Research Article

The Volume-Outcome Relationship in Retroperitoneal Soft Tissue Sarcoma: Evidence of Improved Short- and Long-Term Outcomes at High-Volume Institutions

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Background. We sought to study the association between RPS case volume and outcomes. Although a relationship has been demonstrated between case volume and patient outcomes in some cancers, such a relationship has not been established for retroperitoneal sarcomas (RPSs). Study Design. The National Cancer Database (NCDB) was queried for patients undergoing treatment for primary RPS diagnosed between 2004 and 2013. Mean annual patient volume for RPS resection was calculated for all hospitals and divided into low volume (<5 cases/year), medium volume (5–10 cases/year), and high volume (>10 cases/year). Risk-adjusted regression analyses were performed to identify predictors of 30-day surgical mortality, $R_0$ margin status, and overall survival (OS). Results. Our study population consisted of 5,407 patients with a median age of 61 years, of whom 47% were male and 3,803 (70%) underwent surgical resection. Absolute 30-day surgical mortality and $R_0$ margin rate following surgery for low-, medium-, and high-volume institutions were 2.4%, 1.3%, and 0.5% ($p < 0.027$) and 68%, 65%, and 82% ($p < 0.001$), respectively. Five-year overall survival rates for low, medium, and high-volume institutions were 56%, 57%, and 66%, respectively ($p < 0.001$). Patients treated at low-volume institutions had a significantly higher risk of 30-day mortality (adjusted OR = 4.66, 95% CI 2.26–9.63) and long-term mortality (adjusted HR = 1.56, 95% CI 1.16–2.11) compared to high-volume institutions. Conclusion. We demonstrate the existence of a hospital sarcoma service line volume-oncologic outcome relationship for RPS at the national level and provide benchmark data for cancer care delivery systems and policy makers.

1. Introduction

Retroperitoneal sarcomas (RPSs) are rare tumors that account for 15–20% of all soft tissue sarcomas. The majority of cases present with localized disease, and therefore, surgical resection is the mainstay of treatment. Extirpations are complex procedures that often require removal of adjacent organs and dissection along critical structures, and as a result, they can be associated with significant morbidity. Furthermore, the efficacy of surgery depends on the ability to achieve negative margins, which requires multidisciplinary preoperative and intraoperative expertise in radiology, pathology, and surgical subspecialties.

Hospital surgical volume is a well-studied measure associated with improved outcomes in multiple tumor subtypes [1–4]. In particular, such a relationship has been reported for complex surgical oncologic procedures such as colectomy, nephrectomy, and pancreatectomy, all of which...
are commonly performed for RPS [5–7]. As a result, centralization of complex surgical oncologic procedures to high-volume centers has been advocated [1, 2, 4]. The premise is that high-volume centers have the experience and expertise to perform these complex procedures in an optimal manner with correspondingly superior outcomes compared to low-volume centers.

Such a volume-outcome association has not been demonstrated at the national level for RPS, likely due to the rarity of the disease. Nevertheless, due to the multispecialty expertise required to optimally treat these tumors, an association may exist. Our hypothesis is that high-volume centers treating primary RPS have a lower 30-day postoperative mortality, higher margin negative resection rate, and improved overall survival compared to low-volume centers.

2. Methods

2.1. Data Source. Data from the National Cancer Database (NCDB) were used to conduct this study. The NCDB, a joint program of the Commission on Cancer (CoC) of the American College of Surgeons (ACoS) and the American Cancer Society (ACS), is a nationwide database for more than 1,500 commission-accredited cancer programs in the United States and Puerto Rico. Approximately 70% of all newly diagnosed cases of cancer in the United States are captured at the institutional level and reported to the NCDB. Variables in the database cover demographics, socioeconomic status, tumor stage, treatment received, and hospital characteristics. NCDB data contain no protected health information; hence, this study was exempt from formal IRB review.

2.2. Inclusion/Exclusion Criteria. Patients diagnosed with RPS from 2004 to 2013 were identified from the NCDB and constituted our study population (note that patients with extraabdominal sarcoma and gastrointestinal stromal tumors were not included). This time period was chosen to ensure up-to-date coding in the NCDB for the variables of interest for this study and to provide at least 5 years of follow-up for survival analyses.

Two patient cohorts were created. The first comprised all patients diagnosed with RPS irrespective of whether they underwent surgery or not. This group included all stages and represents the institutional experience with RPS. We believe this group better represents any association between volume and long-term survival as it captures multidisciplinary care. The second cohort is a subset of this group comprising only of patients who underwent curative intent surgery. This group was defined to study the association between surgical volume and short-term outcomes. NCDB surgical codes distinguish between curative intent surgery and procedures such as open biopsies. For this surgery-only group, patients with metastatic disease and those not undergoing curative intent surgery were excluded. For both groups, only patients who had all treatment (surgery, radiation therapy, and/or chemotherapy) at the reporting hospital were included in order to provide valid volume-outcome comparisons.

2.3. Outcome, Exposure, and Independent Variables. The exposure variable was the hospital volume status. Primary outcome variables were overall survival (OS), surgical margins, and 30-day surgical mortality. Surgical margins were defined as negative (R0) or positive (R1/R2). Independent variables included age, sex, race, insurance status, education, modified Charlson score, primary tumor site, pathologic tumor size, grade, histology, radiation therapy, and chemotherapy. Tumor histology was grouped into clinically significant categories by using ICD codes. Tumor grade was divided into GX (unknown), G1 (well differentiated), G2 (moderately differentiated), and G3 (poorly or undifferentiated).

2.4. Hospital Volume Calculations. Average annual volume/hospital of curative intent surgery for RPS was calculated by dividing the total number of surgical resections performed at a hospital by the number of years that data were reported to the NCDB. A histogram of average annual volume/hospital was then plotted, and volume cutoffs were chosen to divide our patient cohorts into three groups: low volume (<5 cases/year), medium volume (5–10 cases/year), and high volume (>10 cases/year) to ensure volume groups with adequate number of patients to enable robust statistical analyses. For analyses involving the all cases cohort, the same volume cutoffs were used to ensure comparability.

