



Marguerite Bride. *West Cornwall Station*. Watercolor, 8" × 11".

The pathology, epidemiology, prognosis, operative and postoperative management, and research frontiers are reviewed for the most common non-endometrioid endometrial carcinomas.

Non-Endometrioid Adenocarcinoma of the Uterine Corpus: A Review of Selected Histological Subtypes

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Background: Understanding the etiology, presentation, evaluation, and management of selected non-endometrioid endometrial adenocarcinomas of the uterine corpus is needed to define optimal treatment regimens.

Methods: The pathology and treatment of selected non-endometrioid endometrial adenocarcinomas of the uterus are reviewed and summarized.

Results: The most common non-endometrioid histology is papillary serous (10%), followed by clear cell (2% to 4%), mucinous (0.6% to 5%), and squamous cell (0.1% to 0.5%). Some non-endometrioid endometrial carcinomas behave more aggressively than the endometrioid cancers such that even women with clinical stage I disease often have extrauterine metastasis at the time of surgical evaluation. Therefore, when technically and medically feasible, comprehensive surgical staging is helpful for women with non-endometrioid endometrial cancer histology. Comprehensive surgical staging includes hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, and cytological evaluation of the abdominal cavity. While whole abdominal radiotherapy has a limited role in early-stage uterine papillary serous carcinoma (UPSC) and clear cell carcinoma (CC), there may be a role for postoperative chemotherapy and volume-directed radiotherapy in both early-stage UPSC and CC. In the setting of optimally debulked advanced-stage disease, a combination of radiation and chemotherapy may be indicated. In the setting of recurrent disease or in women with residual disease after surgery, a platinum-based regimen or enrollment in a clinical trial is recommended.

Conclusions: UPSC and CC are managed similarly since sufficient data to separate treatment recommendations are lacking. Because both histologies are associated with a high rate of recurrence, adjuvant therapy is recommended even in women with early-stage disease. The remaining cell types should be treated similar to endometrioid or other low-grade histologies.

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Abbreviations used in this paper: UPSC = uterine papillary serous carcinoma, CC = clear cell carcinoma, UCCC = uterine clear cell carcinoma, PESCC = primary endometrial squamous cell carcinoma.

Introduction

Endometrial carcinoma is the most common gynecologic malignancy in the United States. In 2008, the American Cancer Society estimated that 40,100 women were diagnosed with endometrial cancer and 7,470 died of their disease.¹ In 1983, Bokhman² first proposed the hypothesis of two distinctly different forms of endometrial carcinoma and their associated differences in risk factors and prognosis. Type 1, or endometrioid carcinoma, was thought to represent an estrogen-stimulated progression, often arising in the setting of endometrial hyperplasia. Features of the type 1 carcinomas include increased exposure to estrogen (nulliparity, early menarche, chronic anovulation, and unopposed exogenous estrogen), obesity, and responsiveness to progesterone therapy. Patients more often are white, are younger in age, and have a better prognosis than their type 2 counterparts (Table 1).³ In contrast, type 2, or non-endometrioid carcinoma, often arises in those who are black, multiparous, and not obese. These tumors do not respond as well to progesterone therapy, and their prognosis is worse. The most common forms of type 2 endometrial cancer include uterine papillary serous carcinoma (UPSC) and clear cell carcinoma (CC). Other non-endometrioid histologies include mucinous and squamous cell carcinoma (Table 2).⁴ This review focuses on the pathology, epidemiology, prognosis, operative

Table 1. — Endometrial Carcinoma: Stages at Presentation and 5-Year Survival Rates

Endometrioid		UPSC/CC	
Present at earlier stage		Present at more advanced stage	
Stage I	73%	Stage I	54%
Stage II	11%	Stage II	8%
Stage III	13%	Stage III	22%
Stage IV	3%	Stage IV	16%
Survival Rates		Survival Rates	
Stage I	85%–90%	Stage I	60%
Stage II	70%	Stage II	50%
Stage III	40%–50%	Stage III	20%
Stage IV	15%–20%	Stage IV	5%–10%

