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# Hospital Volume Threshold for the Treatment of Retroperitoneal Sarcoma

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**Abstract.** *Background: Retroperitoneal sarcomas (RPS) are rare, histologically heterogeneous, and anatomically complex tumors. National Comprehensive Cancer Network guidelines recommend evaluation and management by multidisciplinary teams with experience in sarcoma. Our aim was to determine an appropriate hospital volume threshold for the treatment of RPS. Patients and Methods: Patients undergoing resection of RPS were identified from the National Cancer Data Base (1998-2012). Multivariable modeling with restricted cubic splines was employed to examine the association between hospital volume and survival and identify possible hospital volume threshold. Results: The study included 5,340 patients who underwent surgery at 909 different hospitals. Median annual volume was two cases per year. After adjustment, hospital volume was associated with improved survival (p=0.01), without cutoff. The cohort was then grouped into: Low-volume (≤5 cases/year), intermediate-volume (6-10 cases/year), and high-volume (>10 cases/year). The majority of patients were treated in low-volume hospitals (86%), compared to 9% in intermediate- and 5% in high-volume centers; 44% of patients were treated in hospitals that performed one case per year. Compared to low-volume, high-volume hospitals more often had patients with high-grade and larger tumors. Adjusted 90-day mortality was significantly lower in high- vs. low-volume hospitals (odds ratio(OR)=0.25, p=0.02). With adjustment, treatment in high- vs. low-volume hospitals was associated with lower odds of margin positivity (OR=0.58, p=0.001), and improved overall survival (hazard ratio(HR)=0.61, p=0.002). Conclusion: Treatment of RPS in high-volume centers is associated with significant reduction in short-term mortality and improved long-term survival. Hospital volume may be a surrogate for the infrastructure and support necessary for the optimal management of these complex malignancies.*

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Retroperitoneal sarcoma (RPS) is a rare disease accounting for 0.1-0.2% of all malignancies and 10-15% of all soft-tissue sarcomas (1, 2). The rarity and heterogeneity of these tumors make it difficult to define quality metrics for the management of patients and create marked disparities in case volume distribution between large tertiary cancer centers and smaller or community-based institutions (3, 4).

Management of RPS requires multidisciplinary and tailored management strategies for these patients (5). Surgical resection remains the mainstay of therapy for RPS, with the goal of achieving complete tumor resection. Incomplete resection is a significant risk for early recurrence and compromised survival (1, 6-8). Therefore, surgical therapy frequently requires *en bloc* resection of adjacent visceral and vascular structures if grossly involved (9). This issue increases the complexity of surgical care and requires careful preoperative planning with experience across several specialties (10-12).

Much emphasis has been placed on appropriate referral and management of these patients to high-volume, specialized sarcoma centers in order to achieve optimal outcomes (4, 9). The National Comprehensive Cancer Network (NCCN) guidelines recommend that all patients should be managed by a multidisciplinary team with expertise in sarcoma (8). However, it is unclear whether treatment at specialized cancer centers translates into improved survival (4, 13).

Published data suggest that most patients with RPS in the US are treated in low-volume centers (4). While barriers to high-volume care for RPS patients are complex, the lack of level 1 data demonstrating survival benefit for patients treated at high-volume centers may complicate decision making about referrals for these patients. Therefore, we sought to determine the association between annual hospital procedural volume and survival in patients undergoing treatment for RPS nationally.

## Patients and Methods

The National Cancer Data Base (NCDB) is a joint program of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. It is a nationwide, facility-based, clinical surveillance dataset in the US.

The NCDB file was used to identify all patients with non-metastatic RPS who underwent surgery between 1998 and 2012. Patients <18 years or with distant metastasis, more than one diagnosis, treated at multiple hospitals, or those who did not undergo surgery were excluded.

Patient demographic and clinical characteristics were extracted from the database. Hospital type was provided in the dataset. Clinical and pathological characteristics such as histology, tumor size, tumor grade, and receipt of neoadjuvant radiation were provided. Data about extent of surgery, margin positivity, hospital length of stay, 30-day re-admissions, and mortality within 90 days from surgery were obtained. Annual hospital volume was calculated for each hospital as the number of RPS resections performed per hospital per year. Due to the de-identified nature of the data, the study was granted exemption status by our Institutional Review Board.

*Statistical analysis*. The primary outcome of this study was overall survival. Secondary outcomes included surgical margin positivity, length of stay, 30-day re-admission, and 90-day mortality.