2.5. Statistical Analyses. Bivariate analyses were initially performed to identify demographic, tumor, and treatment differences between different volume categories using the chi-square test or analysis of variance. Logistic regression analyses were used to model the margin negative resection and 30-day mortality following surgery, and adjusted odds ratios (OR) and 95% confidence intervals (CI) were reported. OS was estimated by the Kaplan–Meier method, and the comparison in the survival curves between different surgical volumes was assessed by the log rank test. Cox regression analyses were used to model overall survival, and adjusted hazard ratios (HR) and 95% CIs were reported. Patients who died within 30 days of surgery were excluded from survival analyses. A p value of <0.05 was set as our threshold for statistical significance. The analysis was performed using SAS 9.4 and R 3.3.0.

3. Results

3.1. Demographics. We identified 5,407 patients with primary RPS who comprised our primary study population (Table 1). The median age was 61 years, and 53% were female. The mean tumor size was 18.5 cm (median = 15.5 cm), and a plurality of tumors were well differentiated (36%). Approximately 76% of patients underwent surgery, 26% received radiation therapy, and 17% received systemic therapy. There were 3,807 patients who underwent surgical resection for curative intent of primary RPS (Table 2) excluding stage-4 cancers. The median age was 62 years, and 53% were female. The median tumor size was 16.8 cm. Most tumors were well differentiated (36%).
Table 1: Patient characteristics: all patients.

|                  | High volume (N = 563) | Medium volume (N = 373) | Low volume (N = 4471) | Total (N = 5407) | p value |
|------------------|------------------------|-------------------------|-----------------------|------------------|---------|
| **Age at diagnosis** |                        |                         |                       |                  | 0.0085  |
| Mean (SD)        | 59.6 (14.3)            | 58.5 (14.4)             | 60.7 (14.2)           | 60.4 (14.2)      |         |
| Median            | 60.0                   | 59.0                    | 62.0                  | 61.0             |         |
| Q1, Q3           | 51.0, 70.0             | 50.0, 68.0              | 52.0, 71.0            | 52.0, 71.0       |         |
| Range             | (19.0–90.0)            | (18.0–88.0)             | (18.0–90.0)           | (18.0–90.0)      |         |
| **Sex**          |                        |                         |                       |                  | 0.0001  |
| Male             | 304 (54.0%)            | 193 (51.7%)             | 2028 (45.4%)          | 2525 (46.7%)     |         |
| Female           | 259 (46.0%)            | 180 (48.3%)             | 2443 (54.6%)          | 2882 (53.3%)     |         |
| **Race**         |                        |                         |                       |                  | 0.0010  |
| Black            | 34 (6.0%)              | 30 (8.0%)               | 500 (11.2%)           | 564 (10.4%)      |         |
| Other            | 29 (5.2%)              | 26 (7.0%)               | 271 (6.1%)            | 326 (6.0%)       |         |
| White            | 500 (88.8%)            | 317 (85.0%)             | 3700 (82.8%)          | 4517 (83.5%)     |         |
| **Charlson–Deyo score** |                    |                         |                       |                  | 0.0047  |
| 0                | 472 (83.8%)            | 307 (82.3%)             | 3500 (78.3%)          | 4279 (79.1%)     |         |
| 1                | 79 (14.0%)             | 52 (13.9%)              | 755 (16.9%)           | 886 (16.4%)      |         |
| 2                | 12 (2.1%)              | 14 (3.8%)               | 216 (4.8%)            | 242 (4.5%)       |         |
| **Year of diagnosis** |                    |                         |                       |                  | 0.37    |
| 2004             | 49 (8.7%)              | 20 (5.4%)               | 353 (7.9%)            | 422 (7.8%)       |         |
| 2005             | 41 (7.3%)              | 25 (6.7%)               | 392 (8.8%)            | 458 (8.5%)       |         |
| 2006             | 56 (9.9%)              | 37 (9.9%)               | 404 (9.0%)            | 479 (9.2%)       |         |
| 2007             | 56 (9.9%)              | 38 (10.2%)              | 422 (9.4%)            | 516 (9.5%)       |         |
| 2008             | 66 (11.7%)             | 37 (9.9%)               | 453 (10.1%)           | 556 (10.3%)      |         |
| 2009             | 64 (11.4%)             | 34 (9.1%)               | 452 (10.1%)           | 550 (10.2%)      |         |
| 2010             | 51 (9.1%)              | 38 (10.2%)              | 479 (10.7%)           | 568 (10.5%)      |         |
| 2011             | 68 (12.1%)             | 48 (12.9%)              | 522 (11.7%)           | 638 (11.8%)      |         |
| 2012             | 59 (10.5%)             | 59 (15.8%)              | 508 (11.4%)           | 626 (11.6%)      |         |
| 2013             | 53 (9.4%)              | 37 (9.9%)               | 488 (10.9%)           | 576 (10.7%)      |         |
| **Facility type** |                        |                         |                       |                  | <0.0001 |
| Missing 48       |                        | 39                       | 364                   | 451             |         |
| Community cancer program | 0 (0.0%) | 1 (0.3%) | 230 (5.6%) | 231 (4.7%) |         |
| Comprehensive community cancer program | 0 (0.0%) | 0 (0.0%) | 1428 (34.8%) | 1428 (28.8%) |         |
| Academic/research program | 515 (100.0%) | 283 (84.7%) | 2023 (49.3%) | 2821 (56.9%) |         |
| Integrated network cancer program | 0 (0.0%) | 50 (15.0%) | 426 (10.4%) | 476 (9.6%) |         |
| **Primary payor** |                        |                         |                       |                  | <0.0001 |
| Not insured      | 7 (1.2%)               | 10 (2.7%)               | 181 (4.0%)            | 198 (3.7%)       |         |
| Private insurance| 243 (43.2%)            | 195 (52.3%)             | 2127 (47.6%)          | 2565 (47.4%)     |         |
| Medicaid         | 17 (3.0%)              | 25 (6.7%)               | 271 (6.1%)            | 313 (5.8%)       |         |
| Medicare         | 168 (29.8%)            | 131 (35.1%)             | 1774 (39.7%)          | 2073 (38.3%)     |         |
| Other government | 5 (0.9%)               | 1 (0.3%)                | 61 (1.4%)             | 67 (1.2%)        |         |
| Insurance status unknown | 123 (21.8%) | 11 (2.9%) | 57 (1.3%) | 191 (3.5%) |         |
| **Median income quartiles** |        |            |                        |                  | 0.0078  |
| Missing 36       | 36 (6.8%)              | 41 (11.3%)              | 547 (12.7%)           | 624 (12.0%)      |         |
| <$30,000         | 36 (6.8%)              | 41 (11.3%)              | 547 (12.7%)           | 624 (12.0%)      |         |
| $30,000–$35,999  | 98 (18.6%)             | 67 (18.5%)              | 716 (16.6%)           | 881 (16.9%)      |         |
| $36,000–$45,999  | 139 (26.4%)            | 101 (27.8%)             | 1124 (26.1%)          | 1364 (26.2%)     |         |
| $46,000+         | 254 (48.2%)            | 154 (42.4%)             | 1925 (44.6%)          | 2333 (44.8%)     |         |
| **No high school degree (%)** |       |            |                        |                  | <0.0001 |
| Missing 36       | 58 (11.0%)             | 33 (9.1%)               | 681 (15.8%)           | 772 (14.8%)      |         |
| ≥29%             | 96 (18.2%)             | 91 (25.1%)              | 961 (22.3%)           | 1148 (22.1%)     |         |
| 20–28.9%         | 125 (23.7%)            | 96 (26.4%)              | 994 (23.1%)           | 1215 (23.4%)     |         |
| 14–19.9%         | 248 (47.1%)            | 143 (39.4%)             | 1676 (38.9%)          | 2067 (39.7%)     |         |
| <14%             |                        |                         |                       |                  |         |
| **Distance to treating center (miles)** |        |            |                        |                  | <0.0001 |
| Mean (SD)        | 223.5 (389.7)          | 68.2 (119.1)            | 39.5 (136.1)          | 60.6 (187.7)     |         |
| Median            | 75.9                   | 38.4                    | 12.4                  | 15.4             |         |
| Q1, Q3           | 22.4, 242.7            | 15.0, 89.8              | 5.1, 33.5             | 5.8, 46.2        |         |
| Range             | (1.0–40.1)             | (1.0–1495.6)            | (1.0–4710.1)          | (1.0–4710.1)     |         |
Tables 1 and 2 also provide descriptive data stratified by annual volume (<5 cases, 5–10 cases, and >10 cases). The number of high-volume centers in the United States performing >10 primary surgical resections on average annually was only 3/678 (0.4%), while the overwhelming majority were low volume 671/678 (99%). Using the same volume
cutoffs for all cases of primary RPS treated increased the high-volume centers to four. Correspondingly, low volume centers treated 83% of all patients and also performed 83% of all curative intent surgery, while the same proportion was 10% and 11% for high-volume centers. Overall, high-volume centers were all academic/research centers.

