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The clinico pathological features and survival in serous endometrial cancers

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ABSTRACT

Background & Introduction: Serous cancers are a biologically aggressive variety of endometrial cancer (EC) with a high rate of recurrence and mortality among all the subtypes. Herein we describe our experience with serous endometrial cancer.

Objective: This study was conducted to identify the clinicopathological characteristics, treatment modalities and survival outcomes in women diagnosed with serous endometrial malignancies.

Methods: This was a retrospective descriptive analysis of data on patients diagnosed with serous endometrial tumours between January 2010 to September 2019 in our institute collected from electronic medical records. Descriptive statistics such as proportions, means and standard deviations and Cox regression hazards model on risk factors were performed. Survival was plotted by Kaplan-Meier curves.

Results: During the study period, 32 (5.7%) patients out of 564 diagnosed cases of endometrial cancer had serous histology. The mean age at diagnosis was 62.5 years (SD 7.6) while mean BMI was 26.4 kg/m^2 (SD 4.6). Staging laparotomy was done in 27(84%) of the patients. Advanced stages (III and IV) were detected in 16 patients (50%) at primary surgery.Adjuvant chemo therapy and radiation was received by 21(65.6%) patients therapy. Out of 32 patients, 13 (40%) developed recurrence while another 13 expired. Stage at diagnosis and type of adjuvant therapy were important factors in determining the outcome. Median recurrence free and overall survival was 22 (95% CI 1.4–42) and 36 months (95% CI 10.1–61.8) respectively.

Conclusion: Serous endometrial cancers are an intrusive subtype of EC. Comprehensive surgical staging with optimal cytoreduction should be aimed at. Adequate upfront molecular categorization of these tumors is mandated. Adjuvant therapy with chemotherapy and radiation is given in postoperative setting. Targeted therapies and immunotherapy could be considered in recurrences.

1. Introduction

Endometrial cancer has been on a rise worldwide with an estimated 417,367 new cases and 97,370 deaths reported in 2020 (Sung et al., 2021 May). It is the fourth most common tumor type and accounts for 5% of all cancer cases and 2% of all cancer deaths worldwide (Zhang et al., 2020).

The concept of two types of endometrial cancer(EC) was initially proposed by Bokhman in 1983 (Bokhman, 1983). It is awell-accepted fact that Type I endometrial tumors include endometrioid histology which is usually seen in obese younger patients and attributed to hyperestrogenism while Type II tumors include poorly differentiated endometrioid adenocarcinomas, clear cell and serous types, and are commoner in older patients. These are generally not associated with hormonal influence (Hacker et al., 2015). Recently, a newer classification system based on The Cancer Genome Atlas (TCGA) was proposed (Kandoth et al., 2013; Bell and Ellenson, 2019). This recognizes four distinct EC subgroups based on their genomic features. The first group includes (POLE)-mutant EC, consisting of copy number-stable but ultra-mutated ECs with recurrent mutations in the exonuclease domain of POLE. The second group contains microsatellite instability (MSI) high EC, attributed to dysfunctional DNA mismatch repair (MMR) proteins MLH1, MSH2, MSH6, and PMS2. The third one consists of MMR-proficient ECs having mutations in genes associated with the PI3K/Akt and Wnt signaling pathways. The fourth type incorporates ECs with high frequencies of somatic copy number alterations and TP53 mutations.

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Grade 3 endometrioid cancers as well as serous carcinomas are included in this group.

Serous cancers, accounting for the majority of Type 2 cancers, have been identified as a distinctive variety of EC with unique clinical and pathologic characteristics marked by an aggressive clinical course (Rose, 1996). Though they constitute less than 10% of all endometrial cancers, they are implicated in more than 50% of recurrences and deaths attributed to endometrial carcinoma (del Carmen et al., 2012). Approximately 64% of women with uterine papillary serous cancer have the extrauterine disease (Hamilton et al., 2006) at presentation. Despite this, the management of women with serous endometrial cancer remains unclear. Optimal surgical staging (Creasman et al., 2004) is the standard of care followed by platinum-based chemotherapy (Slomovitz et al., 2003), chemoradiation (de Boer et al., 2018; Moore and Fader, 2011), or adjuvant radiation alone (Burke et al., 2014); these all have been found to be beneficial in prolonged recurrence-free survival and survival. In advanced stages with ascites and peritoneal spread with omental involvement, neoadjuvant chemotherapy followed by surgery is an option. Notwithstanding the different therapeutic modalities, the overall survival outcomes are dismal (Hamilton et al., 2006).