Data from Dunton et al.³

Table 2. — Endometrial Carcinoma Subtypes

Histology	Number
Endometrioid	3,769 (87.4%)
Papillary serous	127 (2.9%)
Clear cell	94 (2.2%)
Mucinous	26 (0.6%)
Squamous cell	7 (0.2%)
Other	289 (6.7%)

Data adapted from Creasman et al⁴ from 4,312 patients treated between 1999–2001 and submitted to FIGO for inclusion in the Annual Report.

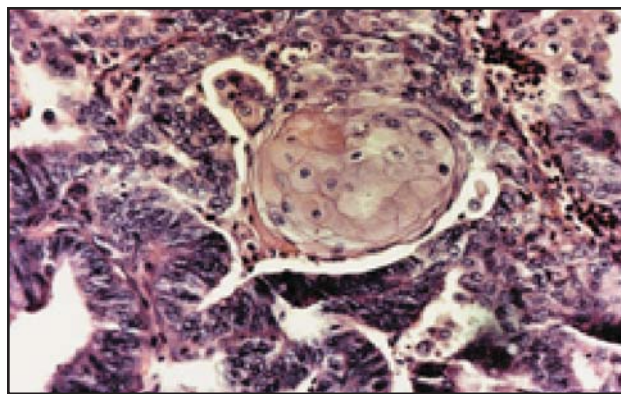


Figure. — Uterine papillary serous carcinoma. From Cavanagh D, Fiorica JV, Hoffman MS, et al. Adenocarcinoma of the endometrium: an institutional review. *Cancer Control*. 1999;6(4):354-360. Reprinted with permission.

and postoperative management, and research frontiers for the most common non-endometrioid endometrial carcinomas. Other forms of uterine endometrial carcinoma, including transitional cell, poorly differentiated, hepatoid, lymphoepithelioma-like, giant cell, neuroendocrine, and undifferentiated, which represent less than 1% of cases, are not discussed in this review.

Uterine Papillary Serous Carcinoma Pathology

UPSC was first described by Hendrickson et al,⁵ who noted histological similarity to ovarian papillary serous adenocarcinoma in 26 of 256 cases of endometrial adenocarcinoma. These cancers were found to have complex papillary architecture, with broad fibrous stalks underlying a tufted stratification of the epithelial lining, profound tumor necrosis, and unusually high amounts of vascular invasion. High numbers of mitotic figures and an increased nuclear-to-cytoplasmic ratio were also identified. Of these cases, 30% were found to have psammoma bodies. Not only is UPSC similar in gross histology to ovarian papillary serous carcinoma (Figure⁶), but also its mechanism of spread is similar in that UPSC tends to have significant peritoneal spread. In 1992, Sherman et al⁷ were the first to describe a precursor lesion to UPSC, similar to endometrial hyperplasia in type 1 carcinomas, designated endometrial intraepithelial carcinoma. In 2003, the World Health Organization adopted this nomenclature. Recently, endometrial glandular dysplasia (EmGD) has also been proposed as a precursor to UPSC. Fadare and Zheng⁸ described EmGD as a morphologically identifiable lesion in 53% of patients with UPSC. They also reported that EmGD was 10 times more common in UPSC than in benign hysterectomy samples.

