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# The effect of microscopic margin status on survival in adult retroperitoneal soft tissue sarcomas

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## Abstract

*Introduction*: Resection is the primary treatment for retroperitoneal (RP) soft tissue sarcomas (STS). Whether obtaining microscopically negative margins (R0) improves overall survival (OS) over microscopically positive margins (R1) remains unclear.
*Methods*: Using the National Cancer Data Base, we identified adult patients diagnosed with RP STS after R0 or R1 resection from 1998 to 2011. We used a multivariable logistic regression model to identify clinicopathologic factors associated with margin status, including radiotherapy receipt. To assess differences in OS, the log-rank test, Cox proportional hazards regression, and propensity score matching were used.
*Results*: We identified 4015 patients; 2593 (64.6%) underwent R0 resection and 1422 (35.4%) underwent R1 resection. The most common histology was liposarcoma (2,371, 59.1%), median age was 60 years, and median follow up was 67 months. Median OS for R0 vs. R1 patients was 92 and 70 months, respectively (log-rank $p < .001$). Pre-operative RT was associated with increased probability of R0 resection (68.0% vs. 57.2%, $p = .012$). Multivariable regression showed R0 vs. R1 resection (HR 0.70, 95% CI 0.60–0.81, $p < .001$) was associated with improved survival, a finding confirmed on propensity score matching. Other significant predictors of OS included low tumor grade, younger age, smaller tumor size, liposarcoma histology, and receipt of RT (HR 0.81, 95% CI 0.70–0.93, $p = .016$).
*Conclusions*: Patients who undergo R0 resection for RP STS appear to experience superior OS compared with patients who had R1 resections.


*Keywords:* Retroperitoneal soft tissue sarcoma; Resection margin; Radiation; R0

## Introduction

Retroperitoneal (RP) sarcomas comprise approximately 15% of all soft tissue sarcomas (STS), with an incidence of 2.7 cases per million in the United States.[1] Surgical resection is the most effective and only potentially curative treatment for RP STS. Unfortunately, anatomical concerns specific to the retroperitoneum (such as asymptomatic tumor progression leading to delayed presentation with large tumor size and invasion of adjacent critical structures) pose unique challenges to surgeons attempting to achieve adequate resection margins. The most important predictor of local recurrence and overall survival in RP STS is complete surgical resection.[2–4]

While historical literature describes a "complete resection" as no gross residual disease after surgery, this definition includes both microscopically negative (R0) and positive (R1) resections. In one of the largest available retrospective series describing surgical resection of RP STS, 80% of margins were deemed "complete" but only 58% of these were true R0 resections.[5] Microscopically positive margins are believed to increase the risk for local recurrence,[4,6] although the impact of this on survival

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remains unclear. Some retrospective studies show that R1 resection patients experience inferior disease specific survival (DSS),[4] while others failed to show a correlation between microscopically positive margins and inferior DSS.[7] Two approaches aimed at reducing the rate of R1 resection include more extensive surgery with en bloc resection of involved structures[8,9] and preoperative radiotherapy (RT).[10] A recent retrospective analysis demonstrated improved local control with RT in RP STS, but no disease specific survival benefit was seen.[11]

The goal of the current study was to determine if R0 vs. R1 margin status was associated with overall survival (OS) using a large national database.

## Patients and methods

### *Data source and study cohort*

We performed a retrospective study of survival outcomes for patients diagnosed with retroperitoneal sarcoma in the National Cancer Data Base (NCDB). The NCDB is a national hospital-based cancer registry established by the Commission on Cancer of the American College of Surgeons and the American Cancer Society, and serves as a comprehensive retrospective data set capturing approximately 70% of all incident cancers in the United States.[12] This data set integrates records from over 1500 Commission on Cancer accredited hospitals. This study was exempt from our Institutional Review Board.

We limited the cohort to patients with ICD-O-3 site code C480 and histology codes for liposarcoma (8850–8858), leiomyosarcoma (8890–8891 and 8896), and other more common sarcoma histologies (9040–9043, 9540, 8800–8811, 8840, 8894, 8895, 9120, and 9170). Inclusion and exclusion criteria are summarized in Fig. 1. We excluded patients younger than 18 years, those with prior cancer diagnoses, those with metastatic disease by clinical or pathological staging, those lacking vital statistics due to diagnosis in 2012, and those who did not undergo surgery. Patients with macroscopic residual tumor (R2) or unknown margin status were excluded from the cohort. Of note, only 455 cases had been coded as R2 resection (comprising 6% of all patients with evaluable margins) and were excluded. Prior to performing outcome analysis using the multivariable model, cases that contained any missing values were dropped.

### *Variables*

Surgical margins were coded as either R0 (“complete resection with no residual tumor, margins grossly and microscopically negative”) or R1 (“residual microscopic residual tumor not visible by naked eye or residual tumor not otherwise specified”). Age at diagnosis was categorized into those above and those below the median cohort age (<60 and ≥60 years). Interactions between gender, race (white vs. other), Charlson/Deyo comorbidity index (C/D scores 0 vs. ≥1), and year of diagnosis were included in

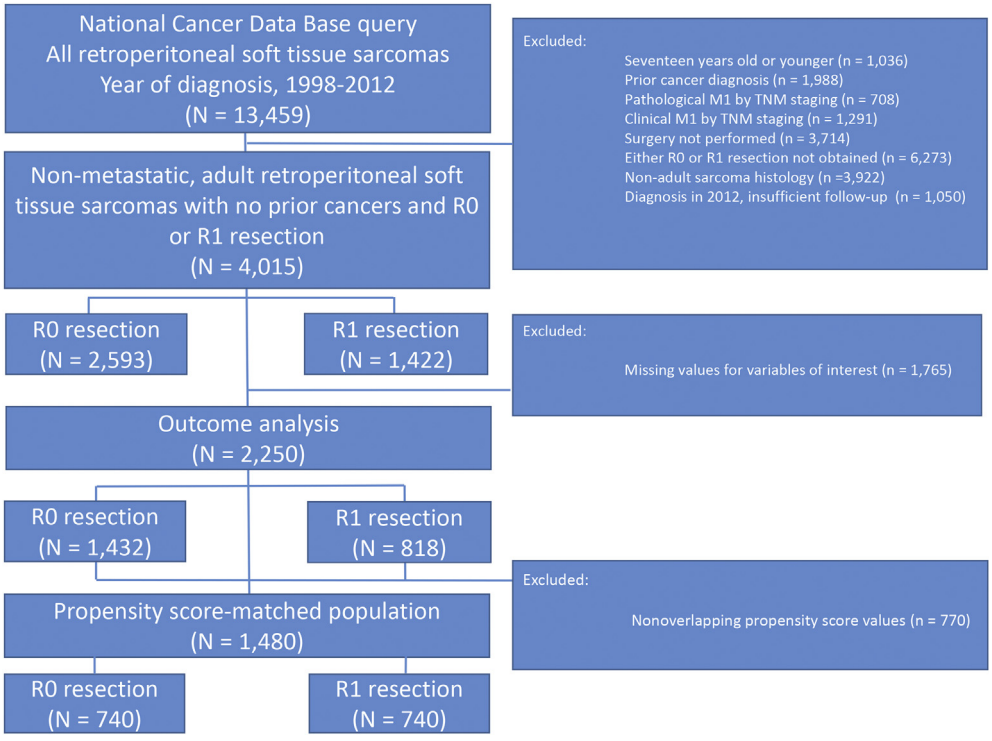


Figure 1. Study flow diagram for cohort selection

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