The rarity of the tumor has been an obstacle in conducting studies addressing this EC subtype exclusively and hence no definite guidelines exist regarding their diagnosis and management. So this study was conducted with the aim of primarily looking into the clinicopathological profile of the patients diagnosed with serous carcinoma and the treatment modalities received by them. The secondary objectives were to review their survival outcomes.

2. Materials and methods

This was a retrospective analysis from a tertiary care center in Southern India. We reviewed the medical records of all patients who were diagnosed with serous endometrial cancer in our institute from January 2010 through September 2019 after approval from the institutional review board. Patients with all histologies other than serous including uterine mesenchymal tumors as well as a metastatic disease were excluded from the study.

Clinical details were retrieved from online electronic medical records. Demographic details, pre-operative investigations, endometrial histology at the initial visit, and intraoperative details were looked into. Pathological details on the size of the tumors inspected during gross examination, post-operative histology including the extent of myometrial invasion and lymphovascular involvement as well as the surgical stage were looked into. The rate of optimal debulking in advanced cases was analyzed. Details regarding adjuvant therapies were also extracted. On follow-up visits, response to treatment or clinical or radiological evidence of recurrence was documented using the Response Evaluation Criteria in Solid Tumours ((RECIST, Version 1.1). Data regarding survival were collected through electronic mail or telephonically in case of patients unable to come for review.

Pre-operative evaluation included an endometrial biopsy and a transvaginal ultrasound (transabdominal in unmarried patients) as an outpatient evaluation. Immunohistochemistry (IHC markers) were not found in preoperative specimens except in a few doubtful cases. An abdominal ultrasound was done to look for any extrauterine spread of disease and if deemed necessary, a contrast-enhanced CT scan was done. The preoperative workup included complete blood counts, renal and liver function tests, a plain radiograph of the chest, and an electrocardiogram. Baseline serum CA125 was done in selected cases where the extrauterine spread of the tumor was suspected. Surgery as the primary treatment modality was considered in patients who were medically fit, had a good performance status, and did not have signs of disseminated disease on imaging. Those with disseminated disease at presentation were given neoadjuvant chemotherapy after discussion in a multidisciplinary tumor board meeting. A full surgical staging procedure comprising of peritoneal washings /ascites for cytology, total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy or omental biopsies, and pelvic and *para*-aortic lymph node dissection with or without peritonectomy were done for the women who were found to have poorly differentiated type 1 or any type 2 histology in their pre-operative biopsies. In some cases where pre-operative biopsies showed non-serous or early-stage disease, subsequent plans on staging procedure were upgraded based on intraoperative frozen section or the degree of myometrial invasion on a cut specimen. The decision for adjuvant therapy was taken after a discussion in the tumor board meeting with post-operative biopsy.

2.1. Statistical analysis

Descriptive statistics of the mean (SD) frequency and percentages were determined. The log-rank test was used to compare the survival probabilities over time. The Cox proportional hazards regression analysis was used to identify the prognostic factors for overall survival and disease-free survival. The overall survival (OS) of the patients was calculated as the time (in months) from the date of surgery to the date of death. Recurrence-free survival (RFS) was calculated as the time (in months) from the date of surgery to the documented first recurrence. If there was no documented recurrence, RFS was calculated from the date of surgery to the date of the last follow-up or death. Follow-up was taken till the time patients had come for a check-up in the hospital. Survival probabilities for different variables were plotted using the Kaplan-Meier curves. A p-value of < 0.05 was considered statistically significant. All analyses were done using Statistical Package for Social Services (SPSS) software Version 21.0 (Armonk, NY; IBM Corp).