Unlike type 1 endometrial cancers, which often possess a gene mutation of PTEN (a tumor suppressor gene) and higher incidence of microsatellite instability, both of which have been associated with an improved prognosis,^{9,10} UPSC is associated with an increased incidence of p53 and HER-2/neu overexpression and a loss

Table 3. — Molecular Alterations in Endometrial Carcinomas

Study	Marker	Type 1	Type 2	
			Serous	Clear Cell
Lax et al ¹¹ An et al ¹⁴	p53	Mutations rare	90% have mutations	14% have mutations
Liu ¹³ An et al ¹⁴	PTEN	80% have mutations	PTEN mutations rare	18% have mutations
Lax et al ¹¹	ER/PR	+	–	–
Liu ¹³	HER-2/neu	10%–30%	45% overexpression	N/A
Herzog et al ¹²	Chromosome 1p	N/A	63% loss of heterozygosity	N/A

N/A = not available, ER/PR = estrogen/progesterone receptor.

of heterozygosity at chromosome 1p, which were associated with a poorer survival compared with their negative counterparts (Table 3).¹¹⁻¹⁴

Because of its histological similarity to ovarian papillary serous carcinoma, researchers have investigated the use of CA-125 to monitor disease activity as well as recurrence. Unfortunately, the data are limited and often conflicting.^{15,16} Although more extensively evaluated in epithelial ovarian carcinoma, CA-125 may serve as a marker for disease progression or recurrence. The utility of monitoring CA-125 may be most useful when it is elevated preoperatively and when it can be monitored postoperatively.

Epidemiology and Prognosis

Compared with their counterparts with type 1 endometrial carcinomas, women with UPSC are typically older and black, with a tendency to be multiparous.^{4,5} While UPSC comprises approximately 5% to 10% of all endometrial cancers, it is responsible for almost 40% of endometrial cancer-related deaths.¹⁷ This is due in part to the fact that approximately 40% of UPSC cases present with stage III or IV disease. In addition, even women who present with early-stage disease often have a disease recurrence. Historically, women with stage I UPSC have a 5-year survival rate of 60% (Table 1). With comprehensive surgical staging, stage I disease survival may be as high as 80% for women with disease limited to the endometrium.¹⁷ The 5-year overall survival rate for all stages of UPSC is 53% compared with 83% for endometrioid carcinoma.^{4,18}

Operative Management for Early-Stage Disease: Comprehensive Surgical Staging

For type 1 endometrial cancers, risk factors that correlate with extrauterine spread include depth of myometrial invasion, grade, and lymphovascular space invasion.¹⁹ In contrast, these traditional risk factors do not apply to women with UPSC as those whose uterine disease is limited to the myometrium may still have metastatic disease.²⁰ As a result, it is imperative in the appropriate

clinical setting that comprehensive surgical staging be performed when UPSC is identified on preoperative biopsy or intraoperative frozen section. Unlike ovarian carcinoma, current International Federation of Gynecology and Obstetrics (FIGO) staging systems for endometrial cancer do not incorporate peritoneal biopsies or omentectomy. However, given the similarities in architecture, spread of metastases, and evidence for distant metastases in clinical stage IA UPSC, several studies have investigated this surgical approach and reported positive microscopic findings present in 20% to 25% of patients.²¹⁻²³ The majority of studies evaluating the role of comprehensive surgical staging for UPSC are limited by their retrospective nature and small numbers of cases.

Operative Management for Advanced-Stage Disease: Utility of Cytoreductive Surgery

Because of the similarities between UPSC and ovarian papillary serous carcinoma, authors have also investigated whether optimal surgical debulking (< 1-cm residual disease) provides a survival benefit in women with UPSC as it does for women with epithelial ovarian carcinoma. Though retrospective, two multi-institutional studies evaluated the role of cytoreductive surgery for stage III/IV UPSC.^{22,23} Both studies showed at least a trend toward a survival benefit in women who were optimally cytoreduced compared with women who had bulky residual disease.

