Original Article

External Validation of a Multi-Institutional Retroperitoneal Sarcoma Nomogram

Chandrajit P. Raut, MD, MSc[1,2]; Rosalba Miceli, PhD[3]; Dirk C. Strauss, MD[4]; Carol J. Swallow, MD, PhD[5,6]; Peter Hohenberger, MD[7]; Frits van Coevorden, MD[8]; Piotr Rutkowski, MD[9]; Marco Fiore, MD[10]; Dario Callegaro, MD[10]; Paolo G. Casali, MD[11]; Rick L. Haas, MD[12]; Andrew J. Hayes, MD[4]; Charles Honore, MD[13]; Amanda J. Cannell, BS[5,6]; Jens Jakob, MD[7]; Milena Szacht, MD, PhD[9]; Mark Fairweather, MD[1,2]; Raphael E. Pollock, MD, PhD[14]; Sylvie Bonvalot, MD[15]; and Alessandro Gronchi, MD[10]

BACKGROUND: A multi-institutional nomogram for predicting disease-free survival (DFS) and overall survival (OS) in patients with primary retroperitoneal sarcoma (RPS) incorporating relevant prognostic factors not included in the American Joint Committee on Cancer staging system for soft tissue sarcoma has been reported. The authors validated this nomogram with an independent, transatlantic cohort. **METHODS:** Data from patients with RPS who were undergoing definitive resection at 1 of 6 sarcoma centers in Europe and North America ("validation set") were used to validate a RPS nomogram developed from 3 other centers ("development set"). The nomogram incorporated 6 variables: age, tumor size, grade, histologic subtype, multifocality, and quality of surgery. Nomogram-predicted probabilities were stratified into 6 subgroups and compared with observed outcomes. Discriminative ability was quantified by Harrell C statistics. **RESULTS:** The validation and development sets included 631 and 523 patients, respectively, all of whom underwent surgical resection at the institutions represented. The 7-year DFS and OS rates for the validation set were 38% (95% confidence interval, 34%-43%) and 58% (95% confidence interval, 53%-63%), respectively. All 6 nomogram variables were found to be independently prognostic. The corrected Harrell C statistics concordance index values for the validation set were 0.69 for DFS and 0.73 for OS, which were similar to those for the development set, suggesting good calibration of the nomogram in the validation cohort. **CONCLUSIONS:** The RPS nomogram was externally validated using a larger, independent cohort. The nomogram can be generalized to patients undergoing surgery for RPS by specialized sarcoma surgeons at sarcoma centers. The nomogram provides a more individualized and disease-relevant estimation of OS compared with the American Joint Committee on Cancer classification. ***Cancer*** **2016;122:1417-24**. *© 2016 American Cancer Society.*

KEYWORDS: grade, histology, multifocality, nomogram, retroperitoneal sarcoma, staging, surgery.

INTRODUCTION

Retroperitoneal sarcomas (RPS) account for approximately 15% of all soft tissue sarcomas (STS).[1] Unique characteristics of RPS make traditional staging using the 7th edition of the American Joint Committee on Cancer (AJCC) system a challenge. Histologic subtype, multifocality, and site of origin are proven risk factors that are prognostic of outcome in patients with STS, but are not included in the AJCC TNM staging for STS or stage grouping.[2-5] Furthermore, the unique locoregional and distant patterns of disease recurrence for specific RPS histologies are not reflected in the stage-based outcomes. Finally, the majority of RPS measure 15 to 20 cm in size, and only approximately 6% of RPS reported in the Surveillance, Epidemiology, and End Results program measure <5 cm in size (the key discriminatory size used in AJCC STS staging).[6,7] This,

Corresponding author: Chandrajit P. Raut, MD, MSc, Division of Surgical Oncology, Department of Surgery, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115; Fax: (617) 394-3052; craut@bwh.harvard.edu

[1]Division of Surgical Oncology, Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [2]Center for Sarcoma and Bone Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts; [3]Department of Medical Statistics, Biometry and Bioinformatics, IRCCS Foundation National Cancer Institute, Milan, Italy; [4]Department of Surgery, Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom; [5]Department of Surgical Oncology, Mount Sinai Hospital and Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [6]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [7]Division of Surgical Oncology and Thoracic Surgery, Mannheim University Hospital, Mannheim, Germany; [8]Department of Surgical Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands; [9]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; [10]Department of Surgery, IRCCS Foundation National Cancer Institute, Milan, Italy; [11]Department of Cancer Medicine, IRCCS Foundation National Cancer Institute, Milan, Italy; [12]Department of Radiation Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands; [13]Department of Surgery, Gustave Roussy Institute, Villejuif, France; [14]Division of Surgical Oncology, Department of Surgery, Ohio State University Medical Center, Columbus, Ohio; [15]Department of Surgery, Curie Institute, Paris, France

Presented at the 18th European Cancer Congress (ECCO)-40th European Society for Medical Oncology (ESMO) European Cancer Congress; September 25-29, 2015; Vienna, Austria.

