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Contribution of lymph node staging method and prognostic factors in malignant ovarian sex cord-stromal tumors: A world wide database analysis

Jieyu Wang [a, b], Jun Li [a], Ruifang Chen [a], Xin Lu [a, b, *]

[a] Department of Gynecology, Obstetrics and Gynecology Hospital of Fudan University, Shanghai, 200032, China
[b] Shanghai Key Laboratory of Female Reproductive Endocrine-Related Disease of Fudan University, Shanghai, 200011, China

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ABSTRACT

Objective: To investigate the clinicopathologic prognostic factors in patients with malignant sex cord-stromal tumors (SCSTs) with lymph node dissection, and at the same time, to evaluate the influence of the log odds of positive lymph nodes (LODDS) on their survival.

Methods: Patients diagnosed with malignant SCSTs who underwent lymph node dissection were extracted from the 1988–2013 Surveillance, Epidemiology, and End Results (SEER) database. Overall survival (OS) and cancer-specific survival (CSS) were estimated by Kaplan-Meier curves. The Cox proportional hazards regression model was used to identify independent predictors of survival.

Results: 576 patients with malignant SCSTs and with lymphadenectomy were identified, including 468 (81.3%) patients with granulosa cell tumors (GCTs) and 80 (13.9%) patients with Sertoli-Leydig cell tumors (SLCTs). 399 (69.3%) patients and 118 (20.5%) patients were in the LODDS < -1 group and $-1 \leq$ LODDS < -0.5 group, respectively. The 10-year OS rate was 80.9% and CSS was 87.2% in the LODDS < -0.5 group, whereas the survival rates for other groups were 68.5% and 73.3%. On multivariate analysis, age 50 years or less ($p < 0.001$), tumor size of 10 cm or less ($p < 0.001$), early-stage disease ($p < 0.001$), and GCT histology ($p \leq 0.001$) were the significant prognostic factors for improved survival. LODDS < -0.5 was associated with a favorable prognosis (OS: $p = 0.051$; CSS:$P = 0.055$).

Conclusions: Younger age, smaller tumor size, early stage, and GCT histologic type are independent prognostic factors for improved survival in patients with malignant SCST with lymphadenectomy. Stratified LODDS could be regarded as an effective value to assess the lymph node status, and to predict the survival status of patients.

Introduction

Sex cord stromal tumors (SCSTs) are rare tumors accounting for approximately 7% of all ovarian malignancies. SCSTs are indolent with early stage at presentation, slow growth, late recurrence, and a very favorable long-term prognosis.

SCSTs include granulosa cell tumors (GCTs), Sertoli-Leydig cell tumors(SLCTs), thecomas, and gynandroblastoma. GCTs derive from the cortical sex cord, whereas SLCTs originate from medullary cords of mesonephric origin. The majority of SCSTs are GCTs, which account for approximately 70% of malignant sex cord–stromal tumors [1,2].

The low incidence and multiplicity of histologic patterns of SCSTs, as well as their variable biologic behavior, represents a limitation in our understanding of their prognostic risk factors. From the current research, the prognostic risk factors are still controversial [1–4]. Furthermore, the prognositic factors have generally been evaluated based on observations of small groups of patients, which leads to limited and often inconsistent conclusions. Adequate risk factor investigation of these neoplasms is imperative to the appropriate therapy.

Lymph node status is generally considered to be a prognostic factor in various cancers, although the conclusion is conflicting. The status of lymph nodes can be evaluated by the number of resected lymph nodes (RLNs) [5] and the lymph node ratio (LNR) [6–8].

* Corresponding author. Department of Gynecology, Obstetrics and Gynecology Hospital of Fudan University, Shanghai, 200032, China.
E-mail address: xinluktz@163.com (X. Lu).

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As an emerging evaluation index, the log odds of positive lymph nodes (LODDS) [9–14], which is defined as the log of odds between PLNs and the number of negative nodes, shows superiority in predicting outcomes in breast [10], pancreatic [9,11], colorectal [12,13], and ovarian cancer [14]. To our knowledge, there is no study exploring the role of LODDS in SCSTs.

In this study, large population-based SCSTs cases are collected from the SEER database. The aims of this study are to determine the clinicopathologic prognostic factors and to evaluate the influence of LODDS for SCSTs.

Patients and methods

All patients diagnosed with primary malignant SCST who underwent lymph node dissection between 1988 and 2013 were extracted from the SEER database. Information on age at diagnosis, race, marital status, FIGO stage, grade, histology, number of lymph nodes resected, number of positive lymph nodes, CA125 level, and tumor size were collected. In addition, cases without a definitive number of removed lymph nodes and active follow-up were excluded. Overall survival (OS) and cancer-specific survival (CSS) were estimated by Kaplan-Meier curves. In the SEER database, the OS represents the number of months from cancer diagnosis to the date of death. CSS is defined as the number of months from cancer diagnosis to the date a patient dies from malignant SCST [15,16].

The frequency distribution of categorical variables was compared with the chi-square test or the Fisher exact test. Survival was estimated by the Kaplan–Meier method, and assessed by the log-rank test. The Cox proportional hazards regression model was used to identify independent predictors of survival. Analyses were performed using SPSS statistical software package, version 19.0 (IBM Corporation, Armonk, NY, USA) and the R version 3.3.0 software (Institute for Statistics and Mathematics, Vienna, Austria; www.r-project.org). All tests were two tailed, and statistical significance remained conventionally defined as $p < 0.05$ in all other cases.

