



Comparative matched analysis for survival endpoints between women with early stage uterine carcinosarcoma and uterine serous carcinoma

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BACKGROUND / OBJECTIVE(s)

- Uterine serous carcinoma (USC) and carcinosarcoma (CS) are rare and aggressive subtypes of endometrial carcinoma (EC) constituting 10% and 2-3%, respectively of women with EC.
- International Federation of Gynecology and Obstetrics (FIGO) stated that uterine CS should be included and staged similarly to endometrial carcinoma.
- Historically, data from several retrospective reports has shown that survival endpoints of women with CS is worse than other aggressive types of EC such as USC. Yet more recently, reports have demonstrated similar outcomes between women with USC and CS
- No prior study compared survival endpoints in women with early stage USC to women with uterine CS using a robust and comprehensive matching analysis.

MATERIAL & METHODS

- Patients: At Henry Ford, 134 women with 2009 FIGO stage I-II USC or CS s/p hysterectomy + BSO + LN evaluation +/- omentectomy and peritoneal cytology from 1990-2019 at Henry Ford with adjuvant management (observation, chemo alone, radiation alone or combined modality treatment) with 3-6 month follow up
- Analysis: Randomly matched 1 CS to 1 USC , blind to patient outcomes. Analyzed variables age, BMI, CCS, FIGO stage, LVSI, percentage of myometrial invasion, status of peritoneal cytology, lower uterine segment involvement, omentectomy, lymphadenectomy, number of pelvic and paraaortic LNs, adjuvant management. Multivariate analysis was performed with Cox regression model using manual stepwise selection with an entry criterion of $p < 0.1$ and stay criteria of $p < 0.05$. A p value of less than 0.05 was considered statistically significant.
- Outcomes: 5 year RFS, DSS, OS.

RESULTS

About the patients:

- N= 134 women were included (67 women with USC and 67 with CS, matched 1:1)
- Median f/up about 8 years
- Pelvic EBRT: mean dose 45 Gy (45-50.4 Gy)
- Vaginal cuff brachytherapy: 192-Ir HDR in 3-5 fractions to the proximal 3-4 cm of the vagina with mean dose 30 Gy in 5 fractions to the vaginal surface using single channel vaginal cylinder. Fractions were once or twice a week
- Chemo: carboplatin and paclitaxel q21d, median cycles was 6

Table 1. Patients demographic, pathologic and management characteristics of study cohort

| Variable | Carcinosarcoma (N=67) | Uterine serous carcinoma (N=67) | p-value |
|---------------------------------------|-------------------------|---------------------------------|---------|
| Median age in years | 68 (range, 40-90) | 69 (range, 51-90) | 0.31 |
| Median body mass index | 34.0 (range, 17.0-52.8) | 32.7 (range, 21.5-51.5) | 0.86 |
| Median follow-up in months | 82.4 (range, 12-280) | 99.7 (range, 12-334) | 0.54 |
| Race | | | 0.47 |
| White | 37 (55%) | 31 (46%) | |
| African American | 28 (42%) | 35 (52%) | |
| Others | 2 (3%) | 1 (1%) | |
| Median Charlson comorbidity Score | 1.0 (range, 0.0-6.0) | 1.0 (range, 0.0-8.0) | 0.61 |
| 2009 FIGOa Stage | | | 1.00 |
| - IA | 42 (63%) | 42 (63%) | |
| - IB | 16 (24%) | 16 (24%) | |
| - II | 9 (13%) | 9 (13%) | |
| Median % of myometrial invasion | 40 (0.1-1.0) | 30 (0.1-1.0) | 0.15 |
| Lymph node (LNb) dissection performed | 56 (84%) | 62 (93%) | 0.11 |
| Median number of examined LN | 12 (range, 0.0-47.0) | 14 (range, 0.0-56.0) | 0.26 |
| Median examined paraaortic LNs | 1 (range, 0.0-20.0) | 2 (range, 0.0-29.0) | 0.43 |
| Lymphovascular space invasion | 29 (43%) | 19 (28%) | 0.07 |
| Omentectomy | 35 (52%) | 37 (55%) | 0.73 |
| Positive peritoneal cytology | 10 (15%) | 11 (16%) | 0.97 |
| Lower uterine segment involvement | 18 (27%) | 30 (45%) | 0.03 |
| Overall adjuvant management | | | 1.00 |
| Observation | 12 (18%) | 12 (18%) | |
| Radiation treatment (RTc) alone | 9 (13%) | 9 (13%) | |
| Chemotherapy alone | 16 (24%) | 16 (24%) | |
| Combined chemotherapy and RT | 30 (45%) | 30 (45%) | |
| Radiation treatment modality | | | 0.07 |
| Vaginal cuff brachytherapy | 25 (64%) | 27 (69%) | |
| Pelvic external beam | 9 (23%) | 2 (5%) | |
| Combination | 5 (13%) | 10 (26%) | |
| Cancer recurrence | 22 (33%) | 24 (36%) | 0.7159 |
| Site of first recurrence | | | |
| Isolated vaginal recurrence | 2 (9%) | 3 (13%) | 1.00 |
| Isolated pelvic recurrence only | 1 (5%) | 2 (8%) | 1.00 |
| Pelvic and vaginal recurrences | 4 (18%) | 2 (8%) | 0.16 |
| Paraaortic recurrence without distant | 1 (5%) | 0 (0%) | 0.77 |
| Any distant recurrence | 14 (64%) | 17 (71%) | 0.76 |