To estimate the adjusted association between annual hospital volume and long-term survival, a multivariable Cox proportional hazards model incorporated with restricted cubic splines (RCS) was used to specify the functional form of annual hospital volume. The RCS methodology examines the adjusted effect of a continuous predictor on an outcome and allows for visualization of the relationship without prior knowledge of the functional form of the association (14). The following covariates were adjusted for in this multivariable model: age, gender, race, comorbidities, histology, tumor size, tumor grade, and extent of surgery.

The RCS model showed a linear association between hospital volume and survival, without a statistically significant cut-off delineating survival difference (15). Thus we made an informed decision to categorize the cohort into three groups: Low-volume hospitals, which performed 1-5 cases/year; intermediate-volume hospitals, performing 6-10 cases/year, and high-volume hospitals, performing >10 cases/year (16). Descriptive data were compared across groups using the Kruskal–Wallis and Chi-square tests.

Separate multivariable logistic regression models were used to examine the adjusted association between hospital volume and margin positivity, 30-day re-admission, and 90-day mortality, with similar adjustment. Linear regression modeling was employed to examine the adjusted relationship between hospital volume and hospital length of stay. Cox proportional hazards modeling were employed to examine the association between hospital volume status and survival. The following covariates were adjusted for in the Cox proportional hazards model: Age, gender, race, insurance status, comorbidities, histology, tumor size, tumor grade, receipt of neoadjuvant radiation, and extent of surgery.

A two-sided significance level of $p<0.05$ was used for all statistical tests. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

## Results

The study included 5,340 patients with RPS who underwent surgery at 909 different hospitals across the US. Median annual hospital volume was only two cases per year (range=1-23). A significant number (44%) of the patients underwent surgery in hospitals that performed just one case per year. Demographic and clinical characteristics of the cohort are detailed in Table I.

*Association between hospital volume and survival*. Median follow-up was 37 months (range=1-190 months). An RCS model was employed to examine the association of annual hospital volume and survival and to determine if a statistically derived threshold of minimum number of hospital volume exists.

After adjustment for patient demographic, clinico-pathological, and treatment characteristics, increasing hospital volume was associated with improving survival ($p<0.0002$). The RCS plot demonstrated a significant linear association between hospital volume and mortality, without a discernable cut-off (Figure 1).

*Hospital volume grouping*. Since the RCS model did not identify a statistically significant hospital volume threshold for dichotomizing the cohort into low- and high-volume groups, we elected to divide the cohort into groups of low-volume, intermediate-volume, and high-volume hospitals.

Comparison of the cohort characteristics according to hospital volume is described in Table I. Comorbidities were similar between groups. Compared to low-volume hospitals, patients treated in high-volume hospitals were significantly more often diagnosed with dedifferentiated liposarcoma (41% *vs*. 18%), larger tumors (median 19 *vs*. 16 cm), and high-grade tumors (61% *vs*. 44%) (all $p<0.01$). Neoadjuvant radiation was used more often in the high- *vs*. low-volume group (8% *vs*. 5%). Patients treated in high-volume hospitals more often underwent radical resections than in those at low-volume hospitals (42% *vs*. 29%, $p<0.0001$). All high-volume hospitals were academic centers, while 52% of the low-volume hospitals were academic centers.

*Surgical outcomes by hospital volume status*. In unadjusted analysis, patients treated at high-volume hospitals had longer hospital stay compared to those treated at low- or intermediate-volume hospitals (median 8 *vs*. 7 *vs*. 7 days, respectively, $p<0.0001$), but similar 30-day re-admissions (Table II). Patients undergoing surgery at high-volume hospitals had a significantly lower 90-day mortality rate compared to both low- and intermediate-volume groups (2% *vs*. 6% *vs*. 6%, respectively, $p=0.04$) (Figure 2).

