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Prognostic factors responsible for survival in sex cord stromal tumors of the ovary—An analysis of 376 women

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Abstract

Objective. To evaluate prognostic factors that impact on the survival of women with ovarian sex cord stromal tumors (SCST).

Methods. Data including age at diagnosis, stage, histology, grade, treatment, and survival were extracted from the 1988–2001 Surveillance, Epidemiology, and End Results Program. Kaplan–Meier and Cox proportional hazards analyses were used to determine the predictors for survival.

Results. 376 women (median age: 51) with ovarian sex cord stromal cell tumors were identified, including 339 with granulosa cell and 37 with Sertoli-Leydig cell tumors. 265 (71%) patients had stage I, 39 (10%) stage II, 40 (11%) stage III, and 32 (8%) had stage IV disease. Women with stage I–II disease had a 5-year disease-specific survival of 95% compared to 59% in those with stage III–IV cancers ($p<0.001$). Patients ≤ 50 years had a survival advantage over those>50 years (93% vs. 84%, $p<0.001$). This age-associated survival advantage was observed for early (97% vs. 92%, $p=0.003$), but not for advanced-staged (68% vs. 53%, $p=0.09$) patients. 110 patients with stage I–II disease underwent conservative surgery without hysterectomy. The survival for this group was similar to patients who underwent a standard surgery including a hysterectomy (94.8% and 94.9%, $p=0.38$). On multivariate analysis, age ≤ 50 ($p=0.001$) and early-stage disease ($p<0.001$) remained significant prognostic factor for improved survival.

Conclusions. Younger age and early-stage disease are important predictors for improved survival in patients with ovarian sex cord stromal tumors. Conservative surgical treatment for early-staged patients wishing to retain fertility appears to be a safe alternative.

Keywords: Sex cord stromal; Prognostic factors; Ovary; Tumor; Survival

Introduction

Sex cord stromal tumors (SCST) are rare tumors comprising less than 5% of all ovarian malignancies. The majority of SCST are granulosa cell tumors, with Sertoli-Leydig cell tumors and theca cell tumors accounting for the remainder of this group. Compared to epithelial ovarian malignancies, SCST tend to present at a younger age with a peak occurrence in the 5th to 6th decade of life.

SCST generally behave in an indolent fashion characterized by early stage at presentation, slow growth, late recurrence, and an overall favorable prognosis. Several clinical and pathological prognostic factors have been reported in the literature, including stage, age, tumor size, and grade. Primary therapy for SCST generally begins with standard surgical staging including a total abdominal hysterectomy and bilateral salpingo-oophorectomy. For younger patients with early-stage disease, conservative surgery has been suggested as a treatment alternative for those

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wishing to retain fertility. However, there is limited evidence in the literature to support the safety of this approach.

The current literature on sex cord stromal tumors of the ovary consists mainly of single or multi-institutional reports with small number of patients, leading to limited and often inconsistent conclusions. Large population-based tumor databases may offer a unique opportunity to collect information on this rare disease. This study identified a large group of women with sex cord stromal tumors of the ovary, and report on the clinical and pathological prognostic factors that influenced outcome. Furthermore, we analyzed the risk associated with conservative surgery in younger patients with early-stage disease.

Materials and methods

Demographic, clinicopathological, treatment, and survival information of all women diagnosed with SCST of the ovary during the period from January 1st, 1992 to December 31st, 2001 were extracted from the Surveillance, Epidemiology, and End Results (SEER) database of the United States National Cancer Institute. Data are reported from 12 population-based registries that represent approximately 14% of the U.S. population [1]. Information on age at diagnosis, FIGO stage, grade, and tumor size was also extracted. Primary surgical treatment was categorized into three groups: no surgery, standard surgical staging including a hysterectomy, and conservative uterine-sparing surgery.

Statistical analysis was performed using the Intercooled STATA 8.0 program (College Station, TX). Survival analysis was performed using the Kaplan–Meier estimates of survival probability, and the Cox-proportional hazards model was used to identify independent predictors of disease-specific survival. A two-sided p-value <0.05 was considered statistically significant.

