The Importance of Surgical Staging in Women With Uterine Serous Carcinoma: Experience in a Single Institution Reveals a Survival Benefit

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Abstract

Objective: To assess the appropriate extent of surgical staging in women with clinically early stage uterine serous carcinoma (USC).

Methods: We conducted a single-institution retrospective cohort study of all women with USC between 2007 and 2012. Treatment practices, outcomes, and factors affecting survival were analyzed using univariate and multivariate analysis.

Results: Eighty-four patients were identified, 76 of whom were included in the analysis. Preoperative pathology correctly identified USC in 73.3% of cases. Surgical stage distribution was 44.7% stage I, 7.9% stage II, 31.6% stage III, and 15.8% stage IV. Women thought to have early stage disease preoperatively encompassed 84.2% (64) of the cohort. Fifty-two (81.3%) of these women with clinically early stage disease had complete surgical staging. Thirty-four (53.1%) were determined to have surgical stage I, and the remaining 30 (46.9%) had occult advanced stage disease. Median follow-up was 43.2 months. Univariate analysis found a significant increase in progression-free survival and overall survival for women with clinically early stage disease with positive lymphovascular space invasion ($P < 0.001$ and $P = 0.002$, respectively), positive peritoneal cytology ($P = 0.022$ and $P = 0.04$, respectively), early stage ($P < 0.001$ and $P = 0.004$, respectively), and elevated serum CA125 at diagnosis ($P = 0.003$ and $P = 0.001$, respectively). On multivariate analysis, early stage (hazard ratio [HR] 9.87; 95% CI 2.79 to 34.92, $P < 0.001$) and complete surgical staging (HR 2.96; 95% CI 1.05 to 8.37, $P = 0.040$) were associated with prolonged progression-free survival, while overall survival was not affected by complete surgical staging (HR 1.92; 95% CI 0.64 to 5.76, $P = 0.79$).

Conclusion: Complete surgical staging prolongs the progression-free survival of women with clinical early-stage uterine serous cancer. Although this does not extend to overall survival, this enables patients to have an improved quality of life with a longer interval without the burden of disease.

Key Words: Uterine serous carcinoma, chemotherapy, survival analysis, surgical staging, uterine cancer treatment

Competing Interests: None declared.

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Résumé

Objectif : Déterminer l'ampleur adéquate de la stadification chirurgicale chez les femmes qui présentent un carcinome séreux de l'utérus (CSU) de stade clinique précoce.

Méthodes : Nous avons mené une étude de cohorte rétrospective portant sur toutes les femmes qui ont présenté un CSU entre 2007 et 2012 au sein d'un seul établissement. Les pratiques de traitement, les issues et les facteurs affectant la survie ont été étudiés au moyen d'analyses univariées et multivariées.

Résultats : Quatre-vingt-quatre patientes ont été identifiées, 76 desquelles ont été admises à l'analyse. L'analyse pathologique préopératoire a correctement identifié le CSU dans 73,3 % des cas. La distribution des stades chirurgicaux était la suivante : stade I, 44,7 %; stade II, 7,9 %; stade III, 31,6 %; et stade IV, 15,8 %. Les femmes qui, avant l'opération, semblaient présenter une maladie de stade précoce représentaient 84,2 % (64) de la cohorte. Cinquante-deux (81,3 %) de ces femmes présentant une maladie de stade clinique précoce ont subi une stadification chirurgicale complète. Il a été déterminé que 34 (53,1 %) de ces 64 femmes présentaient un stade chirurgical I, tandis que les 30 autres (46,9 %) présentaient une maladie occulte de stade avancé. Le suivi médian a été de 43,2 mois. L'analyse univariée a constaté une hausse significative des taux de survie sans progression et de survie globale chez les femmes connaissant une maladie de stade clinique précoce qui avaient obtenu des résultats positifs en ce qui concerne l'invasion de l'espace lymphovasculaire (P < 0,001 et P = 0,002, respectivement), qui avaient obtenu des résultats positifs dans le cadre de la cytologie péritonéale (P = 0,022 et P = 0,04, respectivement), qui présentaient un stade précoce (P < 0,001 et P = 0,004, respectivement) et chez lesquelles un taux sérique élevé de CA125 avait été constaté au moment du diagnostic (P = 0,003 et P = 0,001, respectivement). Dans le cadre de l'analyse multivariée, la présence d'un stade précoce (rapport des risques instantanés [RRI], 9,87; IC à 95 %, 2,79 - 34,92, P < 0,001) et la tenue d'une stadification chirurgicale complète (RRI, 2,96; IC à 95 %, 1,05 - 8,37, P = 0,040) ont été associées à une prolongation de la survie sans progression, tandis que la survie globale n'a pas été affectée par la tenue d'une stadification chirurgicale complète (RRI, 1,92; IC à 95 %, 0,64 - 5,76, P = 0,79).