Between cohorts (traits): similar distribution of median age, BMI, race median morbidity score, 2009 FIGO staging

Between cohorts (pathology): similar distribution of median percentage of myometrial invasion, lymph node dissection, median number and types of LN, LVSI, omentectomy, peritoneal cytology , lower uterine segment involved, recurrence patterns

Between cohorts (adjuvant mgmt): similar distribution of observation, RT alone, chemo alone, combined chemorads, radiation treatment modality (vaginal cuff brachy, pelvic EBRT,

Outcomes:

5 year recurrence-free survival
CS 62% vs USC 59% (p=0.81)

5 year disease-specific survival
CS 67% vs USC 66% (p=0.52)

5 year overall survival
CS 57% vs USC 53% (p=0.70)

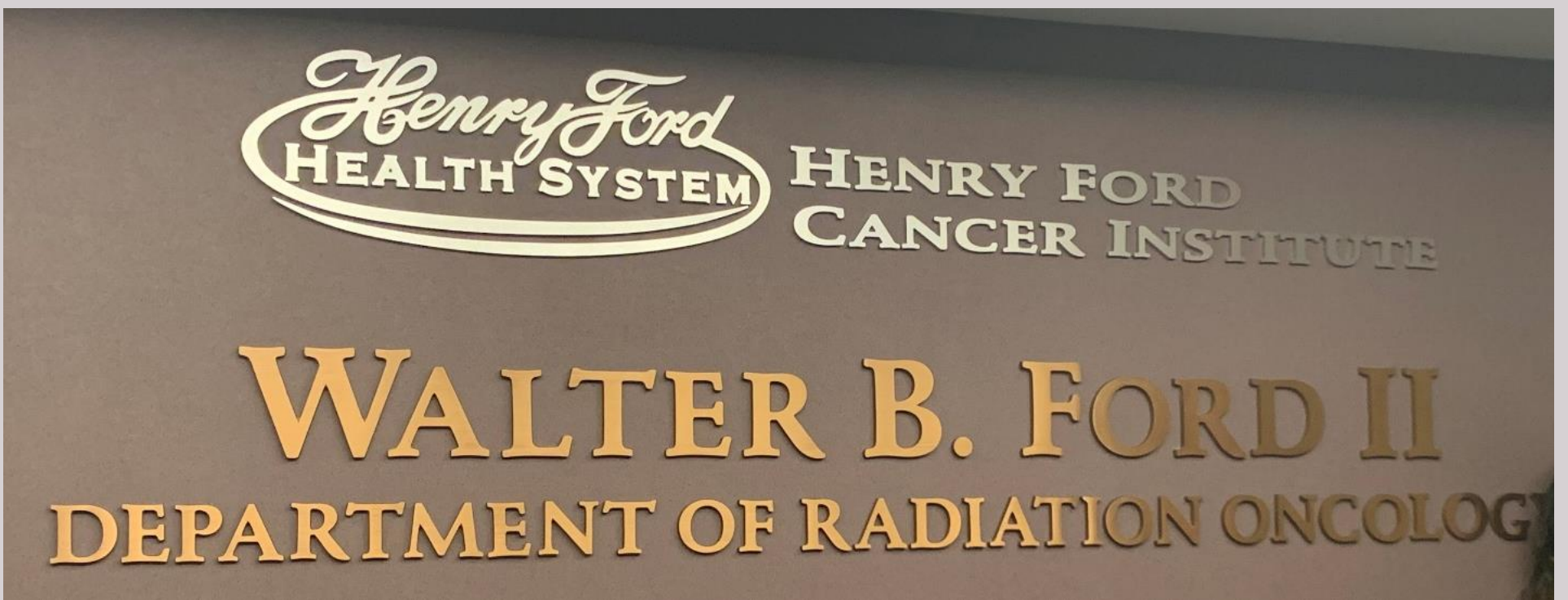
Table 2. Multivariate analysis for survival end points for the study cohort.