3. Results

During the study period, we had around 564 cases of endometrial cancer out of which serous endometrial malignancies were diagnosed in 32(5.7%) patients. The majority [29 (91%)] of them were operated upon at our institute whereas 3 (9%) of them were operated elsewhere. The mean age of the patients was 62.5 years (SD7.6), and the mean BMI was 26.4 kg/m2 (SD 4.6). A majority (84%) of the patients were parous and all were postmenopausal at the time of presentation. The normal menstrual pattern was reported in 23(72%) of them and none had a history of any exogenous hormone intake. Two of our patients (6.3%) had a prior personal history of breast carcinoma and were on Tamoxifen and Letrozole following surgery and chemoradiation. Another patient had a prior history of rectal carcinoma. Among the subjects, 3 (9%) had documented family history of malignancies, and 6 first or second-degree relatives were diagnosed with oesophageal (1 each of first and second-degree), breast (2 first-degree), stomach, and colon malignancies (2 s-degree). Postmenopausal bleeding was the commonest presenting symptom reported by 26(81%) patients while 3(9%) complained of lower abdominal pain in addition to post-menopausal bleeding. CA 125 was done preoperatively in 11(34%) of the subjects only and mean values were 47.4 IU/ml (SD 18) (Table 1).

Preoperatively serous histology was confirmed in only 5(14%) of the 32 serous/ mixed serous with endometrioid tumors. The mean endometrial thickness measured was 12 mm (SD 8). Surgery was the primary treatment modality in 31(96%) patients while one had received neoadjuvant chemotherapy because of extensive disease (Stage IV B) followed by interval cytoreduction after three cycles. Of the patients undergoing upfront surgery, a majority (97%) had a staging laparotomy followed by total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy with or without pelvic and *para*-aortic lymph node dissection while 1(3%) had a completion surgery after an incomplete surgery elsewhere. Lymphadenectomy was done in 75% of patients in our series. Peritoneal cytology was negative in 24(75%) patients of whom 2(6%) had positive cytology. The median number of lymph nodes sampled was 14 (Range 0–27) (Table 2).

A gross examination of the surgical specimens revealed the mean size

Table 1
Demographic and clinical variables.

Demographic and clinical parameters	Numbers (%)
Mean age (SD, in years)	62.5 (7.6)
Mean BMI (SD, in kg/m^2)	26.3(4.6)
Parity	
Parous	27(84%)
Nulliparous	5(16%)
Comorbidity	
Hypertension	17(53%)
Diabetes	14(44%)
Pre op histology	
Well differentiated endometrioid	8(25%)
Moderately differentiated endometrioid	9(28%)
Poorly differentiated endometrioid	6(19%)
Serous	5(16%)
Poorly differentiated endometrioid with clear cell features	2(6%)
No biopsy	2(6%)
Clinical features	
Post menopausal bleeding	26(81.2%)
Post menopausal bleeding with abdominal pain	3(9.3%)
Abdominal pain	2(6.2%)
No symptom	1(3.1%)

Table 2
Surgical parameters.

Variables	Numbers (%)
Types of surgery	
TAH ± BSO	4(12.5%)
TAH + BSO + Omentectomy/Omental biopsy	4(12.5%)
TAH + BSO + PLND	6(18.8%)
TAH + BSO + PLND + PALND	7(21.9%)
TAH + BSO + PLND + PALND + Omentectomy	9(28.1%)
Completion:PLND + PALND + Omentectomy	1(3.1%)
RH + BSO + PLND + PALND + Omentectomy	1(3.1%)
Peritoneal cytology	
Positive	2(6.2%)
Negative	24(75%)
Unsatisfactory	2(6.2%)
Not done	4 (12.5%)
Cytoreduction	
Optimal	27(84.3%)
Suboptimal	5 (15.6%)

TAH BSO: Total abdominal hysterectomy bilateral salpingo-oophorectomy; RH: Radical hysterectomy; PLND: Pelvic lymph node dissection; PALND: Para-aortic lymph node dissection.

of the tumors to be 3.4 cm (SD 2). High-grade serous carcinoma was the commonest histology found in 25 (78.1%) of the post-operative specimens while the rest were of mixed histology (Table 3). Out of 27(84%) biopsy specimen evaluations with immunohistochemical markers, p53 positivity was found in 12 (37.5%) cases; Vimentin was positive in 4 (12.5%) and only 2 patients had Her2 neu testing both of whom were negative. In about half the patients the disease was Stage I disease (50%).