Postoperative Management for Early-Stage Disease

Studies have investigated the use of chemotherapy alone, radiotherapy alone, or a combination of the two. In a prospective trial, the Gynecologic Oncology Group (GOG) studied 21 women with early-stage UPSC (stage I/II) treated with whole abdominal radiotherapy. They found that 8 of 19 evaluable women died of disease recurrence, with over half of recurrent sites within the field of therapy. They concluded that chemotherapy should at least be incorporated into the treatment regimen for UPSC.²⁴ P32 with vaginal brachytherapy has also been investigated in a study that examined early-stage UPSC

and CC. Seventeen women were evaluated with a 2-year overall survival rate of 89.2% for all enrolled patients.²⁵

Several retrospective studies of single-modality adjuvant therapy in women with early-stage UPSC have been reported. In a retrospective, multi-institutional study, Huh et al²⁶ investigated 60 women who underwent adjuvant radiation, platinum-based chemotherapy, or no therapy. The observation group and the adjuvant radiotherapy group had similar risk of recurrence and overall survival. Interestingly, there were no recurrences identified in the adjuvant chemotherapy group. In a retrospective, multi-institutional study, Dietrich et al²⁷ examined 29 patients with stage I disease, 21 of whom received paclitaxel and carboplatin and 8 of whom received other platinum-based chemotherapy. They found that 20 of the 21 patients who received paclitaxel/carboplatin were disease-free (1 had a recurrence, which was treated with chemotherapy and brachytherapy and is now disease-free), with a disease-free survival ranging from 10 to 138 months (mean = 41 months)⁵. Havrilesky et al¹⁷ conducted a large two-center retrospective review of early-stage UPSC. They concluded that women with stage IB/IC disease had a 29% risk of recurrence and that due to the limited role of radiotherapy, systemic therapy is indicated.

As with single-modality therapy, data regarding combination radiotherapy and chemotherapy are limited. Three trials, all from the same institution, have been summarized in the group's most recent publication, which involved 74 patients with stage I UPSC who underwent complete surgical staging followed by adjuvant platinum-based chemotherapy as well as vaginal cuff brachytherapy. While the authors noted that their study was underpowered to detect a difference between platinum-based chemotherapy alone or the combination of vaginal brachytherapy with chemotherapy, they did note a decrease in recurrence as well as an increase in overall survival, both of which were statistically significant, when compared to abdominopelvic radiation or observation.²⁸ In the largest trial to date, Fader et al²⁹ evaluated 129 women with surgically staged I/II UPSC. This study evaluated the effect of adjuvant platinum/taxane chemotherapy with or without radiation in a study involving nine centers. The authors concluded that women with stage I/II disease have a high rate of recurrence in the absence of postoperative therapy (IA = 15.7%, IB = 42.9%, IC = 50%, IIA = 25%, IIB = 100%). However, with platinum and taxane-based chemotherapy with or without volume-directed radiotherapy, the median recurrence rate dropped to 9.6%.

Postoperative Management of Advanced-Stage Disease

Treatment algorithms for advanced-stage disease have also looked at the use of chemotherapy, radiotherapy, or a combination of both. However, as with early-stage disease, the

studies that have examined these regimens and their outcomes are usually retrospective, from a single institution, and limited by sample size. Even the prospective cooperative group trials are limited as they tend to have a relatively small number of women with UPSC enrolled.

For women with advanced-stage disease, the chemotherapy has focused on platinum-based combinations. Zanotti et al³⁰ reported on 18 evaluable women who received paclitaxel and carboplatin for either initial adjuvant therapy or known residual disease, with response rates of 89% in the adjuvant group and 64% in the recurrent disease group. Most studies investigating advanced-stage disease concur with the interpretation that chemotherapeutic regimens are superior in the setting of adjuvant chemotherapy or those with residual disease.³⁰⁻³²

Radiotherapy alone for advanced-stage disease has also been investigated. Grice et al³³ studied 17 women, 8 with stage IIIC disease and 9 with stage IV disease. Four of the 8 patients with stage IIIC disease were alive with evidence of disease at a median of 52.5 months. Three of the 4 patients who received solely radiotherapy died of their disease, with a median time to death of 13 months. Gehrig et al³⁴ compared platinum-based therapy to radiotherapy in a retrospective study of 21 women. They noted statistically significant improvements in outcomes of women receiving chemotherapy over radiotherapy, with increases in time to progression (5.3 months vs 12.4 months, respectively) and mean time to death (8 months vs 18 months, respectively). As part of GOG-94, Sutton et al³⁵ performed a prospective phase II study of whole abdominal radiotherapy for all types of stage III/IV endometrial cancer. The authors concluded that there is a need to add systemic therapy, either concomitantly or sequentially, to the radiation therapy.

