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Assessing the effects of lymphadenectomy and radiation therapy in patients with uterine carcinosarcoma: A SEER analysis ☆

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Abstract

Objective. The purpose of this analysis is to determine the pathologic prognostic factors and treatment outcome of patients with carcinosarcoma of the uterus.

Methods. A retrospective analysis of data from the Surveillance, Epidemiology, and End Results program of the National Cancer Institute between January 1, 1988 and November 1, 2003 was conducted. A total of 1855 with AJCC Stages I–III disease were identified who received primary surgical treatment. Overall survival curves were constructed using Kaplan–Meier curves. Cox proportional hazards model was used to identify factors predictive of overall survival.

Results. AJCC stage of all patients was as follows: 65% Stage I ($n=1099$), 14% Stage II ($n=245$), 21% Stage III ($n=353$). 57% ($n=965$) patients underwent LND. The median number of lymph nodes removed was 12 (SD=10.2); 119 (14%) patients had positive lymph nodes. Five-year overall survival (OS), disease free survival, and median survival were significantly improved for patients receiving lymph node dissection (LND) as compared to patients that received no LND, irrespective of radiotherapy. Adjuvant radiation therapy had no improvement on overall survival regardless of LND. There was no overall survival benefit to the addition of radiotherapy regardless of whether patients underwent a lymph node dissection or not. Age, race, marital status, lymph node dissection and stage were predictive of survival on multivariate analysis.

Conclusions. Lymphadenectomy is significantly associated with improved overall survival in patients with Stage I–III uterine carcinosarcoma compared to no lymphadenectomy. The use of adjuvant radiotherapy conferred no overall survival benefit.

Keywords: Lymph node dissection; Uterine carcinosarcoma; Radiation; Survival; Propensity score

Introduction

Uterine carcinosarcomas, also known as malignant mixed mullerian tumors (MMMT), are rare neoplasms that are associated with a dismal prognosis [1]. The incidence in the United States has been reported to be less than 1% of all gynecologic malignancies and 2–5% of all uterine malignancies. Five-year survival data remain dismal for Stages I–III uterine carcinosarcoma with several studies demonstrating survival rates ranging from 33% to 39% [2-8].

The primary treatment for uterine carcinosarcoma remains total abdominal hysterectomy and bilateral salpingo-oopherectomy (TAH-BSO) [1,2]. No current consensus exists on lymph node dissection (LND) [1,4,9,10].

Despite many recent advances, optimal management of these patients following total abdominal hysterectomy remains controversial [1,11]. The role of adjuvant pelvic radiotherapy (RT) in the post-operative treatment of uterine sarcomas has not been clearly defined and has varied significantly over the past 25 years [1,2,12]. Recently, adjuvant pelvic RT has been shown

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to improve local control with conflicting results on its impact on overall survival [6,12,13].

The aim of this study was to determine whether lymph node dissection resulted in an improvement in survival among patients that underwent TAH-BSO for uterine carcinosarcoma. A secondary goal was to determine if adjuvant RT improves survival.

Materials and methods

Data and study population

A retrospective analysis of all patients with uterine carcinosarcoma registered under the Surveillance, Epidemiology, and End Results (SEER) program of the U.S. National Cancer Institute (NCI) was performed. The SEER database provides information on tumor histology and location, disease stage, individual demographic characteristics, initial treatment as well as survival on incident cancer cases from a set of 16 cancer registries covering 26% of the population [14,15]. Approval by an IRB (institutional review board) committee was not necessary since the SEER database information does not carry any identifying information.

The study population consisted of women diagnosed with American Joint Committee on Cancer (AJCC) Stages I–III uterine carcinosarcoma treated between January 1, 1988 and November 1, 2003. Histological classification was based on the international Classification of Diseases for Oncology codes (ICD 8380) [16-18]. SEER∗STAT software was utilized [19]. The following criteria for exclusion from the analysis were utilized: patients that did not undergo TAH-BSO, AJCC defined stage 4 disease, and those patients with any missing treatment (LND and/or RT) and socioeconomic and/or demographic information. The end point of interest was overall survival. Because patient files in SEER are linked to death certificates regardless of cause of death, this was used as the source of information for overall survival.

Statistical design and analysis

All statistical analyses were carried out using SAS version 9.1 (SAS Institute, Cary, NC) and R version 1.1.1 (The R Foundation for Statistical Computing. Vienna, Austria). Survival time was calculated as the number of months from the diagnosis date to the SEER date of death. Survival was censored as of the last month when patients were known to be alive, or as of November 1, 2003. Univariate associations between type of treatment and clinical and demographic factors were assessed using c^2 tests, *t*-tests and Kruskal–Wallis test. Overall survival curves by LND were constructed using the Kaplan–Meier method and log–rank tests were conducted. The Cox proportional hazards model was used for both univariate and multivariate analysis. The multivariate analysis included all variables found to be statistically significant on univariate analysis ($P<0.05$) and with percentage of missing less than 30%. The proportional hazards assumption underlying the Cox model was tested using −log(−log (survival)) plots.

Table 1
Patient characteristics

Characteristic	LND (with or without RT)		No LND (with or without RT)	
	n	%	*n*	%
Age at diagnosis of breast cancer				
19–24	2	0.21	1	0.14
25–34	5	0.52	3	0.41
35–44	23	2.4	9	1.3
45–54	80	8.3	36	4.9
55–64	264	27.4	121	16.5
65–74	170	17.6	248	34.9
75–84	232	24.0	217	29.6
85+	40	4.2	97	13.3
Period of diagnosis				
1988–1991	110	11.4	139	19.0
1992–1995	159	16.5	204	27.9
1996–1999	258	26.7	132	18.0
2000–2003	448	46.4	257	35.1
Stage				
I	614	63.6	485	66.3
II	121	12.5	124	16.9
III	230	23.8	123	16.8
Race				
White	761	78.9	577	78.8
African American	155	16.1	127	17.3
Other	49	5.1	28	3.8
Marital status				
Married	461	47.8	267	36.5
Divorced/Separated/Widowed	344	35.6	346	47.3
Single	123	12.7	81	11.1
Radiation type				
None	495	51.3	444	60.7
Beam radiation	278	28.8	172	23.5
Combination of beam with implants	111	11.5	67	9.2
Radioactive implants	4	0.41	17	2.3
Radioisotopes	0	0	4	0.55
Other NOS	4	0.41	4	0.55
Recommended	21	2.2	16	2.2
Refused	16	1.7	8	1.1
Seer registry by site:				
Atlanta	22	2.3	14	1.9
California	32	3.3	11	1.5
Connecticut	58	6.0	23	3.1
Detroit	57	5.9	33	4.5
Hawaii	4	0.41	10	1.4
Iowa	39	4.0	41	5.6
Kentucky	6	0.6	5	0.68
Los Angeles	72	7.5	50	6.8
Louisiana	15	1.6	9	1.2
New Jersey	23	2.4	19	2.6
New Mexico	13	1.3	19	2.6
Rural Georgia	2	0.21	0	0
San Francisco—Oakland	50	5.2	24	3.3
San Jose—Monterey	3	0.31	1	0.14
Seattle (Puget Sound)	25	2.6	10	1.4
Utah	23	2.4	19	2.6
% <9th grade education 2000		16.1		16.4
% high school education		38.1		38.9
At least bachelors degree		56.0		53.5
% families below poverty		17.6		18.7
Persons below poverty		23.7		24.8
Median family income in tens		113.8		109.05
Median household income in tens		97.6		93.4
% unemployed		12.32		12.6
% white collar 2000		74.3		72.5
% foreign born		34.3		32.2