The majority of our study population received adjuvant therapy post-operatively. Adjuvant chemotherapy and radiation was received by 21 (65.6%) patients with 4–6 cycles of 3 weekly Carboplatin (AUC 5–6) and Paclitaxel (175 mg/m2) followed by radiation (50.4 Gy in 25 fractions as external beam therapy along with three fractions of high-dose-rate brachytherapy of 7 Gy each). Only chemotherapy was administered in 6(18.7%) while 5 (15.6%) did not receive any adjuvant. The types of radiation received by the patients were in accordance with the GOG 99 protocol. No patient received only radiation as an adjuvant.

Recurrences were seen in 13(40%) of the patients of which 11 expired. Overall survival of the patients recruited in our study was found to be 36 months (95% CI 10.1–61.8 months). Median recurrence-free survival was 22 months (95% CI 1.36–42 months), while the median follow-up period was 27 months (95% CI 4.0–49.5 months) (Table 4).

Table 3
Histopathological variales and FIGO staging.

Pathological variables	Numbers (%)
Postoperative biopsy	
Pure Serous	25(78.1%)
Mixed	
Moderately differentiated endometrioid + serous	1(3.1%)
Poorly differentiated endometrioid + serous	5(16.5%)
Lymphovascular space invasion (LVSI)	
Yes	15 (46.9%)
No	17 (53.1%)
Myometrial Invasion	
<50%	14(43.8%)
≥50%	17(53.1%)
Parametrial involvement	
Yes	4(12.5%)
No	20(62.5%)
Not commented	8(25%)
Immunohisto chemistry	
p53(+)	12(37.5%)
Vimentin(+)	4(12.5%)
ER(−)	9(28%)
FIGO Stage	
I	16(50%)
III	11(34.5%)
IV	5(15.6%)

Table 4
Patterns of recurrence.

Stage	Adjuvant therapy received	Site(s) of recurrence	Outcome
I B	Chemo RT	Retroperitoneal nodes (Para aortic)	Alive
	Chemo RT	Supraclavicular nodes,lungs	Dead
	Chemo	Retroperitoneal nodes,lungs	Dead
	Chemo	Vaginal vault	Dead
	Not taken	Retroperitoneal nodes (External and common iliac)	Dead
	Not taken	Liver	Dead
IIIA	Chemo RT	Retroperitoneal nodes (External and common iliac)	Dead
	Chemo	Lungs	Dead
IIIC	Chemo RT	Lungs	Dead
	Chemo RT	Omentum	Dead
IV A	Chemo	Lungs	Alive
IV B	Chemo	Retroperitoneal nodes	Dead
	Not received	Retroperitoneal nodes	Dead

Chemo RT- chemotherapy and Radiation Therapy.

Analyses using the Cox proportional hazards regression model showed that the surgical stage, as well as the adjuvant treatment received, were

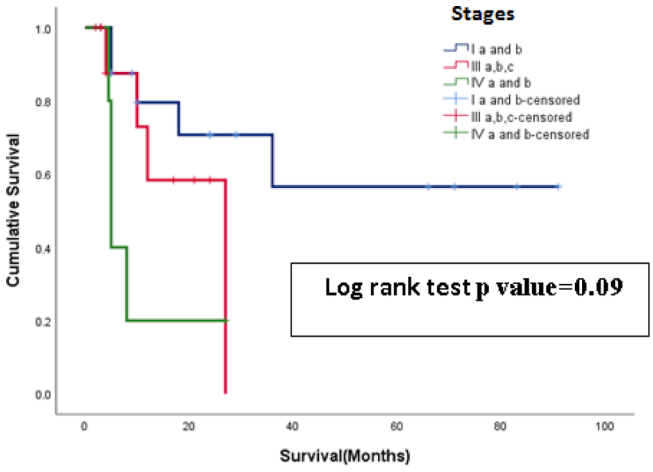

Fig. 1. Kaplan–Meier curve showing overall survival with Stage of the disease.

statistically significant predictors of overall but not disease-free survival as shown in the Kaplan Meir curves (Figs. 1 and 2). Other clinicopathological features like myometrial invasion and lymphovascular space invasion or even the comprehensive surgical staging were not found to be significant in predicting survival. At the completion of our study, 19 (60%) patients were alive. While 11(34.3%) deaths occurred due to recurrent disease, 1(3.2%) patient had succumbed to progressive disease, and 1(3.2%) died of natural causes.