After adjustment, length of hospital stay and 30-day re-admission rates were similar between groups (Table III); however, the likelihood of 90-day mortality was significantly

Table I. *Demographic, clinicopathological, and hospital characteristics of patients with retroperitoneal sarcoma who underwent surgery (National Cancer Data Base 1998-2012).*

| | | Hospital volume | | | | |
|---|---|---|---|---|---|---|
| | | Low (N=4,597) | Intermediate (N=466) | High N=277) | All (N=5,340) | *p*-Value |
| Patient age, years | N | 4,597 | 466 | 277 | 5,340 | 0.0117 |
| | Median | 63.0 | 61.0 | 60.0 | 62.0 | |
| | Q1, Q3 | 53.0, 73.0 | 53.0, 69.0 | 51.0, 70.0 | 53.0, 72.0 | |
| Gender, n (%) | Female | 2,551 (55.5%) | 212 (45.5%) | 127 (45.8%) | 2,890 (54.1%) | <0.0001 |
| Race, n (%) | White | 3,878 (84.4%) | 402 (86.3%) | 248 (89.5%) | 4,528 (84.8%) | 0.0690 |
| | Black | 472 (10.3%) | 36 (7.7%) | 17 (6.1%) | 525 (9.8%) | |
| | Other | 247 (5.4%) | 28 (6.0%) | 12 (4.3%) | 287 (5.4%) | |
| Annual income, n (%) | Low | 1,323 (30.0%) | 152 (34.3%) | 59 (22.8%) | 1,534 (30.0%) | 0.0057 |
| | High | 3,082 (70.0%) | 291 (65.7%) | 200 (77.2%) | 3,573 (70.0%) | |
| Insurance states, n (%) | Insured | 4,330 (96.7%) | 389 (97.7%) | 203 (98.1%) | 4,922 (96.8%) | 0.3055 |
| Charlson-Deyo score, n (%) | 0 | 2,522 (76.8%) | 335 (80.9%) | 215 (81.1%) | 3,072 (77.5%) | 0.1353 |
| | 1 | 602 (18.3%) | 63 (15.2%) | 43 (16.2%) | 708 (17.9%) | |
| | ≥2 | 161 (4.9%) | 16 (3.9%) | 7 (2.6%) | 184 (4.6%) | |
| Year of diagnosis, n (%) | 1998 | 266 (5.8%) | 6 (1.3%) | 0 (0.0%) | 272 (5.1%) | <0.0001 |
| | 1999 | 241 (5.2%) | 7 (1.5%) | 0 (0.0%) | 248 (4.6%) | |
| | 2000 | 247 (5.4%) | 10 (2.1%) | 0 (0.0%) | 257 (4.8%) | |
| | 2001 | 285 (6.2%) | 13 (2.8%) | 0 (0.0%) | 298 (5.6%) | |
| | 2002 | 273 (5.9%) | 16 (3.4%) | 12 (4.3%) | 301 (5.6%) | |
| | 2003 | 320 (7.0%) | 6 (1.3%) | 28 (10.1%) | 354 (6.6%) | |
| | 2004 | 261 (5.7%) | 13 (2.8%) | 18 (6.5%) | 292 (5.5%) | |
| | 2005 | 299 (6.5%) | 23 (4.9%) | 12 (4.3%) | 334 (6.3%) | |
| | 2006 | 302 (6.6%) | 39 (8.4%) | 21 (7.6%) | 362 (6.8%) | |
| | 2007 | 340 (7.4%) | 18 (3.9%) | 30 (10.8%) | 388 (7.3%) | |
| | 2008 | 326 (7.1%) | 44 (9.4%) | 38 (13.7%) | 408 (7.6%) | |
| | 2009 | 330 (7.2%) | 43 (9.2%) | 36 (13.0%) | 409 (7.7%) | |
| | 2010 | 354 (7.7%) | 56 (12.0%) | 19 (6.9%) | 429 (8.0%) | |
| | 2011 | 388 (8.4%) | 65 (13.9%) | 44 (15.9%) | 497 (9.3%) | |
| | 2012 | 365 (7.9%) | 107 (23.0%) | 19 (6.9%) | 491 (9.2%) | |
| Histology, n (%) | DDLS | 842 (18.3%) | 122 (26.2%) | 113 (40.8%) | 1,077 (20.2%) | <0.0001 |
| | Fibrosarcoma | 29 (0.6%) | 2 (0.4%) | 2 (0.7%) | 33 (0.6%) | |
| | Fibrous | 240 (5.2%) | 17 (3.6%) | 6 (2.2%) | 263 (4.9%) | |
| | LMS | 1,246 (27.1%) | 99 (21.2%) | 53 (19.1%) | 1,398 (26.2%) | |
| | Liposarcoma | 626 (13.6%) | 54 (11.6%) | 11 (4.0%) | 691 (12.9%) | |
| | MPNST | 60 (1.3%) | 9 (1.9%) | 2 (0.7%) | 71 (1.3%) | |
| | Other | 229 (5.0%) | 27 (5.8%) | 9 (3.2%) | 265 (5.0%) | |
| | Sarcoma NOS | 191 (4.2%) | 13 (2.8%) | 7 (2.5%) | 211 (4.0%) | |
| | WDLS | 1,134 (24.7%) | 123 (26.4%) | 74 (26.7%) | 1,331 (24.9%) | |
| Tumor size, cm | N | 4,204 | 434 | 260 | 4,898 | |
| | Median | 160.0 | 180.0 | 190.0 | 160.0 | <0.0001 |
| | Q1, Q3 | 97.0, 240.0 | 100.0, 280.0 | 104.5, 290.0 | 100.0, 250.0 | |
| Tumor grade, n (%) | 1 | 1,526 (39.1%) | 163 (40.8%) | 85 (35.3%) | 1,774 (39.0%) | <0.0001 |
| | 2 | 627 (16.0%) | 52 (13.0%) | 8 (3.3%) | 687 (15.1%) | |
| | 3 | 1,754 (44.9%) | 185 (46.3%) | 148 (61.4%) | 2,087 (45.9%) | |
| Neoadjuvant RT, n (%) | Received | 216 (4.8%) | 65 (14.6%) | 23 (8.3%) | 304 (5.9%) | <0.0001 |
| Extent of resection, n (%) | Local | 915 (19.9%) | 46 (9.9%) | 7 (2.5%) | 968 (18.1%) | <0.0001 |
| | Radical | 1,353 (29.4%) | 189 (40.6%) | 116 (41.9%) | 1,658 (31.0%) | |
| | Simple | 2,329 (50.7%) | 231 (49.6%) | 154 (55.6%) | 2,714 (50.8%) | |
| Hospital location, n (%) | Midwest | 1,130 (24.6%) | 168 (36.1%) | 0 (0.0%) | 1,298 (24.3%) | <0.0001 |
| | Northeast | 989 (21.5%) | 38 (8.2%) | 185 (66.8%) | 1,212 (22.7%) | |
| | South | 1,636 (35.6%) | 191 (41.0%) | 92 (33.2%) | 1,919 (35.9%) | |
| | West | 842 (18.3%) | 69 (14.8%) | 0 (0.0%) | 911 (17.1%) | |
| Hospital type, n (%) | Academic | 2,375 (51.7%) | 454 (97.4%) | 277 (100.0%) | 3,106 (58.2%) | <0.0001 |
| | Community | 274 (6.0%) | 0 (0.0%) | 0 (0.0%) | 274 (5.1%) | |
| | Comprehensive | 1,947 (42.4%) | 12 (2.6%) | 0 (0.0%) | 1,959 (36.7%) | |
| Annual hospital volume, cases | N | 4,597 | 466 | 277 | 5,340 | |
| | Median | 1.0 | 7.0 | 19.0 | 2.0 | <0.0001 |
| | Q1, Q3 | 1.0, 2.0 | 6.0, 9.0 | 16.0, 21.0 | 1.0, 3.0 | |