| Table 1: Continued. | High volume (N = 563) | Medium volume (N = 373) | Low volume (N = 4471) | Total (N = 5407) | p value |
|----------------------|-----------------------|-------------------------|-----------------------|------------------|---------|
| Histologic subtype   |                       |                         |                       |                  | <0.0001 |
| Dedifferentiated liposarcoma | 160 (28.4%) | 81 (21.7%) | 755 (16.9%) | 996 (18.4%) |          |
| Fibrosarcoma          | 10 (1.8%)            | 5 (1.3%)                | 67 (1.5%)             | 82 (1.5%)        |          |
| Leiomyosarcoma        | 98 (17.4%)           | 88 (23.6%)              | 1069 (23.9%)          | 1255 (23.2%)     |          |
| Liposarcoma           | 188 (33.4%)          | 98 (26.3%)              | 1468 (32.8%)          | 1754 (32.4%)     |          |
| MFH                  | 5 (0.9%)             | 5 (1.3%)                | 96 (2.1%)             | 106 (2.0%)       |          |
| MPNST                | 6 (1.1%)             | 6 (1.6%)                | 42 (0.9%)             | 54 (1.0%)        |          |
| Rare/NOS             | 96 (17.1%)           | 90 (24.1%)              | 974 (21.8%)           | 1160 (21.5%)     |          |
| Grade                |                       |                         |                       |                  | <0.0001 |
| Missing              | 97                    | 71                      | 992                   | 1160             |          |
| Well differentiated   | 172 (36.9%)          | 85 (28.1%)              | 1256 (36.1%)          | 1513 (35.6%)     |          |
| Mod differentiated    | 23 (4.9%)            | 38 (12.6%)              | 587 (16.9%)           | 648 (15.3%)      |          |
| Poorly differentiated | 99 (21.2%)           | 111 (36.8%)             | 1019 (29.3%)          | 1229 (28.9%)     |          |
| Undifferentiated      | 172 (36.9%)          | 68 (22.5%)              | 617 (17.3%)           | 857 (20.2%)      |          |
| Tumor size           |                       |                         |                       |                  | 0.35    |
| Missing              | 36                    | 17                      | 327                   | 380              |          |
| 5–10 cm              | 98 (18.6%)           | 80 (22.5%)              | 848 (20.5%)           | 1026 (20.4%)     |          |
| <5 cm                | 42 (8.0%)            | 27 (7.6%)               | 391 (9.4%)            | 460 (9.2%)       |          |
| >10 cm               | 387 (73.4%)          | 249 (69.9%)             | 2905 (70.1%)          | 3541 (70.4%)     |          |
| AJCC stage group     |                       |                         |                       |                  | <0.0001 |
| Stage I              | 180 (32.0%)          | 90 (24.1%)              | 1322 (29.6%)          | 1592 (29.4%)     |          |
| Stage II             | 49 (8.7%)            | 39 (10.5%)              | 560 (12.5%)           | 648 (12.0%)      |          |
| Stage III            | 204 (36.2%)          | 140 (37.5%)             | 1278 (28.6%)          | 1622 (30.0%)     |          |
| Stage IV             | 38 (6.7%)            | 20 (5.4%)               | 314 (7.0%)            | 372 (6.9%)       |          |
| AJCC staging not applicable | 22 (3.9%) | 27 (7.2%) | 275 (6.2%) | 324 (6.0%) | |
| AJCC stage group unknown | 70 (12.4%) | 57 (15.3%) | 722 (16.1%) | 849 (15.7%) | |
| Surgery              |                       |                         |                       |                  | <0.0001 |
| No                   | 53 (9.4%)            | 73 (19.6%)              | 1198 (26.8%)          | 1324 (24.5%)     |          |
| Yes                  | 510 (90.6%)          | 300 (80.4%)             | 3273 (73.2%)          | 4083 (75.5%)     |          |
| Radiation            |                       |                         |                       |                  | <0.0001 |
| Missing              | 0                     | 1                       | 79                    | 80               |          |
| No                   | 453 (80.5%)          | 293 (78.8%)             | 3196 (72.8%)          | 3942 (74.0%)     |          |
| Yes                  | 110 (19.5%)          | 79 (21.2%)              | 1196 (27.2%)          | 1385 (26.0%)     |          |
| Chemotherapy         |                       |                         |                       |                  | 0.0001  |
| Missing              | 6                     | 11                      | 188                   | 205              |          |
| No                   | 469 (84.2%)          | 270 (74.6%)             | 3569 (83.3%)          | 4308 (82.8%)     |          |
| Yes                  | 88 (15.8%)           | 92 (25.4%)              | 714 (16.7%)           | 894 (17.2%)      |          |
| Last contact or death, months from Dx | 41.7 (27.4) | 42.3 (31.6) | 43.8 (32.2) | 43.5 (31.7) | 0.68 |
| Median               | 37.6                  | 35.8                    | 37.2                 | 37.1             |          |
| Q1, Q3               | 20.0, 58.0           | 16.8, 61.0              | 17.9, 64.8           | 18.1, 63.5       |          |
| Range (0.6–133.1)    | (1.2–132.5)          | (0.0–142.6)             | (0.0–142.6)          | (0.0–142.6)      |          |
| Vital status         |                       |                         |                       |                  | <0.0001 |
| Dead                 | 177 (31.4%)          | 151 (40.5%)             | 1954 (43.7%)          | 2282 (42.2%)     |          |
| Alive                | 386 (68.6%)          | 222 (59.5%)             | 2517 (56.3%)          | 3125 (57.8%)     |          |
| Hospital volume      |                       |                         |                       |                  | <0.0001 |
| Mean (SD)            | 153.7 (46.5)         | 62.6 (3.0)              | 14.4 (12.5)           | 32.2 (47.1)      |          |
| Median               | 134.0                | 64.0                    | 10.0                 | 13.0             |          |
| Q1, Q3               | 114.0, 212.0         | 62.0, 65.0              | 5.0, 22.0            | 6.0, 35.0        |          |
| Range (103.0–212.0)  | (51.0–68.0)          | (1.0–47.0)              | (1.0–212.0)          | (1.0–212.0)      |          |
| Table 2: Patient characteristics: all surgical cases. |
|---------------------------------------------------|
|                                                    |
|                                                    |
| Age at diagnosis                                   |
| Mean (SD)                                          |
| High volume (N = 401)                              |
| 59.6 (13.7)                                        |
| Medium volume (N = 235)                            |
| 58.7 (14.5)                                        |
| Low volume (N = 3167)                              |
| 61.2 (13.9)                                        |
| Total (N = 3803)                                   |
| 60.9 (14.0)                                        |
| p value                                           |
| 0.0045                                             |
|                                                    |
| Median                                             |
| High volume (N = 401)                              |
| 60.0                                               |
| Medium volume (N = 235)                            |
| 60.0                                               |
| Low volume (N = 3167)                              |