Conclusion : La tenue d'une stadification chirurgicale complète prolonge la survie sans progression des femmes qui présentent

un carcinome séreux de l'utérus de stade clinique précoce. Bien que cette intervention n'exerce pas d'effets sur la survie globale, elle permet aux patientes de connaître une amélioration de leur qualité de vie (prolongation de l'intervalle dans le cadre duquel les patientes n'ont pas à vivre avec le fardeau de la maladie).

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INTRODUCTION

Uterine papillary serous carcinoma is responsible for only 2% to 10% of all uterine cancers. It is a highly aggressive cancer and accounts for approximately 50% of deaths from uterine cancer.[1,2] It is often diagnosed at an advanced stage, with 47% of uterine serous cancers diagnosed as stage II to IV.[2] This is in contrast with endometrioid adenocarcinoma, which is most often diagnosed at an early stage and generally has a good prognosis. The prognosis for women with USC is known to be poor even when the disease is diagnosed at an early stage, because occult metastases at the time of diagnosis are frequent; recurrences are also frequent. Indeed, Goff et al. reported a 72% incidence of extrauterine spread at the time of surgery in women with clinically stage I disease, in comparison with 25% of women with endometrioid adenocarcinoma.[3] Thomas et al. also described a cohort of 42 women with clinically early stage disease who had routine intraoperative biopsies, pelvic lymphadenectomy, omentectomy, and peritoneal washings; 30% of these women subsequently had upstaging of their disease.[4]

The classification of uterine cancers into type I and type II is based on histological, molecular, and clinical features; these features underlie the aggressive nature of type II cancers such as USC. The histological similarity of USC to serous ovarian cancer and its propensity for intra-abdominal spread has led many clinicians to treat USC using an approach similar to that used for epithelial ovarian cancer. A combination of surgery and chemotherapy is usually offered, although radiotherapy is sometimes also used.

Because of the increasing evidence of clinicopathological features common to both ovarian and uterine serous carcinoma, aggressive surgery and adjuvant chemotherapy have become the mainstay of treatment for USC.[3,5,6] Chemotherapy generally consists of a platinum agent in combination with paclitaxel.[7,8] As in women with ovarian cancer, the extent of surgical staging that should be performed in women with clinically early stage disease is controversial. However, the weight of evidence from several published studies regarding the surgical management of USC has advocated for complete staging in order to properly assign stage, identify prognostic factors, and select appropriate adjuvant therapy.[3,9,10]

The focus of this study was to examine the management and outcomes of women with USC over a five-year period at the Tom Baker Cancer Centre, focusing primarily on those who were deemed preoperatively to have clinically early stage disease. Furthermore, we wished to determine what factors affected survival in these women.

ABBREVIATIONS

AUC	area under the curve
HR	hazard ratio
LVI	lymphovascular space invasion
OS	overall survival
PFS	progression-free survival
USC	uterine serous carcinoma

METHODS

We conducted a retrospective cohort study of all women with a diagnosis of USC between 2007 and 2012 at the Tom Baker Cancer Centre in Calgary, Alberta. This cancer centre provides management for all women with USC in southern Alberta and border populations in adjacent provinces, representing a catchment of approximately two million people.

All women with USC who are fit for surgery undergo full surgical staging. This consists of a hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omentectomy, and peritoneal cytology. Other procedures may be performed to debulk tumour to microscopic residual disease (e.g., bowel resection). Following surgery, each case is reviewed and discussed by a multidisciplinary tumour board review panel to confirm the pathology and establish an individualized treatment plan. Historically, the chemotherapy regimen used most commonly has been carboplatin (using target AUC 5) and paclitaxel (175 mg/m^2) every three weeks. More recently, carboplatin (AUC 5) every three weeks and dose-dense paclitaxel (80 mg/m^2 weekly) has been used, applying the Calgary modification of dose-dense chemotherapy.[11] In select patients, single-agent carboplatin (using target AUC 6) has been used.

Patients were identified using the Alberta Cancer Registry. Data were extracted from patient charts contained on the ARIA Oncology Information System (Varian Medical Systems, Palo Alto CA). Demographic data such as patient age, BMI, date of diagnosis, and Eastern Cooperative Oncology Group performance status[12] were collected. Stage was determined according to the FIGO 2009 guidelines.[13] Clinical data such as surgical