NCDB: National Cancer Data Base; DDLS: dedifferentiated liposarcoma; LMS: leiomyosarcoma; MPNST: malignant peripheral nerve sheath tumor; NOS: not otherwise specified; WDLS: well-differentiated liposarcoma; RT: radiation. Percentages may not add up to 100 due to rounding or missing values.

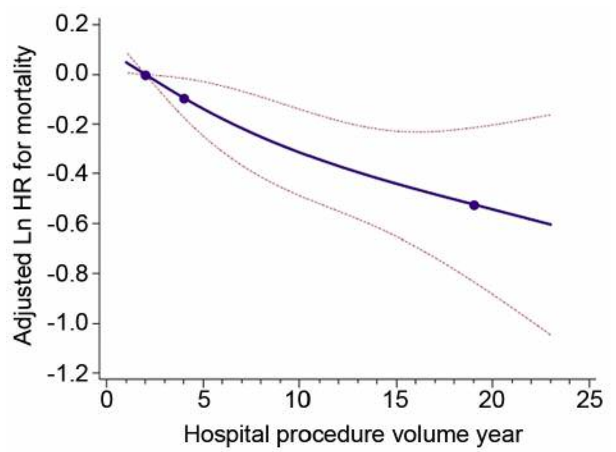


Figure 1. *Smoothed restricted cubic splines plot of the adjusted association of annual hospital procedure volume and long-term mortality in patients with retroperitoneal sarcoma. The blue solid curve represents the adjusted regression line for each model; the dotted lines represent the 95% confidence intervals. Ln HR: Natural log of the hazard ratio.*