| 62.0                                               |
| Total (N = 3803)                                   |
| 62.0                                               |
|                                                    |
| Q1, Q3                                            |
| High volume (N = 401)                              |
| 51.0, 69.0                                         |
| Medium volume (N = 235)                            |
| 50.0, 69.0                                         |
| Low volume (N = 3167)                              |
| 52.0, 71.0                                         |
| Total (N = 3803)                                   |
| 52.0, 71.0                                         |
|                                                    |
| Range                                             |
| High volume (N = 401)                              |
| (20.0–90.0)                                        |
| Medium volume (N = 235)                            |
| (19.0–87.0)                                        |
| Low volume (N = 3167)                              |
| (18.0–90.0)                                        |
| Total (N = 3803)                                   |
| (18.0–90.0)                                        |
|                                                    |
| Sex                                               |
| Male                                               |
| 216 (53.9%)                                        |
| Female                                             |
| 185 (46.1%)                                        |
|                                                    |
| Race                                              |
| Black                                              |
| 21 (5.2%)                                          |
| Other                                              |
| 22 (5.5%)                                          |
| White                                              |
| 358 (89.3%)                                        |
|                                                    |
| Charlson–Deyo score                               |
| 0                                                  |
| 336 (83.8%)                                        |
| 1                                                  |
| 55 (13.7%)                                         |
| 2                                                  |
| 10 (2.5%)                                          |
|                                                    |
| Year of diagnosis                                  |
| 2004                                               |
| 30 (7.5%)                                          |
| 2005                                               |
| 31 (7.7%)                                          |
| 2006                                               |
| 40 (10.0%)                                         |
| 2007                                               |
| 43 (10.7%)                                         |
| 2008                                               |
| 51 (12.7%)                                         |
| 2009                                               |
| 44 (11.0%)                                         |
| 2010                                               |
| 36 (9.0%)                                          |
| 2011                                               |
| 38 (9.5%)                                          |
| 2012                                               |
| 44 (11.0%)                                         |
| 2013                                               |
| 44 (11.0%)                                         |
|                                                    |
| Facility type                                      |
| Missing                                            |
| 31                                                 |
| Community cancer program                           |
| 0 (0.0%)                                           |
| Comprehensive community cancer program              |
| 0 (0.0%)                                           |
| Academic/research program                          |
| 370 (100.0%)                                       |
| Integrated network cancer program                  |
| 0 (0.0%)                                           |
|                                                    |
| Primary payor                                      |
| Not insured                                        |
| 2 (0.5%)                                           |
| Private insurance                                  |
| 175 (43.6%)                                        |
| Medicaid                                           |
| 6 (1.5%)                                           |
| Medicare                                           |
| 102 (25.4%)                                        |
| Other government                                    |
| 3 (0.7%)                                           |
| Insurance status unknown                           |
| 113 (28.2%)                                        |
| Median income quartiles                            |
| Missing                                            |
| 24                                                 |
| <$30,000                                           |
| 25 (6.6%)                                          |
| $30,000–$35,999                                    |
| 61 (16.2%)                                         |
| $36,000–$45,999                                    |
| 93 (24.7%)                                         |
| $46,000+                                           |
| 198 (52.5%)                                        |
|                                                    |
| No high school degree quartiles (%)                |
| Missing                                            |
| 24                                                 |
| ≥29%                                               |
| 43 (11.4%)                                         |
| 20–28.9%                                           |
| 62 (16.4%)                                         |
| 14–19.9%                                           |
| 85 (22.5%)                                         |
| <14%                                               |
| 187 (49.6%)                                        |
| Distance to treating center (miles)                |
| Mean (SD)                                          |
| 259.0 (433.2)                                      |
| Median                                             |
| 80.4                                               |
| Q1, Q3                                             |
| 22.9, 306.5                                       |
| Range                                              |
| (1.0–4040.1)                                       |
whereas approximately 24% of low-volume centers met that CoC designation. High-volume centers were more likely to provide care to males, Caucasians, those with lower Charlson–Deyo scores, and those who lived in high educational attainment zip codes. The median distance travelled for treatment at a high-volume hospital was 76 miles, compared to 12 miles for a low-volume hospital. High-volume centers were more likely to treat patients whose tumors were larger (17.5 cm versus 15 cm) and of higher grade (58% versus 47%) than low-volume centers. It is important to note that, since the NCDB does not report recurrence, these data only reflect the management of primary RPS and do not provide insight into the management of recurrent RPS.