4. Discussion

Serous endometrial cancers have been recognized as a rare subgroup of endometrial carcinomas with features different from the commoner endometrioid histology. The diagnosis and management of these cancers have always been challenging due to their distinctive histopathologic characteristics. This subtype has generally a poor prognosis (Nicklin and Copeland, 1996) and its aggressiveness is similar to high-grade serous carcinoma of the ovary with a propensity to involve peritoneal surfaces and rapid metastasis (Hendrickson et al., 1982).

These tumors are more common in older age group women with a lower BMI (del Carmen et al., 2012). In our series serous endometrial cancers comprised 6% of the total endometrial cancers with a mean age of 62 years at presentation. There was a significant familial tendency as 50% of the patients had either a family history of breast, ovarian, bowel, or endometrial cancer in a first-degree relative or a personal history of treatment for breast carcinoma with tamoxifen therapy (Gitsch et al., 1995).

Diagnosing serous carcinoma preoperatively on biopsy specimens has been found difficult due to the serous cancers mimicking a wide spectrum of histological pictures from well-differentiated adenocarcinomas to the clear cell variety (Hendrickson et al., 1982). The diagnosis of serous cancers on such biopsies was less specific when compared to other high-grade endometrial histologies. Unlike high-grade endometrioid histologies which express ER, PR positivity, and inactivation of the PTEN suppressor gene, serous carcinoma is mostly p53 positive and in some cases demonstrates HER-2neu gene amplification (Murali et al., 2019; Santin et al., 2002). In our study of these uterine papillary serous carcinomas, 78% percent had pure tumors while 22% had admixed endometrioid components, (). According to GOG criteria, serous tumors classified as mixed type should have more than 50% serous histology (del Carmen et al., 2012). However, a recent study reported that serous tumors with even a minor component (<10%) also had poorer prognoses as compared to grade 3 pure endometrioid histology (Boruta et al., 2004). The patients with mixed histologies behaved as aggressively as pure serous histologies.

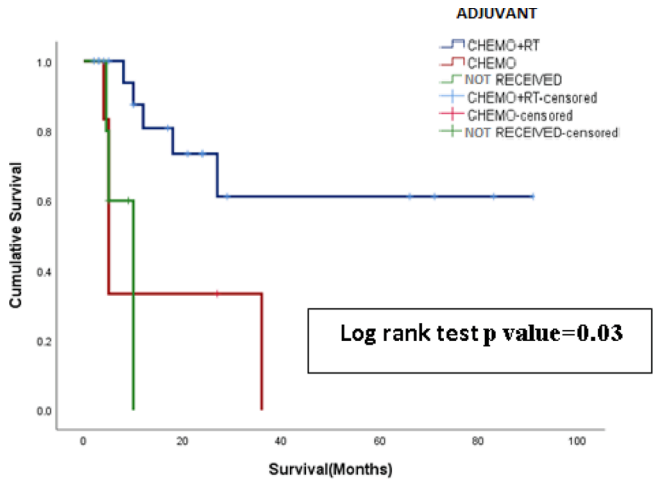

Fig. 2. Kaplan–Meier curve showing overall survival with adjuvant treatment received.

Serous carcinoma could be detected in preoperative histology in only 16% of the patients. This could have been the reason behind all the patients not undergoing comprehensive surgical staging in a few of them. Endometrial thickness may also be misleading as serous carcinomas often arise in the background of endometrial atrophy (del Carmen et al., 2012). In a study of type 2 endometrial cancers, the endometrial thickness was found to be ≤ 35% while it was < 4 mm in 17% (Wang et al., 2006). The mean thickness of the endometrium in our group was 12 mm. CA 125 has been favored in some studies as having some role in the pre-operative evaluation of patients with uterine papillary serous carcinoma but its importance has not been proven (Olawaiye et al., 2008). Other markers like HE4, Prolactin, and YKL-40 have been proposed but none of them could be validated (del Carmen et al., 2012).To increase the detection of serous carcinomas use of molecular markers and immunohistochemistry in doubtful histology of preoperative biopsies can be utilized. That would help in accurate counseling and treatment planning with comprehensive surgical staging and optimal cytoreduction with a better survival outcome for the patients with these cancers.