Adjuvant therapies that have combined radiotherapy and chemotherapy have also been studied. A single-institution phase II trial of women with advanced-stage UPSC was performed using "sandwich" therapy, in which patients received 3 cycles of paclitaxel/carboplatin (PC) followed by pelvic and volume-directed radiation therapy followed by an additional 3 cycles of PC. Nine patients received this regimen, with progression-free survival of 46 months. Similarly, Low et al³⁶ examined 13 women with advanced-stage UPSC. Women were treated with 4 cycles of PC or epirubicin/cisplatin followed by whole pelvic and vaginal brachytherapy. The stage III 5-year overall survival rate was 59%. In a retrospective multi-institutional trial, Alvarez Secord et al³⁷ evaluated 356 women with advanced endometrial cancer, including 86 who had UPSC. Women with UPSC had a worse progression-free survival (hazard ratio [HR] = 1.55) and overall survival (HR = 1.78) compared to women with other histological subtypes. The GOG recently conducted a prospective phase III study, GOG-184, which closed in 2004, to

evaluate the role of volume-directed radiotherapy followed by cisplatin and doxorubicin with or without paclitaxel. Of the 552 women who were eligible in this study, 18% had either UPSC or CC. These women had an increased risk of death (UPSC = 4.43, CC = 3.45) compared to the women with endometrioid histology.³⁸ The final results of this trial are not yet available to determine if there are any differences in patterns of failure or responsiveness to chemotherapy between the groups. GOG-122 was a randomized phase III trial of whole abdominal radiotherapy vs doxorubicin and cisplatin in women with advanced endometrial carcinoma. The authors concluded that chemotherapy was superior to whole abdominal radiation in this patient population. Of the 422 women enrolled, 83 had UPSC. Similar to the other studies, the women with UPSC had an increased risk of recurrence (HR = 1.39) and death (HR = 1.56) compared to all other histologies.³⁹

Uterine Clear Cell Carcinoma

Pathology

Uterine clear cell carcinoma (UCCC) was first described by de Bonneville in 1911.⁴⁰ It is characterized by the clearing of cellular cytoplasm (glycogen) and configured in an array of shapes and patterns ranging from solid and glandular to papillary structures. One group studied 16 cases of UCCC and found PTEN mutations in 3 of 14 cases of UCCC (2 cases were pure UCCC and 1 case was mixed UCCC/endometrioid histology). The PTEN mutations resulted in missense, frameshift, or nonsense mutations. Microsatellite instability was seen in 2 of 14 cases, with loss of heterozygosity in 4 cases. Strong nuclear expression of p53 was found in 5 of 16 cases, but only 1 of 11 pure UCCC showed a mutation in p53 (Table 3).¹⁴

Epidemiology and Prognosis

While diethylstilbestrol (DES)-exposed CC of the vagina and cervix is generally seen in young premenopausal women, UCCC is almost exclusively seen in the postmenopausal period and generally is more aggressive. The mean age of diagnosis is 68 years, which is similar to that for UPSC. Patients with UCCC are more likely to be black, present with higher-stage disease, and have a worse survival than patients with endometrioid carcinoma (Table 1).⁴¹ The recurrence rate is approximately 50% at 3 years.⁴² The 5-year survival rate for UCCC ranges from 79% for early disease to 21% for advanced disease.⁴³ Although UCCC accounts for only 4% of uterine cancers, it accounts for approximately 8% of uterine cancer-related deaths.⁴⁴