Results

A total of 576 women with malignant SCSTs of the ovary who underwent lymph node dissection were identified. Table 1

Table 1
Demographic and clinicopathological characteristics of patients with sex cord-stromal tumors (SCSTs) stratified by LODDS.

	LODDS < −1	−1 ≤ LODDS < −0.5	−0.5 ≤ LODDS < 0	LODDS ≥ 0	Total
	N = 399 (69.3%)	N = 118 (20.5%)	N = 45 (7.8%)	N = 14 (2.4%)	N = 576 (100%)
Age					
< 50	215 (66.2%)	78 (24.0%)	24 (7.4%)	8 (2.5%)	325 (56.4%)
≥50	184 (73.3%)	40 (15.9%)	21 (8.4%)	6 (2.4%)	251 (43.6%)
Tumor size					
≤5 cm	66 (71.7%)	19 (20.7%)	5 (5.4%)	2 (2.2%)	92 (16.0%)
5–10 cm	98 (76.6%)	17 (13.3%)	12 (9.4%)	1 (0.8%)	128 (22.2%)
10–15 cm	64 (67.4%)	24 (25.3%)	5 (5.3%)	2 (2.1%)	95 (16.5%)
15–20 cm	37 (68.5%)	12 (22.2%)	4 (7.4%)	1 (1.9%)	54 (9.4%)
> 20 cm	57 (69.5%)	16 (19.5%)	8 (9.8%)	1 (1.2%)	82 (14.2%)
Unknown	77 (34.2%)	30 (24.0%)	11 (8.8%)	7 (5.6%)	125 (21.7%)
Race					
White	279 (70.1%)	80 (20.1%)	32 (8.0%)	7 (1.8%)	398 (69.1%)
Black	84 (65.1%)	29 (22.5%)	12 (9.3%)	4 (3.1%)	129 (22.4%)
American indian or Alaska native	2 (66.7%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	3 (0.5%)
Asiansa or pacific islander	30 (75.0%)	6 (15.0%)	1 (2.5%)	3 (7.5%)	40 (6.9%)
Unknown	4 (66.7%)	2 (33.3%)	0 (0.0%)	0 (0.0%)	6 (1.0%)
Marital status					
Single-never married	98 (65.3%)	33 (22.0%)	14 (9.3%)	5 (3.3%)	150 (26.0%)
Married	213 (71.5%)	58 (19.5%)	23 (7.7%)	4 (1.3%)	298 (51.7%)
Separated	8 (61.5%)	4 (30.8%)	1 (7.7%)	0 (0.0%)	13 (2.3%)
Divorced	34 (73.9%)	12 (26.1%)	0 (0.0%)	0 (0.0%)	46 (8.0%)
Widowed	30 (62.5%)	9 (18.8%)	5 (10.4%)	4 (8.3%)	48 (8.3%)
Unknown	16 (76.2%)	2 (9.5%)	2 (9.5%)	1 (4.8%)	21 (3.6%)
Stage of disease					
Stage I	286 (71.9%)	76 (19.1%)	32 (8.0%)	4 (1.0%)	398 (69.1%)
Stage II	51 (64.6%)	22 (27.8%)	5 (6.3%)	1 (1.3%)	79 (13.7%)
Stage III	45 (67.2%)	15 (22.4%)	3 (4.5%)	4 (6.0%)	67 (11.6%)
Stage IV	3 (60.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)	5 (0.9%)
Unknown	14 (51.9%)	5 (18.5%)	4 (14.8%)	4 (14.8%)	27 (4.7%)
Grade of disease					
Grade 1	21 (65.6%)	8 (25.0%)	3 (9.4%)	0 (0.0%)	32 (5.6%)
Grade 2	28 (66.7%)	10 (23.8%)	4 (9.5%)	0 (0.0%)	42 (7.3%)
Grade 3	69 (68.3%)	24 (23.8%)	5 (5.0%)	3 (3.0%)	101 (17.5%)
Unknown	281 (70.1%)	76 (19.0%)	33 (8.2%)	11 (2.7%)	401 (69.6%)
Histology					
GCT	335 (71.6%)	89 (19.0%)	35 (7.5%)	9 (1.9%)	468 (81.3%)
SLCT	52 (65.0%)	17 (21.3%)	9 (11.3%)	2 (2.5%)	80 (13.9%)
SCST-NOS	7 (46.7%)	5 (33.3%)	0 (0.0%)	3 (20.0%)	15 (2.6%)
Other	5 (38.5%)	7 (53.8%)	1 (7.7%)	0 (0.0%)	13 (2.3%)
CA125					
Negative	95 (80.5%)	17 (14.4%)	4 (3.4%)	2 (1.7%)	118 (20.5%)
Positive	69 (69%)	27 (27%)	2 (2%)	2 (2%)	100 (17.4%)
Borderline	1 (50%)	1 (50%)	0 (0.0%)	0 (0.0%)	2 (0.3%)
Unknown	234 (65.7%)	73 (20.5%)	39 (11.0%)	10 (2.8%)	356 (61.8%)

GCT = Granulosa cell tumor.
SLCT = Sertoli-leydig cell tumor.
SCST-NOS = sex-cord stromal tumor not otherwise specified.

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