTS: There were 25 patients with a median age of 55 years (36–78 years). The Eastern Cooperative Oncology Group performance status was 1 in 23 patients (92%) and 2 in 1 patient (4%) and 3 in 1 patient (4%). 22 patients (88%) had disease restricted to endometrium while 3 patients (12%) had cervical involvement. The surgery done was Type I hysterectomy in 24 patients (96%), Type II in 1 patient (4%). Pelvic lymph node dissection was done in 22(88%) patients while para-aortic (infra-hilar) dissection was done in 2 patients (8%). The pathological stages were Stage IA in 13 patients, Stage IB in 3 patients, Stage II in 4 patients, Stage IIIC1 in 3 patients, and Stage IV in 2 patients. Grade 1 tumors were seen in 21 patients, Grade 2 in 2 patients, Grade 3 in 2 patients. The histology was endometrioid in 23 patients, clear cell in 1 patient, and carcinosarcoma in 1 patient. Adjuvant treatment was received by 5 patients.

CONCLUSION: Endometrial cancer is 4th most common gynaecological cancer in our series, 3.5% of all cancer patients. Risk factors including menopause. Other risk factors not statistically significant. Endometrioid adenocarcinoma most common histology with early stage is most common among all surgically treated patients. Simple hysterectomy sufficient for stage 1 & 2. Adjuvant therapy needed in stage 3 & 4. DFS and OS are good in younger age groups, well-differentiated, early stage endometrial cancers but very poor in older age group, poorly differentiated, stage 3C and stage 4 patients.

Key Words: Endometrial cancer, India, operable

INTRODUCTION

Endometrial cancer is the fourth most common cancer in women worldwide.[1] However, it is the third most common malignancy in Indian women. The declining incidence of cervical cancer and the predicted rise of endometrial cancer in this century mean that endometrial cancer will be a significant issue in India. [2] The traditional management of operable endometrial cancer is by staging laparotomy followed by appropriate adjuvant therapy (as per indication). However, multiple controversies exist in this management.[3] The role of lymphadenectomy, adjuvant radiation, and chemotherapy is not well defined.[4,5,6] As a result, variability in the management of endometrial cancer across centres is common. This variability may have an impact on outcomes. However, there is limited literature about the prognosis and practices in the management of endometrial cancer available from India. Lack of such information hampers the development of strategies to improve the outcome and prognosis. This retrospective review was planned to evaluate the outcomes of endometrial cancer patients from central India.

METHOD

This was descriptive retrospective analysis of all endometrial cancer patients who were treated in between January 2013 and February 2017 at a tertiary cancer care centre, Sri Aurobindo Institute of Medical Science and Post Graduate Institute, Indore (M.P.). After surgical staging, all patients were evaluated in multispecialty board discussion for further treatment planning. These patients were treated in accordance with the NCCN (National Comprehensive Cancer Network guidelines) of respective years.

Data collection: The cases selected from institutional recorded data and then demographic and clinical details were reviewed. This included details about diagnosis, staging details, details about outside surgery, details of procedures at our centre, postopera-

tive complications, adjuvant treatment, sites of failure, date of progression, and date of death.

Data analysis: SPSS 16 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Descriptive statistics was performed. The time-to-event analysis was done by Kaplan–Meier method. Disease-free survival (DFS) was calculated from the date of surgery to the date of first failure. Overall survival (OS) was calculated from the date of surgery to the date of death. Patients who were alive were censored at their last follow-up. COX regression analysis was performed to identify factors affecting DFS and OS. The factors tested were age (>55 years or 55 years and below), stage (I–II vs. III–IV), Grade (1–2 vs. 3), recipient of adjuvant treatment (yes or no), and Eastern Cooperative Oncology Group performance status (ECOG PS) (0–1 vs. 2-3).

Table 1: Stage-wise Disease-free survival (DFS) and Overall Survival (OS)

Stage	DFS(%)-3yrs	OS(%)-3yrs
1	94%	96%
2	84%	86%
3	76%	74%
4	40%	36%
All	84%	92%

Table 2: Factors affecting Disease-free survival (DFS) and Overall Survival (OS) on multivariate analysis

Variable	Hazard Ratio	95% CI	P value
Elderly age	11.02	1.29–94.40	0.028
Grade 3 status	6.024	1.171–31.25	0.032
Stage III-IV status	5.780	1.189–28.571	0.035

RESULTS

Demographics: Endometrial cancer is 4th most common gynaecological cancer in our series. A total of 25 patients were treated at our centre. Median age was 55years (36–78 years). 24 (96%) patients were post-menopausal. 5 patients have history of late menopause. 1 patient is nullipara. The Eastern Cooperative Oncology Group performance status was 1 present in 23 patients (92%) and score 2 present in 1 patient (4%) and score 3 present in 1 patient (4%). 5 (20%) patient has DM-2 alone and 3 (12%) patients has both DM-2 and Hypertension and 1 patient has history of IHD. None of the patient has history of OCP uses. 2 patients have positive history of endometrial cancer in first degree relatives. 4 patients have BMI >30 kg/m^2 with one patient had BMI 42kg/m^2. Per vaginal bleeding is most common symptoms, 24 patients in our series and lower pelvic pain present in 4 patients. No symptoms of locally advanced or metastatic disease in our series. All patients preoperatively diagnosed with endometrial biopsy. MRI pelvis with contrast done in all patients for clinical staging purpose.

