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# Retroperitoneal lymph node staging in paratesticular rhabdomyosarcoma—are we meeting expectations?

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ABSTRACT

*Background:* Staging retroperitoneal lymph node dissection (RPLND) for paratesticular rhabdomyosarcoma (RMS) is recommended for all patients aged ≥10 y. The purpose of this study was to evaluate adherence with surgical resection guidelines for RPLND in patients with paratesticular RMS as a measure for surgical quality.

*Materials and methods:* All patients with paratesticular RMS were identified in the Surveillance, Epidemiology, and End Results database from 1973 to 2012. Patients were divided into two eras to reflect before (1973-2002) and after (2003-2012) the release and dissemination of the 2001 surgical guidelines for staging ipsilateral RPLND in all patients aged ≥10 y with paratesticular RMS. Survival outcomes associated with lymph node dissection were calculated using the Kaplan–Meier method and Cox proportional hazards analysis.

*Results:* Two hundred thirty-five patients with paratesticular RMS were identified and included in the study, among whom 111 were adolescents aged 10-20. RPLND did not significantly increase after 2003 among adolescents (45%-61%, $P = 0.09$). The benefit of RPLND on improved 5-y overall survival was evident among adolescents (92% *versus* 64%, $P = 0.003$). Adjusting for histology, age, stage at diagnosis, and race/ethnicity, RPLND was associated with improved overall survival among patients aged ≥10 y (hazard ratio 0.37, 95% confidence interval 0.17-0.83).

*Conclusions:* Despite surgical guidelines recommending RPLND in pediatric patients aged ≥10 y, nearly one-third of adolescent patients did not undergo RPLND. These findings are disturbing considering the survival benefit associated with RPLND among adolescent patients and indicate an opportunity for improvement in surgical quality.



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## Introduction

Assessing and improving the quality and safety of surgical care have become increasingly important to providers, patients, and health-care systems. However, there are few studies that have examined quality among pediatric surgical patients with cancer. There is considerable debate to define the best patient-centered outcome measures.[1-4] Donabedian proposed that health-care quality can be measured by its structure, processes, and outcomes.[3] The surgical literature has historically focused on the reporting of direct outcomes such as mortality and postoperative complications as indicators of quality. However, the use of mortality as a direct outcome for pediatric oncology is limited by small sample sizes. Moreover, if the case volume is low, there may not be sufficient adverse events to report.[4]

Adherence to evidence-based surgical guidelines has been proposed as a surrogate marker of surgical quality among oncology patients. As quality indicators, process-based measures such as adherence to treatment guidelines must have a strong relationship with a given outcome.[3] Surgical guidelines for the management of cancer are developed based on the best available evidence for optimizing disease-free and survival outcomes.

Paratesticular rhabdomyosarcoma (RMS) is a rare disease with an incidence of two to seven cases per million.[5,6] Much of the management of pediatric patients with paratesticular RMS has been based on the results of studies from the Intergroup Rhabdomyosarcoma Study Group (IRS). Accurate staging of patients is important for determining adjuvant chemotherapy regimen and radiation therapy. Results from the IRS-IV suggested that computer tomography imaging alone was inadequate for staging of lymph nodes in adolescents aged ≥10 y and led to a higher rate of regional relapse and mortality.[7] Based on these findings, the Soft Tissue Sarcoma Committee of the Children's Oncology Group (COG-STS) released guidelines for staging ipsilateral retroperitoneal lymph node dissection (RPLND) among all adolescent patients ≥ 10 y of age with paratesticular RMS.[7] The purpose of this study was to evaluate adherence with surgical resection guidelines for RPLND in patients with paratesticular RMS as a measure of surgical quality.

## Material and methods

The study design was a retrospective cohort analysis using the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. The SEER database is a population-based cancer registry derived from 20 cancer registries and represents approximately 28% of the United States population. Patients with a diagnosis of paratesticular RMS from 1972 to 2012 within the SEER database were identified by the International Classification of Disease for Oncology, Third Edition histology codes 8900, 8901, 8902, 8903, 8904, 8910, 8912, 8920, 8921, and 8991 and primary site codes C62.0, C62.1, C62.9, C653.0, C63.1, and C63.2. We further selected cases with adequate data regarding staging, primary surgery, nodal management, and survival.

We characterized variation in performance of RPLND for patients before and after the release of the COG-STS RMS surgical guidelines for staging ipsilateral RPLND in all patients aged ≥10 y with paratesticular RMS. Patients were considered to not have undergone an RPLND if the patient was coded as "no nodes examined" under the variable "regional nodes examined (1988+)"; "no regional lymph nodes removed or aspirated; diagnosis at autopsy", "biopsy or aspiration of regional lymph node, not otherwise specified", "sentinel lymph node biopsy" under "treatment summary - scope of regional lymph node surgery (2003+)"; or "no regional lymph nodes examined" in the variable "treatment summary - regional lymph node examined (1998-2002)". Patients with missing nodal information were excluded from the analysis.

Patients were divided into children (<10 y), adolescents (10-20) and adults (>20) as based on the inclusion criteria for the IRS-III and IRS-IV studies. The listed year of diagnoses was used to categorize patients into one of two treatment eras: 1973-2002 and 2003-2012. We chose to use this cutoff as defined by the publication of the guidelines for staging RPLND in adolescents aged ≥10 y by the COG-STS in 2001 and a 1-year period for dissemination of the guidelines.

In addition to topography and morphology, case characteristics of patients with paratesticular RMS were extrapolated from SEER including age, sex, year of treatment, race/ethnicity, stage of disease, surgical procedure performed, number of lymph nodes dissected, and number of positive lymph nodes. Stage of disease was classified as local, regional, distant, and unknown according to the SEER historic stage A variable.

Patient parameters were statistically compared between age groups using Student's *t*-test for continuous variables and Pearson's chi-square test for categorical variables. Performance of an RPLND among adolescents aged 10-20 y was compared between the two treatment eras using a chi-square test. Comparison of RPLND among children aged <10 y and adults aged >20 y between the two treatment eras was also performed as controls for temporal trend.

The outcomes of pediatric, adolescent, and adult patient groups were primarily compared on the basis of overall survival (OS) using the Kaplan–Meier method. Estimates of differences between survival curves of patient groups were compared using the log-rank test. Multivariate Cox proportional hazards regression models were constructed to adjust for the effect of different variables on survival. Lymph node status was not included in the final multivariate model because of collinearity with performance of an RPLND (i.e. all patients with positive nodes had undergone an RPLND). Furthermore, SEER does not include preoperative imaging findings, and a large proportion of adolescent and adult patients ($n = 88$, 56%) had unknown lymph node status because the nodes were not sampled or biopsied. All statistical analyses were performed with STATA, version 14.0 (StataCorp, College Station, TX). All tests were two-sided, and a $P < 0.05$ was considered statistically significant.