Operative Management for Early-Stage Disease: Comprehensive Surgical Staging

As with patients with UPSC, comprehensive surgical staging in UCCC is paramount in order to direct appropriate adjuvant therapy. Patients should undergo total

hysterectomy, bilateral salpingo-oophorectomy, comprehensive pelvic and para-aortic lymphadenectomy, pelvic and abdominal cytology, and resection of gross disease. In a retrospective study by Thomas et al,⁴³ 99 patients were identified with UCCC, 69 of whom showed no gross extension of cancer beyond the corpus. However, on final pathologic inspection, 36 patients (52%) had extension beyond the pelvis and 20% were upstaged due to lymphatic spread. Patients with endometrioid histologies typically present with early-stage disease, especially low-grade histology (75%). However, patients with UCCC present with true stage I disease in only 30% of cases.^{42,45}

Operative Management for Advanced-Stage Disease: Utility of Cytoreductive Surgery

Several retrospective studies have evaluated the success of treatment in advanced-stage UCCC. In those patients with gross extrauterine disease, attempts at optimal cytoreduction are critical. The absence of residual disease is an independent predictor of survival in stage III/IV disease. Thomas et al⁴³ compared patients with and without gross residual disease and reported a statistically significant improvement in progression-free survival (7 vs 17 months, respectively) and overall survival (18 vs 40 months, respectively). Factors that can serve as independent prognostic indicators of survival are myometrial invasion and lymphovascular space invasion. Abeler and Kjørstad⁴⁰ studied 97 patients with UCCC. Of those tumors with positive lymphovascular space invasion, only 17% survived 5 years and 8% survived 10 years. The further importance of meticulous cytoreductive surgery can be illustrated by a GOG study that reported no long-term survivors among those left with residual disease. Despite adjuvant whole abdominal radiation, median progression-free survival was 4.8 months.³⁵

Postoperative Management for Early-Stage Disease

Treatment for stage I/II disease has typically been composed of adjuvant radiation, and much of the available information has been translated from the treatment of UPSC and grade III uterine cancers. Data on the exclusive adjuvant treatment of UCCC are limited because many of the studies have combined UPSC and UCCC in their analysis, and many of these tumors are of mixed histologies. Two retrospective studies have evaluated radiotherapy for UCCC. Cirisano et al⁴⁴ reported on 38 patients with UCCC who were treated with primary surgery. Twenty-two patients underwent radiation therapy (13 received whole-pelvic radiation therapy, 2 underwent vaginal brachytherapy, and 7 received both). The authors noted no recurrences in the radiation field. Another study examined 22 patients who underwent comprehensive staging.⁴³ Eleven patients received no adjuvant therapy and 11 received additional therapy

after surgery (5 external beam radiation therapy, 2 vaginal brachytherapy, and 4 chemotherapy). At 44 months of follow-up, only 1 patient in the adjuvant therapy cohort recurred at the vaginal cuff. Among 27 patients with stage I or II disease, 9 patients recurred, with 6 patients having received no adjuvant therapy. These data suggest that adjuvant radiotherapy may provide local disease control.

Postoperative Management of Advanced-Stage Disease

Management of advanced-stage UCCC is similar to that of UPSC. There are currently no randomized trials specifically evaluating UCCC and much of the data available is from retrospective studies that include UPSC with or without UCCC, and often the number of women with UCCC is so limited that no separate conclusions can be drawn.³⁴ For example, GOG-122 included only 17 women with UCCC. In this study of whole abdominal radiation vs cisplatin and doxorubicin, women with UCCC did not have an increased risk of recurrence or death compared to their endometrioid counterparts. However, validation of this risk is difficult since the study was not powered to determine this.³⁹ Thomas et al⁴³ reported on 11 patients with stage IIIA disease and noted a 67% risk of recurrence at 41 months, with the majority of patients suffering lymphatic or hematologic spread, thus suggesting a role for adjuvant chemotherapy. As for stage IV, it is imperative to reduce the tumor volume to no gross residual disease. The only predictor of survival in multivariate analysis in patients with stage IV disease was in those with no gross residual disease (median survival 40 vs 18 months).