### 3.2. Short-Term Outcomes (Surgery-Only Cohort)

A total of 82 patients (2.2%) died within 30 days after surgery was performed. The absolute 30-day mortality rates were 0.5%, 1.3%, and 2.4% at high, medium, and low volume centers, respectively. Following adjustment (Table 3), patients undergoing RPS surgery at a low-volume hospital had a greater

| Table 2: Continued. | High volume \(N = 401\) | Medium volume \(N = 235\) | Low volume \(N = 3167\) | Total \(N = 3803\) | \(p\) value |
|---------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| **Histologic subtype** |                        |                      |                      |                      | <0.0001               |
| Dedifferentiated liposarcoma | 125 (31.2%) | 69 (29.4%) | 585 (18.5%) | 779 (20.5%) |                      |
| Fibrosarcoma | 6 (1.5%) | 4 (1.7%) | 45 (1.4%) | 55 (1.4%) |                      |
| Leimyosarcoma | 64 (16.0%) | 38 (16.2%) | 715 (22.6%) | 817 (21.5%) |                      |
| Liposarcoma | 143 (35.7%) | 64 (27.2%) | 1078 (34.0%) | 1285 (33.8%) |                      |
| MFH | 2 (0.5%) | 4 (1.7%) | 70 (2.2%) | 76 (2.0%) |                      |
| MPNST | 3 (0.7%) | 2 (0.9%) | 25 (0.8%) | 30 (0.8%) |                      |
| Rare/NOS | 58 (14.5%) | 54 (23.0%) | 649 (20.5%) | 761 (20.0%) |                      |
| **Grade** |                        |                      |                      |                      | <0.0001               |
| Missing | 62 | 53 | 617 | 732 |                      |
| Well differentiated | 133 (39.2%) | 53 (29.1%) | 919 (36.0%) | 1105 (36.0%) |                      |
| Mod differentiated | 15 (4.4%) | 19 (10.4%) | 426 (16.7%) | 460 (15.0%) |                      |
| Poorly differentiated | 57 (16.8%) | 53 (29.1%) | 774 (30.4%) | 884 (28.8%) |                      |
| Undifferentiated | 134 (39.5%) | 57 (31.3%) | 431 (16.9%) | 622 (20.3%) |                      |
| **Tumor size** |                        |                      |                      |                      | 0.11                  |
| Missing | 29 | 6 | 206 | 241 |                      |
| 5-10 cm | 56 (15.1%) | 55 (24.0%) | 556 (18.8%) | 667 (18.7%) |                      |
| <5 cm | 29 (7.8%) | 17 (7.4%) | 236 (8.0%) | 282 (7.9%) |                      |
| >10 cm | 287 (77.2%) | 157 (68.6%) | 2169 (73.3%) | 2613 (73.4%) |                      |
| **AJCC stage group** |                        |                      |                      |                      | 0.016                 |
| Stage I | 128 (31.9%) | 63 (26.8%) | 989 (31.2%) | 1180 (31.0%) |                      |
| Stage II | 38 (9.5%) | 29 (12.3%) | 409 (12.9%) | 476 (15.2%) |                      |
| Stage III | 158 (39.4%) | 96 (40.9%) | 1044 (33.0%) | 1298 (34.1%) |                      |
| AJCC staging not applicable | 17 (4.2%) | 18 (7.7%) | 196 (6.2%) | 231 (6.1%) |                      |
| AJCC stage group unknown | 60 (15.0%) | 29 (12.3%) | 529 (16.7%) | 618 (16.3%) |                      |
| **Margins** |                        |                      |                      |                      | 0.0001                |
| Missing | 153 | 43 | 810 | 1006 |                      |
| Grossly positive \((R2)\) | 6 (2.4%) | 6 (3.1%) | 128 (5.4%) | 140 (5.0%) |                      |
| Microscopically positive \((R1)\) | 40 (16.1%) | 61 (31.8%) | 621 (26.3%) | 722 (25.8%) |                      |
| Negative \((R0)\) | 202 (81.5%) | 125 (65.1%) | 1608 (68.2%) | 1935 (69.2%) |                      |
| **30-day mortality** |                        |                      |                      |                      | 0.027                 |
| Patient alive or died more than 30 days after surgery performed | 399 (99.5%) | 232 (98.7%) | 3090 (97.6%) | 3721 (97.8%) |                      |
| Patient died 30 or fewer days after surgery performed | 2 (0.5%) | 3 (1.3%) | 77 (2.4%) | 82 (2.2%) |                      |
| **90-day mortality** |                        |                      |                      |                      | 0.0012                |
| Patient alive or died more than 90 days after surgery performed | 396 (98.8%) | 220 (93.6%) | 3000 (94.7%) | 3616 (95.1%) |                      |
| Patient died 90 or fewer days after surgery performed | 5 (1.2%) | 15 (6.4%) | 167 (5.3%) | 187 (4.9%) |                      |
| **Hospital volume** |                        |                      |                      |                      | <0.0001               |
| Mean (SD) | 143.5 (38.4) | 60.9 (12.1) | 12.8 (11.2) | 29.5 (44.0) |                      |
| Median | 108.0 | 53.0 | 8.0 | 11.0 |                      |
| Q1, Q3 | 108.0, 185.0 | 53.0, 78.0 | 4.0, 18.0 | 5.0, 32.0 |                      |
| Range | (108.0–185.0) | (51.0–78.0) | (1.0–45.0) | (1.0–185.0) |                      |
than fourfold increase in the risk of dying within 30 days of surgery compared to patients undergoing surgery at a high-volume hospital (OR = 4.66, 95% CI 2.26–9.63; \( p < 0.001 \)).