No definite consensus has been arrived at regarding the management of uterine serous carcinomas as the data is mostly from retrospective studies. Complete surgical staging in early stages or debulking in cases of advanced-stage disease is the treatment of choice as initial management (del Carmen et al., 2012; Boruta et al., 2009). Neoadjuvant chemotherapy has also been suggested for patients who were poor candidates for upfront surgery (de Lange et al., 2019). Selective surgical staging based on uterine features such as myometrial invasion or lymphovascular space invasion has not been encouraged as most patients present with extrauterine disease and up to 70% of cases of metastatic disease may be detected only with the comprehensive surgical staging (Boruta et al., 2009). A study evaluating women with high-risk endometrial cancers including serous histology by sentinel lymph node biopsy followed by both pelvic and *para*-aortic lymphadenectomy found 95% sensitivity with a negative predictive value of 98% supporting its use even in high-risk patients (Soliman et al., 2017). Lymphadenectomy was found to have therapeutic benefits in these tumors (Chan et al., 2006). Two-thirds (77.4%) of our patients underwent lymphadenectomy of whom 29.1% had positive nodes. Recently, researchers have found comprehensive pelvic lymph node dissection along with paraaortic lymph node sampling (Li et al., 2020). As uterine serous cancers tend to metastasize to peritoneal surfaces, omentectomy and peritoneal biopsies have been recommended in some studies whereas others have not favored omentectomy as it was not found to be associated with better overall and cause-specific survival in serous carcinoma. The added benefit of these procedures was to establish staging accuracy with minimal perioperative morbidity (Geisler et al., 1999; Gehrig et al., 2003). Optimal cytoreduction (≤1 cm maximal diameter of the largest residual tumor nodule) has shown an improved median survival (Moller et al., 2004). Our study detected 50% of the patients to be in advanced stages(III and IV) at presentation but had optimal cytoreduction in 84.3%. An average of 10 and 3–4 nodes per side were dissected in the pelvic and *para*-aortic basin, respectively. This is an important component of staging and was at par with the literature (Li et al., 2020).

Adjuvant therapy in these patients has been an area of debate as to whether chemotherapy alone is better versus chemotherapy with radiation. National Comprehensive Cancer Network (NCCN) guidelines as well as the recently published ESMO/ESTRO guidelines on management of endometrial cancers recommend observation for very early-stage IA serous endometrial cancers without myometrial invasion (Concin et al., 2021). Chemotherapy with or without vaginal brachytherapy and External Beam Radiation Therapy with or without vaginal brachytherapy could be considered for IA myoinvasive as well as IB or greater disease (Koh et al., 2018). Recent literature has emphasized the survival benefit of adjuvant chemotherapy (with or without radiotherapy) even for uterine serous carcinoma confined to the endometrium while there was no difference in subjects who underwent observation versus

radiation only (Nasioudis et al., 2020). Another study demonstrated that adjuvant Carboplatin Paclitaxel chemotherapy with concurrent intravaginal radiation (IVRT) yielded good outcomes in stage I–II uterine serous carcinomas (Kiess et al., 2012). Adjuvant chemotherapy is mostly preferred in serous cancers with any myometrial invasion due to their invasive nature (Charo and Plaxe, 2015).

The GOG 249 study included stages I or II serous endometrial tumors along with intermediate and high-risk endometrioid histologies and randomly assigned them to either pelvic radiation(RT) or vaginal brachytherapy (VCB) followed by intravenous Paclitaxel with Carboplatin for three cycles. The combined treatment was not found to be superior to pelvic RT but led to more severe toxicity. Hence the authors opined that pelvic RT alone could be considered sufficient as an adjuvant treatment even in high-risk early-stage (Stage I&II) endometrial carcinomas of all histologies with the exclusion of chemotherapy (Randall et al., 2019). In the PORTEC III study, women with high-risk endometrial cancer including stage I-III and serous/clear cell histology received either pelvic radiotherapy alone or chemoradiotherapy and chemotherapy (consisting of two cycles of Cisplatin given during radiotherapy, followed by four cycles of Carboplatin and Paclitaxel). The chemoradiation group recorded a higher progression-free survival but there was no effect on overall survival. The effect on survival seemed to be more obvious in the non-endometrioid (serous and clear cell) and advanced stage disease. An updated analysis of the same study concluded significantly improved overall survival and failure-free survival with chemoradiotherapy versus radiotherapy alone across all groups of high-risk endometrial cancer and this option has to be offered as treatment in these groups (de Boer et al., 2018; de Boer et al., 2019).