Mucinous and Squamous Cell Uterine Carcinomas

UPSC and UCCC are the most common non-endometrioid endometrial carcinomas. Two additional subtypes, mucinous and squamous cell, also represent a significant percentage of non-endometrioid histology.⁴⁶ Endometrial carcinomas of other cell types also exist but comprise less than 1% of cases and are not discussed in this review. Gestational trophoblastic disease also affects the endometrium but is beyond the scope of this review.

Mucinous Adenocarcinoma

Endometrial carcinoma with mucinous histology comprises 0.6% to 5% of uterine cancers and is rarely found as a pure cell type.^{46,47} The mucinous areas have a microglandular pattern with intraluminal and intracytoplasmic secretions and micropapillary formation. They have a consistent low-grade appearance and are likely a variant of endometrioid histology. These cancers behave in the type 1, estrogen-driven fashion and are almost exclusively seen in postmenopausal women. A review by Giordano et al⁴⁸ summarized 24 cases previously reported in the literature, and all but 1 patient

presented with postmenopausal vaginal bleeding. Mucinous endometrial carcinomas have a similar prognosis as low-grade endometrial adenocarcinoma and are managed in a similar fashion.

Squamous Cell Carcinoma

Primary endometrial squamous cell carcinoma (PESCC) is uncommon. It accounts for 0.1% to 0.5% of all uterine cancers.^{49,50} Many of the presumed squamous cell carcinomas thought to be of uterine origin are most likely from the cervix. The criteria for establishing the diagnosis of PESCC are coexisting primary adenocarcinoma of the endometrium, no connection between PESCC and cervical squamous epithelium, no coexisting primary squamous cell carcinoma of the cervix, and clear evidence of squamous differentiation such as intercellular bridges and/or keratin.⁴⁹ Goodman et al⁵⁰ reviewed 64 cases of PESCC. Patients tended to be white, non-obese, and older than 67 years of age. Vaginal bleeding was present in 69% of these patients. Estrogen use was not found to be a predisposing factor in development of disease. Nulliparity was found in 36% of cases. Human papilloma infection has not been found in patients with PESCC. The presence of lymphovascular space invasion and myometrial invasion were found to be poor prognostic indicators. Postsurgical treatment many include radiation and/or chemotherapy. Due to the paucity of cases, the role of adjuvant therapy has not been evaluated. In a review of 42 cases of PESCC, 16 patients received radiation therapy before or after surgery, with 10 patients surviving an average of 40 months. Those patients who did not undergo radiation therapy survived an average of 21 months following surgery.⁵¹ Overall treatment should be directed at comprehensive surgical staging and accurate diagnosis.

Conclusions

Many questions regarding the management of UPSC and CC remain answered. Large, prospective, multi-institutional clinical trials need to be conducted to address these questions. While these women represent a minority of the patients who present with endometrial carcinoma, they represent a disproportionate number of recurrences and deaths due to this disease. Based on the available literature, several conclusions can be drawn. Women with clinical stage I UPSC or CC should undergo comprehensive surgical staging with consideration of adjuvant chemotherapy with or without volume-directed radiotherapy (pelvic and/or vaginal cuff brachytherapy). The precise chemotherapeutic regimen has not been determined in a prospective fashion, but the majority of the available literature is based on carboplatin and paclitaxel. In women with advanced-stage disease, efforts should be made to achieve optimal cytoreduction followed by adjuvant chemotherapy. When available and appropriate, these women should be

offered the opportunity to enroll in clinical trials. In the absence of an appropriate clinical trial, chemotherapy with either paclitaxel/carboplatin or doxorubicin/cisplatin is recommended.

Disclosures

No significant relationship exists between the authors and the companies/organizations whose products or services may be referenced in this article.

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