On sensitivity analyses, 90-day mortality rates followed a similar trend for absolute and adjusted risk of perioperative mortality.

The overall R0 margin rate was 69%. The R0 rate was 82%, 65%, and 68% for high-, medium-, and low-volume centers, respectively. Table 4 displays the multivariable analysis for R0 margin status; low-volume centers were less likely to achieve R0 margin status compared to high-volume centers (OR = 0.46, 95% CI 0.31–0.70; \( p = 0.0003 \)).

3.3. Long-Term Outcomes (All Cases). The median follow-up to last contact or death is 37 months. There were 2,282 deaths (42%) from all causes over the duration of the study. For all RPS patients, the 5-year overall survival was 57.1% (95% CI 55.6–58.7%). When stratified by the hospital volume, the 5-year overall survival for high-, medium-, and low-volume centers was 66%, 57%, and 56% (\( p < 0.001 \); Figure 1(a)). For RPS patients who underwent surgical resection for curative intent, the 5-year overall survival rate was 58.6% (95% CI 56.8–60.5%). When stratified by the hospital volume, the 5-year overall survival rates for patients undergoing curative intent surgery in high-, medium-, and low-volume centers was 69%, 56%, and 57%, respectively (\( p < 0.001 \); Figure 1(b)).

Table 5 displays the multivariable analysis for overall survival. After controlling for patient and tumor variables, patients who were treated at a low-volume hospital had a 52% greater risk of all-cause long-term mortality compared to those treated at a high-volume hospital (HR 1.56, 95% CI 1.16–2.11; \( p = 0.0032 \)).

4. Discussion

In this study of patients diagnosed with primary RPS, we show that patients treated at high-volume centers were four times less likely to die within 30 days of the procedure, 54% more likely to have an R0 margin status, and 52% more likely to be alive by the end of follow-up when compared to patients in low-volume centers. These results are consistent with a strong volume-outcome association for RPS for both short- and long-term outcomes.

Hospital surgical volume has been suggested to be a proxy for superior outcomes for multiple complex surgical oncologic procedures. Although surgical volume in itself impacts outcomes, it is likely that case volume is also associated with the quality of other processes at the institution. Optimal outcomes in this disease require team-based multidisciplinary care including medical oncology, radiation oncology, radiology, and pathology. The rarity of RPS means that tumor boards, compliance to NCCN guidelines, and coordination of survivorship care are all likely to contribute to better oncologic outcomes. For patients who did undergo surgery, the complexity of the surgical procedure requires processes designed to optimize perioperative care and manage complications such as subspecialty trained surgical oncologists, urologists, vascular surgeons, tertiary anesthesiologists, interventional radiologists, and critical care teams to optimize short-term outcomes. It is likely that increased surgical volume allows for a gain in proficiency both within the operating room as well as at the institutional level, which translates into better perioperative outcomes.

Although an argument could be made that our choice of cutoff to define what constitutes a high-volume institution is somewhat arbitrary, and this is consistent with another large study on the subject. The Transatlantic Retroperitoneal Sarcoma Working Group (TARPSWG) has published on 1,007 primary RPS patients treated in eight North American and European sarcoma centers from 2002 to 2011 [8, 9]. These centers are considered high volume and as a group averaged approximately 12 cases/year, similar to the threshold in this study. When we compare high-volume centers identified in the current study to the TARPSWG, we note other similarities in the outcomes measured. The group investigated the safety of resection of primary RPS and

### Table 3: Logistic regression analysis of 30-day postoperative mortality.

| Variable                | Odds ratio | 95% Wald Confidence limits | \( p \) value |
|-------------------------|------------|---------------------------|--------------|
| Age                     | 1.06       | 1.04–1.09                 | <0.0001      |
| Female (reference = male) | 0.92       | 0.61–1.40                 | 0.71         |
| Race (reference = white) |            |                           |              |
| Black                   | 1.16       | 0.56–2.39                 | 0.69         |
| Other                   | 0.74       | 0.23–2.37                 | 0.61         |
| Charlson–Deyo (reference = 2) |       |                           |              |
| 0                       | 1.13       | 0.65–1.95                 | 0.66         |
| 1                       | 1.67       | 0.79–3.50                 | 0.18         |
| Hospital volume (reference = high) | |                  |              |
| Medium                  | 2.73       | 0.65–11.51                | 0.17         |
| Low                     | 4.66       | 2.26–9.63                 | <0.0001      |

### Table 4: Logistic regression analysis of R0 margin status.

| Variable                | Odds ratio | 95% Wald Confidence limits | \( p \) value |
|-------------------------|------------|---------------------------|--------------|
| Age                     | 0.98       | 0.98–0.99                 | <0.0001      |
| Female (reference = male) | 1.11       | 0.94–1.31                 | 0.215        |
| Race (reference = white) |            |                           |              |
| Black                   | 1.20       | 0.90–1.60                 | 0.21         |
| Other                   | 0.98       | 0.69–1.40                 | 0.93         |
| Charlson–Deyo (reference = 2) |       |                           |              |
| 0                       | 0.86       | 0.69–1.07                 | 0.19         |
| 1                       | 0.76       | 0.51–1.13                 | 0.17         |
| Hospital volume (reference = high) | |                  |              |
| Medium                  | 0.38       | 0.21–0.70                 | 0.0019       |
| Low                     | 0.46       | 0.31–0.70                 | 0.0003       |
reported that Clavien–Dindo $\geq 3$ events occurred in 16% of patients and that the 30-day mortality was 1.8%. In the current study, high-volume centers had a 30-day mortality of 0.5%, suggesting that the cutoff used in the current study may be appropriate to optimize 30-day mortality.