Results

A total of 376 women with sex cord stromal tumors of the ovary were identified. 339 of these patients had granulosa cell tumors and 37 (10%) had Sertoli-Leydig cell tumors. The median age of women in this group was 51 years (9–93). 280 (75%) of patients were Caucasian, 65 (17%) were Black, 18 (5%) Asian, and 13 (3%) of other racial backgrounds (Table 1).

234 women (63%) received standard primary surgical staging that included a hysterectomy, whereas 129 (34%) underwent surgical treatment without hysterectomy. 70% of patient presented with stage I disease, 10% stage II, 11% stage III, and 9% with stage IV cancers. Of the 106 patients with information on grade, 65 (61%) had low grade (1–2) disease and 41 (39%) had grade 3 disease. Tumor size was recorded for 210 cases with a median size of 11 cm (range: 0.5–50).

The overall 5-year and 10-year disease-specific survival for all patients was 88% and 79%. Patients with early-stage (Stage I–II) disease had a 5-year and 10-year survival of 95% and 84%, compared to only 59% and 57% for those with advanced stage disease ($p<0.001$) (see Fig. 1). Younger women (≤ 50 years) had a 5-year survival advantage over older (>50 years) women (93% vs. 84%, $p<0.001$) (see Fig. 2). Patients with grade 1–2 tumors had better 5-year survival than those with grade 3 disease (96% vs. 64%, $p<0.001$) (see Fig. 3). Tumor size was not an important predictor for survival; for, those with tumors ≤ 10 cm vs. >10 cm had a survival of 91% vs. 89%, respectively ($p=0.42$).

To determine the outcomes of young women who underwent uterine-sparing procedures, we analyzed the survival for the group of 134 younger patients (≤ 50 years) with stage I disease. The outcome for this group of young patients with stage I disease was excellent with a 5-year and 10-year disease-specific survival of 97% and 94%. Sixty-one (46%) of these patients underwent standard surgical which included a hysterectomy and 71 (54%) had a uterine-sparing procedure. There was no difference in the outcome of women who had a standard vs. conservative surgery (97% vs. 98%, $p=0.61$).

The factors that were significant in univariate analysis were then analyzed in a multivariate analysis using the Cox proportional hazards model. Younger age at diagnosis (hazard ratio = 1.03; 95% C.I. = 1.01–1.05) and early-stage (Stage I–II) of disease (hazard ratio = 1.79; 95% C.I. = 1.43–2.25) remained as significant prognostic factors for improved disease-specific survival (Table 2).

Discussion

Ovarian sex cord stromal tumors (SCST) are relatively rare malignancies. As such, most studies of this disease have been hindered by small number of patients that limit conclusive statistical analysis. To our knowledge, this current report represents the largest series of women with sex cord stromal tumors in the literature. Consistent with the well-known indolent nature of this disease, our series showed an extremely favorable prognosis

Table 1
Demographic and clinicopathologic information

Characteristics	Total ($n=376$)
Age of diagnosis	
Mean (years)	52.1 ± 0.9
Median (range)	51 (9–93)
Race	
White	280 (74.5%)
Black	65 (17.3%)
Asian	18 (4.8%)
Other	13 (3.5%)
Surgery	
Surgical staging with hysterectomy	234 (63.0%)
Uterine preserving surgery	129 (34.0%)
No surgery	13 (13.0%)
Stage at diagnosis	
Stage I	265 (70.5%)
Stage II	39 (10.4%)
Stage III	40 (10.6%)
Stage IV	32 (8.5%)
Histology	
Granulosa	339 (90.0%)
Sertoli-Leydig	37 (10.0%)
Grade of disease	
Grade 1	24 (6.4%)
Grade 2	41 (10.9%)
Grade 3	41 (10.9%)
Unknown	270 (71.8%)
Tumor size (median)	11 cm (range: 0.5–50)
Radiation	
No radiation	367 (97.6%)
Radiation	8 (2.1%)
Unknown	1 (0.3%)