Surgical details: All patients were treated with surgery primarily. The surgery done was Type I hysterectomy in 24 patients (96%), Type II in 1 patient (4%). Pelvic lymph node dissection was done in 22 (88%) patients while para-aortic (infra-hilar) dissection was done in 2 patients (8%). Bilateral salpingo-oophorectomy was performed in all patients. Pelvic lymph node dissection was done in 22(88%) patients while para-aortic (infra-hilar) dissection was done in 2 patients (8%). One patient had done liver metastesectomy. The median intraoperative time was 180 min (100–400 min). The median postoperative stay was 8 days (5–33 days).

Adverse events: Grade 3–4 surgical morbidity occurred in only 2 (8%) patients. Median blood loss was 300 ml (100–1000 ml). Intraoperative bowel injury occurred in 2 patients and one patient had ureteric injury which required suturing with stenting. Surgical site wound infection occur in 4 patients and 1 patient had history of wound dehiscence.

Histopathological details: The histology was endometrioid in 23 patients, clear cell in 1 patient, and carcinosarcoma in 1 patient. Tumors were staged according to the FIGO 2009 staging system of endometrial cancers, The pathological stages were Stage IA in 13 patients, Stage IB in 3 patients, Stage II in 4 patients, Stage IIIC1 in 3 patients, and Stage IV in 2 patients. Grade 1 tumors were seen in 21 patients, Grade 2 in 2 patients, Grade 3 in 2 patients.

Adjuvant treatment details: Adjuvant treatment was received by 5 patients. 3 patients received adjuvant radiation, External beam radiation (EBRT). The median EBRT dose was 50.4 Gy (50.4–50.4 Gy). Grade 3–4 toxicity post-radiation was seen in 4 patients (16%). The three most common acute reactions during radiation were vomiting in 4 patients, diarrhea in 3 patients, and urinary tract infection in 2 patients.

Adjuvant chemotherapy was received by 3 patients. The chemotherapy regimen was paclitaxel and carboplatin in 2 patients and Ifosfamide and cisplatin were used in patients with mixed mullerian tumor. The median chemotherapy cycles were 6 (1–6 cycles). One patient had Grade 4 febrile neutropenia. Common acute adverse events seen during chemotherapy were anemia in 3 patients and vomiting in 2 patients.

Recurrences: Three (12%) patients had recurrence within 3 years follow-up period. One had distant metastasis and two had local recurrence. In the two patients who had local recurrence, one patient had salvaged with pelvic radiation. The second patient underwent surgical excision as salvage therapy. Of the

one patient who had distant metastasis, she had initial disease with advanced stage IIIC1. The site of distant metastasis was lung.

Outcomes: The median follow-up was 2.5 years. The 3-year DFS and OS were 84% and 92%, respectively. The DFS and OS of each stage are shown in Table 1. The factors affecting DFS and OS on multivariate analysis are shown in Table 2.

DISCUSSION

Carcinoma endometrium is the second most common gynecological malignancy at our centre. The median age in our cohort was 55 years. In endometrial cancer series reported from the West, this age is consistently above 60 years[1] while studies reported from India show a median age consistently near 50 years. This reflects the differential life expectancy in the state in which the centre is located.[2] The majority of patients were postmenopausal with 5 patients have history of late menopause and 1 patient is nullipara, 5 (20%) patient has DM-2 alone and 3 (12%) patients has both DM-2 and Hypertension and 1 patient has history of IHD and 2 patients have positive history of endometrial cancer in first degree relatives. These factors are consistent with the known risk factors associated with endometrial cancers.[4] None of the patients have a history of smoking and alcohol intake. Obesity is also one of the risk factor which was present in 4 patients.

Unlike breast and prostate cancer where screening tests are available to the general population, endometrial cancer is most commonly diagnosed at endometrial biopsy in symptomatic patients, i.e., after a postmenopausal patient reports vaginal bleeding. No generally applicable screening test is available. For patients who receive a pelvic ultrasound for another indication, an enlarged endometrial stripe or other intrauterine anomaly, such as a polyp, may prompt biopsy in the absence of vaginal bleeding. However, most experts agree that ultrasound is not recommended as a screening tool in asymptomatic patients.