The TARPSWG also studied oncologic outcomes on the same patients and reported an $R_0/R_1$ resection rate of 95%. In the current study, high-volume centers had a comparable $R_0/R_1$ resection rate of 98%; when the negative margin was defined by assessment of microscopic disease; high-volume centers were significantly more likely to achieve $R_0$ resection than low-volume centers. However, it should be noted that, since microscopic assessment of the entire tumor surface is not feasible, not all institutions routinely report microscopic margin status. Indeed, approximately 26% of all surgical cases had missing margin data, and therefore, extraction of margin information from pathology reports and subsequent reporting to the NCDB for RPS will need to be improved. Finally, TARPSWG reported a 5-year overall survival rate of 67%, which compares with the 69% seen in our study for high-volume centers. Overall, the comparison with the TARPSWG data suggests that high-volume centers both within and outside of the United States have comparable outcomes.

A review of soft tissue sarcomas identified in the Florida Cancer Data System (FCDS) suggested that high-volume centers—defined as $\geq 5$ surgical cases/year—had superior 30-day mortality and 5-year overall survival [10]. Subset analysis of truncal/retroperitoneal sarcomas ($n = 1,745$) showed improved 5-year overall survival for high-volume centers (low volume, 32% versus high volume, 36%). Margin status was not available for analysis. When compared to the 5-year overall survival observed at high-volume centers in the current study and in the TARPSWG study (67% and 69%, resp.), the FCDS study reported a lower 5-year overall survival at high-volume centers (36%).

### Table 5: Cox regression model for overall survival: all patients.

| Variable                      | Odds ratio | 95% Wald Confidence limits | $p$ value |
|-------------------------------|------------|---------------------------|----------|
| Age                           | 1.02       | 1.02–1.03                 | <0.0001  |
| Female (reference = male)     | 0.79       | 0.72–0.87                 | <0.0001  |
| Race (reference = white)      |            |                           |          |
| Black                         | 0.81       | 0.69–0.96                 | 0.015    |
| Other                         | 0.88       | 0.71–1.09                 | 0.23     |
| Insurance (reference = private) |       |                           |          |
| Medicaid                      | 1.38       | 1.11–1.70                 | 0.0034   |
| Medicare                      | 1.14       | 1.00–1.30                 | 0.056    |
| No insured                    | 1.38       | 1.07–1.79                 | 0.014    |
| Other government              | 1.18       | 0.75–1.86                 | 0.47     |
| Unknown                       | 1.23       | 0.85–1.78                 | 0.28     |
| No high school degree (reference $\geq 29\%$) | | | |
| $<$14%                        | 0.77       | 0.67–0.90                 | 0.0007   |
| 14–19.9%                      | 0.86       | 0.73–1.00                 | 0.055    |
| 20–28.9%                      | 0.92       | 0.79–1.08                 | 0.30     |
| Charlson–Deyo (reference = 2) |            |                           |          |
| 0                             | 0.72       | 0.58–0.88                 | 0.0011   |
| 1                             | 0.81       | 0.65–1.01                 | 0.055    |
| Tumor size (reference $<$5 cm) |       |                           |          |
| 5–10 cm                       | 1.02       | 0.83–1.25                 | 0.85     |
| $>$10 cm                      | 1.43       | 1.19–1.73                 | 0.0001   |
| Grade (reference = grade 3)   |            |                           |          |
| Grade 1                       | 0.34       | 0.28–0.40                 | <0.0001  |
| Grade 2                       | 0.52       | 0.44–0.61                 | <0.0001  |
| Unknown                       | 0.64       | 0.56–0.73                 | <0.0001  |
| Margins (reference = $R_0$)   |            |                           |          |
| $R_1$                         | 1.31       | 1.15–1.49                 | <0.0001  |
| $R_2$                         | 2.18       | 1.73–2.75                 | <0.0001  |
| Unknown                       | 1.61       | 1.44–1.80                 | <0.0001  |
| Surgery (reference = yes)     |            |                           |          |
| No                            | 0.93       | 0.83–1.04                 | 0.21     |
| Radiation (reference = yes)   |            |                           |          |
| No                            | 0.80       | 0.72–0.90                 | <0.0001  |
| Chemotherapy (reference = yes)|            |                           |          |
| No                            | 1.26       | 1.11–1.42                 | 0.0004   |
| Hospital volume (reference = high) |       |                           |          |
| Medium                        | 1.44       | 0.98–2.10                 | 0.064    |
| Low                           | 1.57       | 1.16–2.11                 | 0.0032   |

Figure 1: Overall survival stratified by hospital volume. (a) All cases. (b) Surgical cases.
in overall survival highlights the importance of establishing a cutoff (10 versus 5 cases in this instance) that offers better outcomes for RPS patients.

The association between institutional volume and improved outcomes has been used to advocate regionalization of complex procedures to high-volume centers. Even in the absence of health care policy change, this phenomenon had been observed for a variety of cancer types requiring complex surgery [11, 12]. Finks et al. used Medicare data to examine trends in hospital volume and the proportion of patients undergoing surgical resection in high-volume centers. The authors reported that regionalization of complex cancer resections appears to have occurred in the decade following reports that there is an inverse relationship between hospital volume and outcomes [11]. In the context of regionalization, it is important to note that, in our study, only 3 hospitals met the threshold for high volume (>10 surgical cases/year on average) out of a hospital cohort of 678. However, it is also important to note that the data presented in this study refer to treatment of primary RPS and not recurrent disease. Multiple reports from large volume centers suggest that resection of recurrent RPS constitutes approximately 32–44% of their RPS patient population [13–15]. Since the NCDB does not record recurrence and surgery for recurrence, the number of high-volume centers managing and resecting RPS is certainly underestimated by the current data. Nevertheless, the number of high-volume centers appears to be low, and further research will be needed, likely using qualitative or mixed methods, to investigate why significant regionalization has not occurred with regard to RPS. One clue may be the proximity of patients to a high-volume center. The median distance travelled for treatment at a high-volume center was 76 miles compared to 12 miles for a low-volume center. Whether this was due to referral networks, patient education/income insurance contracts, or other factors is unknown.

In this study, only 3 hospitals qualified as high-volume centers. All commission on cancer-approved hospitals are required to report to the NCDB, and these centers diagnoses account for 70% of new cancers diagnosed in the United States. Since the cancer programs that report to the NCDB include 19 of 20 National Comprehensive Cancer Network (NCCN) hospitals, 33 or 37 NCI-designated cancer centers, and 69 of 121 major inpatient VA hospitals, it is likely that our study captures most of the major sarcoma centers in the US. One likely explanation for only identifying 3 high-volume hospitals is that the current study only reports treatment for primary RPS and not recurrent RPS. Multiple retrospective studies from large sarcoma centers report that treatment of locally recurrent RPS accounts for 24–35% of all RPS cases [13, 14, 16]. It is highly likely that the inclusion of recurrent RPS would increase the number of high-volume centers and that the current analysis underestimates the number of high-volume centers.