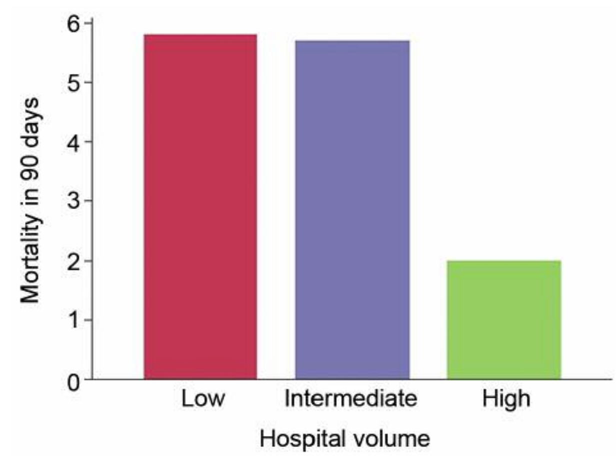


Figure 2. *Average risk of death within 90 days after surgery according to hospital volume of treatment of patients with retroperitoneal sarcoma.*

lower in the high- *vs*. low-volume groups [odds ratio (OR)=0.25, *p*=0.02], but not for those at intermediate-volume hospitals (OR=0.86, *p*=0.65).

In unadjusted analysis, the rates of margin positivity were similar across hospital volumes (Table II). However, after adjustment, receipt of surgical treatment at high-volume *vs*. low-volume hospitals was associated with a lower odds of margin positivity (OR=0.58, *p*=0.001); a similar but less benefit was seen for those at intermediate-volume hospitals (OR=0.72, *p*=0.02).

*Survival according to hospital volume*. Unadjusted overall survival estimate at 10 years was compromised among patients treated at low-volume hospitals (33%) compared to patients treated at intermediate-volume hospitals (39%) or high-volume hospitals (35%) (*p*=0.0003).

After adjustment, surgical treatment at low-volume hospitals was significantly associated with compromised survival in comparison to that at intermediate-volume (hazard ratio=0.73, *p*=0.02) and high-volume hospitals (hazard ratio=0.61, *p*=0.002) (Table IV).

## Discussion

This nationwide study examined the association between hospital procedural volume and survival among patients undergoing RPS resections in the US. After adjustment for patient demographic, clinicopathological, and treatment characteristics, increasing hospital volume was significantly associated with improved long-term survival in a linear fashion. While there were no differences in comorbidities, patients undergoing surgery at high-volume hospitals were less likely to die within 90 days from surgery. The overwhelming majority of patients underwent RPS resection at low-volume hospitals, with nearly half of the population undergoing surgery at hospitals that performed only one case per year.

The NCCN guidelines recommend that evaluation and management of RPS be carried out in a multidisciplinary setting where extensive expertise and experience in the treatment of the disease is present (8). While the volume–outcomes relationship is well established for many procedures,(17-19) limited data exist demonstrating a survival benefit associated with hospital volume in the management of RPS. Gutierrez *et al*. examined the significance of hospital volume in a cohort of patients with soft-tissue sarcoma who were treated in the state of Florida between 1981 and 2001. The study included 4,205 patients, with only 41.5% of whom had truncal or RPS. Patients treated at high-volume hospitals (≥5 cases/year) had a significantly improved overall survival (3). While their conclusion is similar to our study's that hospital volume is associated with improved survival, it is important to note that our study only included patients with RPS and attempted to identify a hospital volume threshold associated with a marked survival difference. RPS is distinctly different from sarcoma of the extremities and is associated with worse survival (20). Since overall survival was examined as the primary endpoint, we accounted for the presence of comorbidities, a limitation of the previous study.