| Variables | Recurrence-free survival | | | Overall survival | | | Disease-specific survival | | |
|---|--------------------------|--------------|---------|------------------|--------------|---------|---------------------------|--------------|---------|
| | HR | 95% CI of HR | p-value | HR | 95% CI of HR | p-value | HR | 95% CI of HR | p-value |
| Age | N/A | N/A | N/A | 1.00 | 0.97 – 1.04 | 0.85 | N/A | N/A | N/A |
| Body mass index | 0.97 | 0.93 – 1.02 | 0.19 | N/A | N/A | N/A | N/A | N/A | N/A |
| Charlson comorbidity index | N/A | N/A | N/A | 1.10 | 0.94 – 1.29 | 0.23 | N/A | N/A | N/A |
| Deep myometrial invasion | 2.81 | 0.65 – 12.17 | 0.17 | 1.91 | 0.70 – 5.23 | 0.21 | N/A | N/A | N/A |
| No lymph node dissection | N/A | N/A | N/A | 2.44 | 1.17 – 5.11 | 0.02 | 2.23 | 0.92 – 5.40 | 0.08 |
| No LUS involvement | 0.58 | 0.30 – 1.15 | 0.12 | N/A | N/A | N/A | 0.36 | 0.19 – 0.70 | 0.003 |
| FIGO stage IA vs. II | 0.36 | 0.11 – 1.19 | 0.09 | N/A | N/A | N/A | N/A | N/A | N/A |
| FIGO stage IB vs. II | 0.37 | 0.12 – 1.18 | 0.09 | N/A | N/A | N/A | N/A | N/A | N/A |
| Adjuvant CT alone vs. combined modality (CMT) | 1.71 | 0.68 – 4.28 | 0.25 | 1.16 | 0.53 – 2.53 | 0.72 | 1.20 | 0.50 – 2.84 | 0.69 |
| Observation vs. CMT | 3.04 | 1.24 – 7.49 | 0.02 | 2.65 | 1.29 – 5.42 | 0.01 | 2.82 | 1.29 – 6.20 | 0.010 |
| Radiation treatment alone vs. CMT | 0.32 | 0.07 – 1.39 | 0.13 | 1.35 | 0.56 – 3.22 | 0.51 | 0.41 | 0.09 – 1.82 | 0.24 |

Abbreviations: HR = hazard ratio, CI = confidence interval, LUS = lower uterine segment, FIGO = International Federation of Gynecology and Obstetrics, CT = chemotherapy, CMT = combined modality treatment, N/A = not applicable as it was not included in multivariate analysis.

SUMMARY / CONCLUSION

- In simple terms, uterine CS is not an isolated aggressive histology.
- When matched based on age, tumor stage, adjuvant treatment our study suggests there is no statistically significant difference in any 5-year survival endpoints between early stage USC and CS.
- Lack of combined modality therapy and lack of LN dissection negatively affected outcomes across the board.
- Limitation: retrospective design within single institution, though we did use a robust matching analysis on numerous variables.



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