Staging: In 2009, the International Federation of Gynecology and Obstetrics (FIGO) revised the staging system for carcinomas of the vulva, cervix, and endometrium [8]. The primary changes made for endometrial cancer included the grouping of stages IA and IB together as stage IA with the loss of prior IC and the division of stage IIIC (metastasis to the pelvic and/or paraaortic lymph nodes) into stage IIIC1 (positive pelvic nodes) and IIIC2 (positive paraaortic lymph nodes). Specifically the old staging system defined stage IA as no invasion into the myometrium, stage IB as less than 50% invasion into the myometrium, and stage IC as equal to or greater than 50% invasion into the myometrium, whereas the new FIGO 2009 system defines stage IA as cancer confined to the uterus with less than 50% myometrial invasion, and stage IB as equal to or greater than 50% myometrial invasion, with both IA and IB including any tumor grade. This was modified after data from the FIGO Annual Report showed no difference in survival between previous stage IA grade 1 or 2 and stage IB grade 1 or 2 tumors. The other significant change involved patients with positive pelvic or paraaortic lymph nodes. Under the old FIGO guidelines, patients with positive pelvic and/or paraaortic lymph nodes were staged as IIIC, and under the new system patients with positive pelvic lymph nodes are separated from those with positive paraaortic +/− pelvic lymph nodes, stage IIIC1 and IIIC2, respectively. This change was made because many studies demonstrated worse survival for patients with positive paraaortic lymph nodes when compared to positive pelvic lymph nodes.

In surgical treatment, uterus, fallopian tubes, ovaries, and lymph nodes (pelvic ± para-aortic) are removed. Type 1 hysterectomy also known as extra-fascial hysterectomy done in most of the patients with type-2 hysterectomy which also including surrounding parametrium done 1 patient. Pelvic lymphnodes removal is part of staging laparotomy in most of the patients which judgment mainly decided with preoperative imaging. Para-aortic lymphnodes removal was based on clinical suspicion. Open approach done in all patients. One patient had done liver metastesectomy. The median intraoperative time was 180 min (100–400 min). The median postoperative stay was 8 days (5–33 days) which is comparable to other studies.[5]

Intra-operative complications occur in 3 patient and immediate post-operative complications occur in 5 patients.

Endometrioid adenocarcinoma most common histology in our group with 20 patient diagnosed with early stage (stage1-2) endometrial cancer.

Adjuvant radiation done in 3 patients who has stage 3C diagnosed with histopathological examination. 3 patients received adjuvant chemotherapy out of whom 2 patients have stage 4 disease and one patient diagnosed with carcinosarcoma.

The recurrence pattern in this study is similar to those reported in other Indian and Western studies.[9] Local recurrence rate is 12% in our group of patients with 3 years follow-up. Surveillance protocol in our institute- history and clinical examination done in every 1 month for 6 months then 2-3 months for next 6 months, 4-6months in 2nd and 3rd year. USG done every 6months. CT/MRI as clinically indicated. We have salvaged 2 patients with recurrence. DFS and OS are good in early stage endometrial cancers but very poor in stage 3C and stage 4 patients.

CONCLUSION

Endometrial cancer is 4th most common gynaecological cancer in our series, 3.5% of all cancer patients. Risk factors including menopause. Other risk factors not statistically significant. Endometrioid adenocarcinoma most common histology with early stage is most common among all surgically treated patients. Simple hysterectomy sufficient for stage 1 & 2. Adjuvant therapy needed in stage 3 & 4. DFS and OS are good in younger age groups, well-differentiated, early stage endometrial cancers but very poor in older age group, poorly differentiated, stage 3C and stage 4 patients.

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REFERENCES

1. Globocan 2018 – Home. Available from: http://www.globocan.iarc.fr/Default.aspx.
2. Nandakumar A, Ramnath T, Chaturvedi M. The magnitude of cancer cervix in India. Indian J Med Res 2009;130:219-21.
3. SGO Clinical Practice Endometrial Cancer Working Group, Burke WM, Orr J, Leitao M, Salom E, Gehrig P, et al. Endometrial cancer: A review and current management strategies: Part II. Gynecol Oncol 2014;134:393-402.
4. Schmandt RE, et al. Understanding obesity and endometrial cancer risk: opportunities for prevention. Am J Obstet Gynecol. 2011;205(6):518–25.
5. Benedetti Panici P, Basile S, Maneschi F, Alberto Lissoni A, Signorelli M, Scambia G, et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: Randomized clinical trial. J Natl Cancer Inst 2008;100:1707-16.
6. Nout RA, van de Poll-Franse LV, Lybeert ML, Wárlám-Rodenhuis CC, Jobsen JJ, Mens JW, et al. Long-term outcome and quality of life of patients with endometrial carcinoma treated with or without pelvic radiotherapy in the post operative radiation therapy in endometrial carcinoma 1 (PORTEC-1) trial. J Clin Oncol 2011;29:1692-700.
7. Hogberg T, Signorelli M, de Oliveira CF, Fossati R, Lissoni AA, Sorbe B, et al. Sequential adjuvant chemotherapy and radiotherapy in endometrial cancer – Results from two randomised studies. Eur J Cancer 2010;46:2422-31.
8. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet. 2009;105(2):103–4.
9. Lurain JR, et al. Prognostic factors associated with recurrence in clinical stage I adenocarcinoma of the endometrium. Obstet Gynecol. 1991;78(1):63–9.