Maurice *et al*. examined the impact of hospital volume on use of surgery and completeness of resection. Their study included 3,141 patients with RPS from the NCDB. Patients

Table II. *Unadjusted clinical and short-term oncological outcomes of surgery for retroperitoneal sarcoma by hospital volume.*

| | Hospital volume status | | | | |
|---|---|---|---|---|---|
| | Low (N=4597) | Intermediate (N=466) | High (N=277) | All (N=5340) | *p*-Value |
| Surgical margins, n (%) | | | | | |
| Negative | 2,272 (60.0%) | 220 (60.9%) | 136 (67.3%) | 2,628 (60.4%) | 0.1132 |
| Positive | 1,515 (40.0%) | 141 (39.1%) | 66 (32.7%) | 1,722 (39.6%) | |
| Length of stay, days | | | | | |
| N | 2,794 | 351 | 207 | 3,352 | |
| Median | 7.0 | 7.0 | 8.0 | 7.0 | <0.0001 |
| Q1, Q3 | 5.0, 9.0 | 5.0, 10.0 | 6.0, 10.0 | 5.0, 9.0 | |
| 30-Day re-admission, n (%) | | | | | |
| No | 3,037 (94.6%) | 385 (93.7%) | 254 (96.2%) | 3,676 (94.6%) | 0.3599 |
| Yes | 172 (5.4%) | 26 (6.3%) | 10 (3.8%) | 208 (5.4%) | |
| 90-Day mortality, n (%) | | | | | |
| No | 3,894 (94.2%) | 330 (94.3%) | 246 (98.0%) | 4,470 (94.4%) | 0.0404 |
| Yes | 238 (5.8%) | 20 (5.7%) | 5 (2.0%) | 263 (5.6%) | |

Percentages may not add up to 100 due to rounding or missing values.

Table III. *Summary of adjusted outcomes of surgery for retroperitoneal sarcoma by hospital volume status. Each outcome was examined in a separate multivariable model where the adjusted association of each outcome was modeled against hospital volume status while adjusting for the effects of patient age, gender, race, insurance status, comorbidities, tumor size, tumor grade, receipt of neoadjuvant radiation, and extent of surgery.*

| | Length of stay | | 30-Day re-admission | | 90-Day mortality | |
|---|---|---|---|---|---|---|
| Hospital volume | Increase | *p*-Value | OR (95% CI) | *p*-Value | OR (95% CI) | *p*-Value |
| Low | Reference | | Reference | | Reference | |
| Intermediate | 1% | 0.91 | 1.06 (0.64-1.76) | 0.83 | 0.86 (0.43-1.69) | 0.65 |
| High | 4% | 0.34 | 0.61 (0.29-1.27) | 0.19 | 0.25 (0.08-0.80) | 0.02 |

CI: Confidence interval; OR: odds ratio.

treated at high-volume hospitals (≥5 cases/year) were more likely to have undergone complete resection. With a follow-up of 31 months, survival was equivalent between high- and low-volume groups. The authors acknowledged the limited follow-up time which restricted the ability to draw conclusions about the effect on survival (4). In contrast to Maurice *et al*.'s study, our study primarily focused on survival as the main endpoint and examined it in a multivariable fashion to account for potential confounders. Our median follow-up time was longer (range=1-190 months). The definition of high-volume status (≥5 cases/year) that was used in Maurice *et al*.'s study may not be adequate.

Our study demonstrated a linear association between hospital volume and survival, which was examined using a multivariable model with RCS function. The RCS function permitted us to determine if a statistically derived cut-off existed. Since the association was linear and in order to better represent the distribution of hospital volume, we analyzed the cohort as three groups. We showed that hospital volume was associated with improved survival in a dose-dependent fashion. Our designation of high-volume hospitals (>10 cases/year) seems more appropriate, as evidenced by its correlation with academic hospital status; 100% of our high-volume hospitals were also academic, compared to 97% of hospitals in the intermediate-volume group and 52% for the low-volume group.

Table IV. *Adjusted overall survival of patients who underwent surgery for retroperitoneal sarcoma by hospital volume.*

| Hospital volume | Hazard ratio | 95% Confidence Interval | *p*-Value |
|---|---|---|---|
| Low | Reference | | |
| Intermediate | 0.731 | 0.57-0.95 | 0.017 |
| High | 0.614 | 0.45-0.84 | 0.002 |

Adjusted for patient age, gender, race, insurance status, comorbidities, histology, tumor size, tumor grade, receipt of neoadjuvant radiation, and extent of surgery.