A limitation of this study is that it does not provide surgeon-specific volume data. There is evidence that a surgeon’s volume is what drives good outcomes, and that when a surgeon relocates, those good outcomes also relocate to the new institution. Whether this is true for rare malignancy such as RPS is not entirely clear. Another limitation is that the NCDB does not contain ECOG performance status, American Society of Anesthesiologists physical status level, and other indicators of functional status. It does contain components of the Charlson Comorbidity Index which allows for a certain degree of adjustment for functional status. The NCDB also does not report the number of organs resected, the number of intestinal anastomoses, and post-operative complications, and therefore, we cannot comment on complexity of the surgery performed at the institutions. Many of the RPS histologic subtypes were unknown. Recent data suggest that RPS histologic subtype influences pattern of failure and death [8]. Whether histologic subtype influenced the results for high-volume centers cannot be determined. The NCDB also does not report on recurrence and disease-specific mortality. RPS has a high rate of local recurrence, and whether institutional volume affects local recurrence and disease-specific death cannot be ascertained. Moreover, the number of patients undergoing treatment for recurrent RPS cannot be determined, and therefore, the actual patient volume per institution is underestimated in this analysis. Finally, since re-resection for recurrent RPS is not captured in this study, and there may be a separate volume-outcome association that may be stronger than the one we observe for primary tumors.

5. Conclusions

Despite superior short- and long-term outcomes for high-volume institutions treating RPS, the overwhelming majority of patients continue to be seen at low-volume institutions. While it may be impractical to regionalize all RPS care to the few existing high-volume institutions, there is certainly room for consolidation. Other efforts to disseminate expertise, such as remote tumor boards, centralizing pathology review such as seen in Europe, visits by expert surgeons, and teledicine may need to be explored.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] C. B. Begg, L. D. Cramer, W. J. Hoskins, and M. F. Brennan, “Impact of hospital volume on operative mortality for major cancer surgery,” JAMA, vol. 280, no. 20, pp. 1747–1751, 1998.
[2] P. B. Bach, L. D. Cramer, D. Schrag, R. J. Downey, S. E. Gelfand, and C. B. Begg, “The influence of hospital volume on survival after resection for lung cancer,” New England Journal of Medicine, vol. 345, no. 3, pp. 181–188, 2001.
[3] J. D. Birkmeyer, A. E. Siewers, E. V. Finlayson et al., “Hospital volume and surgical mortality in the United States,” New
England Journal of Medicine, vol. 346, no. 15, pp. 1128–1137, 2002.

[4] B. E. Hillner, T. J. Smith, and C. E. Desch, “Hospital and physician volume or specialization and outcomes in cancer treatment: importance in quality of cancer care,” Journal of Clinical Oncology, vol. 18, no. 11, pp. 2327–2340, 2000.

[5] Y. Fong, M. Gonen, D. Rubin, M. Radzyner, and M. F. Brennan, “Long-term survival is superior after resection for cancer in high-volume centers,” Annals of Surgery, vol. 242, no. 4, pp. 544–547, 2005.

[6] D. Schrag, L. D. Cramer, P. B. Bach, A. M. Cohen, J. L. Warren, and C. B. Begg, “Influence of hospital procedure volume on outcomes following surgery for colon cancer,” JAMA, vol. 284, no. 23, pp. 3028–3035, 2000.

[7] M. Sun, M. Bianchi, Q. D. Trinh et al., “Hospital volume is a determinant of postoperative complications, blood transfusion and length of stay after radical or partial nephrectomy,” Journal of Urology, vol. 187, no. 2, pp. 405–410, 2012.

[8] A. Gronchi, D. C. Strauss, R. Miceli et al., “Variability in patterns of recurrence after resection of primary retroperitoneal sarcoma (RPS): a report on 1007 patients from the multi-institutional collaborative RPS working group,” Annals of Surgery, vol. 263, no. 5, pp. 1002–1009, 2016.

[9] A. J. MacNeill, A. Gronchi, R. Miceli et al., “Postoperative morbidity after radical resection of primary retroperitoneal sarcoma: a report from the transatlantic RPS working group,” Annals of Surgery, vol. 267, no. 5, p. 1, 2017.

[10] J. C. Gutierrez, E. A. Perez, F. L. Moffat, A. S. Livingstone, D. Franceschi, and L. G. Koniaris, “Should soft tissue sarcomas be treated at high-volume centers? an analysis of 4205 patients,” Annals of Surgery, vol. 245, no. 6, pp. 952–958, 2007.

[11] J. F. Finks, N. H. Osborne, and J. D. Birkmeyer, “Trends in hospital volume and operative mortality for high-risk surgery,” New England Journal of Medicine, vol. 364, no. 22, pp. 2128–2137, 2011.

[12] P. A. Learn and P. B. Bach, “A decade of mortality reductions in major oncologic surgery the impact of centralization and quality improvement,” Medical Care, vol. 48, no. 12, pp. 1041–1049, 2010.

[13] J. J. Lewis, D. Leung, J. M. Woodruff, and M. F. Brennan, “Retroperitoneal soft-tissue sarcoma: analysis of 500 patients treated and followed at a single institution,” Annals of Surgery, vol. 228, no. 3, pp. 355–365, 1998.

[14] T. Lehnert, S. Cardona, U. Hinz et al., “Primary and locally recurrent retroperitoneal soft-tissue sarcoma: local control and survival,” European Journal of Surgical Oncology (EJSO), vol. 35, no. 9, pp. 986–993, 2009.

[15] D. A. Anaya, G. Lahat, J. Liu et al., “Multifocality in retroperitoneal sarcoma: a prognostic factor critical to surgical decision-making,” Annals of Surgery, vol. 249, no. 1, pp. 137–142, 2009.

[16] A. Gronchi, R. Miceli, C. Colombo et al., “Frontline extended surgery is associated with improved survival in retroperitoneal low- to intermediate-grade soft tissue sarcomas,” Annals of Oncology, vol. 23, no. 4, pp. 1067–1073, 2012.