Recently, biomarkers and molecular alterations have emerged as attractive targets to guide newer treatment modalities like immunotherapy. The importance of presence of the surrogate marker for TP53, i.e. p53 on IHC, has gained importance after the incorporation of the TCGA molecular subtypes into the risk groups for adjuvant therapy. Based on that, these serous tumors may be proven to be p53 positive and hence categorized as High intermediate/ high risk indicating the need for adjuvant chemotherapy. In a multicentre, randomized phase II trial comparing Carboplatin Paclitaxel with or without Trastuzumab in advanced or recurrent uterine serous carcinoma patients overexpressing HER 2 neu, the addition of Trastuzumab to chemotherapy was found to increase progression-free survival (Fader et al., 2018). Another study documented increased PD-L1 expression in about 33% of patients with Type II endometrial cancers (Mo et al., 2016). This has been explored in several reports and initial results were in favor of the checkpoint inhibitor, Pembrolizumab (an anti-PD L1 monoclonal antibody) as a treatment for advanced endometrial cancer (Ott et al., 2017). The recent NCCN guidelines advocate using Trastuzumab along with platinum and taxane-based chemotherapy as the preferred regimen in advanced or recurrent HER2-positive uterine serous carcinomas. Also, a combination of Pembrolizumab (a PD-1 inhibitor) and Lenvatinib, a multi-kinase inhibitor has also proven beneficial in improving OS and PFS in women with serous endometrial cancers (Ferriss et al., 2021). As our study entailed patients diagnosed between 2010 and 2019 when the guidelines for HER2 Neu testing were not very clear, it had not been done in majority of them. Even so, HER 2 neu remains an important therapeutic target in patients diagnosed with serous endometrial cancers.

Majority of our patients received adjuvant treatment in the form of chemoradiotherapy irrespective of the stage of the disease. Platinum-based chemotherapy with either EBRT or VBT or both was used in our study. Combined treatment was found to be a prognostically significant factor in predicting overall survival signifying the importance of adjuvant treatment even in the early stages emphasized in literature (Nasioudis et al., 2020; Kiess et al., 2012; Huang et al., 2014) and patients receiving adjuvant chemoradiation did better than other patients. Our median overall survival and follow-up period of 36 and 27 months, respectively, were in keeping with existing data (Bristow et al., 2001; Benito et al., 2009; Wang et al., 2018; Rauh-Hain et al., 2010). Recurrence developed in 40% of our subjects as seen previously (Havrilesky et al., 2007) while our median recurrence-free survival was also comparable to studies (Hoskins et al., 2001). The stage of the disease at presentation was found to be statistically significant in predicting survival while optimality of cytoreduction or other clinicopathological features like lymph node status, LVSI, and depth of myometrial invasion were not significant in contrary to existing studies (Slomovitz et al., 2003; Bristow et al., 2001). The advanced stage at diagnosis was a poor prognostic factor in our participants.

The major drawback of our study was the retrospective design with a small sample size. The lack of immunohistochemistry details of the specimens was also a hindrance. Nevertheless, our study was a small step towards highlighting the factors influencing the management of patients diagnosed with serous endometrial carcinoma. Prospective multicentric trials concentrating solely on this histology with immunohistochemistry and molecular classifiers in correlation with adjuvant treatment modalities and optimal adjuvant therapy are the need of the hour.

5. Conclusion

Serous endometrial carcinomas are aggressive endometrial tumors with distinctive clinicopathological features associated with high recurrence and mortality rates. Comprehensive surgical staging with optimal cytoreduction should be aimed at. The tumors need to be typed upfront using molecular classification. Adjuvant therapy with chemoradiation could be considered in all the stages as it extended a survival benefit. Alternate targeted therapies could be of great implication in these tumors.

CRediT authorship contribution statement

Amrita Datta: Conceptualization, Methodology, Data curation, Validation, Writing – original draft. **Vinotha Thomas:** Writing – review & editing. **Rachel George:** Writing – review & editing. **Anitha Thomas:** Conceptualization, Methodology, Data curation, Validation, Writing – original draft. **Thomas Samuel Ram:** Visualization, Investigation, Resources, Supervision, Writing – review & editing. **Sherin Daniel:** Investigation, Validation, Writing – review & editing. **Abraham Peedicayil:** Visualization, Investigation, Resources, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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