The current study is aligned with other reports that show a survival benefit associated with hospital volume for complex surgical procedures and surgery for other complex cancer types (16, 17, 21). The volume–outcomes relationship seems to be more relevant for complex cancer surgery. RPS is a rare and heterogeneous entity (with over 50 histological subtypes), posing complexity in clinical and pathological diagnosis, decision for preoperative therapy, determination and quality of extent of resection, and postoperative management (8). High-volume hospitals have more resources and often have expert pathologists, radiologists, medical and radiation oncologists, and surgeons. In our study, all high-volume hospitals were also academic hospitals that have multidisciplinary care, compared to only 50% of low-volume hospitals (22). In a study of 12,528 patients with sarcoma from France, Blay *et al.* showed that care tailored by multidisciplinary sarcoma tumor boards is associated with improved compliance with clinical guidelines and improved relapse-free survival (23). In addition, completeness of surgical resection was greater in the high- *vs.* low-volume group, similar to another reports (24). Margin positivity has been associated with increased risk of recurrence and compromised survival in RPS (1, 4, 25, 26).

With adjustment, 90-day mortality was significantly higher in low- compared to high-volume centers. This increased risk of mortality may be related to the complexity of surgical resection employed for RPS. Oncological principles dictate complete tumor resection with the goal of achieving at least grossly negative margins (8, 27). *En bloc* resection may involve high-risk procedures such as pancreaticoduodenectomy, distal pancreatectomy, nephrectomy, biliary reconstruction, and complex visceral or vascular resection (9). High-volume hospitals are more likely to have experienced surgeons who can perform complex resections with reduced morbidity, and may more effectively utilize the expertise of various surgical disciplines.

The vast majority of patients with RPS were treated at low-volume hospitals, with nearly half of the population receiving surgical care at hospitals that performed one case per year. This finding raises significant concerns about patterns of care for RPS in the US, given our reported compromised short-term and long-term survival when resection is performed in the low-volume setting. While access to high-volume hospitals may be a barrier, it is hard to justify the preponderance of hospitals performing just one case per year.

Limitations of this study include its retrospective nature and the possibility of coding errors. The cut-off of 10 used to defined high-volume hospitals may seem arbitrary. However, before choosing this, we employed an RCS model to examine the functional form of the relationship between hospital volume and survival and determine if a statistically appropriate cut-point existed. Since we observed a linear association with no apparent cut-off, we divided the cohort into three groups in order to better represent hospital volume distribution in the analysis, including a cut-off of 10 cases/year, in line with other studies (16, 28). While the element of selection bias is inherent in retrospective studies, patients treated at high-volume centers more often had larger and high-grade tumors. This suggests that the estimate of survival benefit provided may be more conservative than in reality. It was not possible to examine surgeon volume; however, hospital volume may be relevant for complex forms of cancer such as RPS as it acts as surrogate for multidisciplinary care and availability of experienced and specialized surgeons. Data about recurrence were not available. Information about cause of death was not provided and only overall survival was reported. To minimize this effect, we adjusted for factors including demographics and comorbidities.

This national study provides important information about patterns of surgical care and outcomes of RPS in the US. The NCCN guidelines recommend management of patients with these rare and heterogeneous tumors in a multidisciplinary setting in order to optimize for patient outcomes. Despite this, the overwhelming majority of patients with RPS were treated at low-volume centers, with nearly half of all patients receiving care at hospitals that performed only one case per year. The finding of this study that hospital volume is associated with improved postoperative mortality and survival is important and strongly supports the NCCN guidelines advocating for specialized care for RPS.

While barriers to implementation of high-volume care exist, it is hard to justify the practice of performing only one case per year. This indicates that there might be opportunities for improvement with regard to regionalization of care when the volume threshold of 10 is not attainable. Our results are timely and relevant, given the anticipated change in payers' reimbursement structure from fee-for-service to risk-based (29). Hospitals are increasingly focusing on quality and improved outcomes. Importantly, surgeons and non-surgeon providers are obligated to counsel patients with RPS about the survival benefits associated with high-volume care to help them make informed decisions regarding the best treatment setting for this complex malignancy.

## Authors' Contributions

MA Adam: Conception and design, analysis and interpretation, data collection, writing the article, critical revision of the article; Dimitrios Moris: Analysis and interpretation, data collection, writing the article, critical revision of the article. Shay Behrens: Analysis and interpretation, data collection, writing the article, critical revision of the article; Daniel Nussbaum: Conception and design, data collection, writing the article, critical revision of the article; Oliver Jawitz: Analysis and interpretation, data collection, writing the article, critical revision of the article. Megan Turner: Analysis and interpretation, data collection, writing the article, critical revision of the article; Michael Lidsky: Analysis and interpretation, data collection, writing the article, critical revision of the article; Dan Blazer III: Conception and design, interpretation, writing the article, critical revision of the article, obtaining funding. The data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator.

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