DOI: 10.1002/cncr.29931, **Received:** December 15, 2015; **Accepted:** January 7, 2016, **Published online** February 24, 2016 in Wiley Online Library (wileyonlinelibrary.com)

coupled with the finding that all RPS are by definition "deep," means that approximately 94% of RPS are by definition T2b tumors, and therefore tumor grade is the only variable that discriminates the majority of RPS into the discrete stages of IIB and III.

Nomograms provide a more disease-specific and clinically relevant prognostic model for predicting various outcomes, including overall survival (OS), disease-free survival (DFS), and local recurrence-free survival rates within a specific time frame compared with the AJCC system, particularly for STS. An initial STS nomogram from the Memorial Sloan Kettering Cancer Center (MSKCC) incorporated a variety of histologies and sites of origin.[5] Although RPS were included, RPS/intra-abdominal sarcomas accounted for only 13% of the original development cohort. The limited usefulness of the AJCC STS staging system for RPS was a critical impetus to the eventual development of the initial single-institution, RPS-specific nomograms from high-volume sarcoma centers.[2,4] These were critical in the evolution of expert opinion that has supported the use of such nomograms. However, a shortcoming of most single-institution nomograms is that they may reflect the treatment biases of experienced sarcoma centers and thus may not be more broadly applicable.

The first multi-institutional RPS nomogram (to the best of our knowledge) was developed from patients undergoing surgical resection of primary RPS between 1999 and 2009 at the sarcoma centers at the National Cancer Institute in Milan, Italy; The University of Texas MD Anderson Cancer Center in Houston, Texas; and the University of California at Los Angeles and was externally validated using another data set from 2001 to 2010 from the Gustave Roussy Institute (Villejuif, France).[8] Unlike prior nomograms, this one included size and age as continuous rather than categorical variables, as well as relevant RPS histologies, tumor grade, multifocality, and completeness of surgical resection. The 7-year DFS and OS rates could be predicted with accuracy (Fig. 1 A and B). This provided a more broadly applicable nomogram.

This multi-institution RPS nomogram is currently under consideration for inclusion in the forthcoming 8th edition of the AJCC staging system. To determine whether adoption of this nomogram by the AJCC is justified, we decided to critically evaluate the nomogram by externally validating it with a larger data set collected from other high-volume sarcoma centers.

MATERIALS AND METHODS

Data regarding patients with primary RPS undergoing surgery with curative intent at 6 dedicated sarcoma centers in 6 countries from January 2002 through December 2011 were collected ("validation set"). Patients who had undergone macroscopically incomplete initial surgical resection of RPS at an outside referring institution were excluded. Patients with retroperitoneal presentations of gastrointestinal stromal tumor, desmoplastic small round cell tumor, extraosseous Ewing sarcoma/primitive neuroectodermal tumor, uterine sarcoma histologic subtypes, alveolar/embryonal rhabdomyosarcoma, and desmoid fibromatosis were excluded.

Histologic subtypes incorporated within the multi-institutional RPS nomogram included well-differentiated liposarcoma, dedifferentiated liposarcoma, leiomyosarcoma, unclassified/undifferentiated pleomorphic sarcoma, malignant peripheral nerve sheath tumor, solitary fibrous tumor, and other. Liposarcomas were classified as "well differentiated" if only a well-differentiated component and no dedifferentiated component was present and as "dedifferentiated" if such a component was present regardless of tumor extent. All tumors were graded using the Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) (National Federation of Centers for the Fight Against Cancer) grading system.[9] The one treatment variable that was included in the nomogram was extent of surgical resection, with macroscopically complete (R0, negative microscopic margin; R1, positive microscopic margin) surgical resections classified as "complete" and macroscopically incomplete (R2) surgical resections classified as "incomplete." Patients were followed prospectively with clinical examination and routine imaging (usually computed tomography scans of the chest, abdomen, and pelvis) every 3 months to 4 months for the first 2 years, every 6 months for the following 3 years, and yearly thereafter. Local and distant disease recurrence and death were recorded as events.

The multi-institutional RPS nomogram incorporated 6 clinical characteristics and treatment variables to predict DFS and OS: age (in years) at the time of diagnosis as a continuous variable (OS only), tumor size (in centimeters) as a continuous variable, FNCLCC grade (1, 2, or 3), histologic subtype (well-differentiated liposarcoma, dedifferentiated liposarcoma, leiomyosarcoma, unclassified/undifferentiated pleomorphic sarcoma, malignant peripheral nerve sheath tumor, solitary fibrous tumor, and other), multifocality at the time of initial presentation (yes/no), and extent of surgical resection (complete, incomplete [for OS only]).[8]

Statistical Analysis

Cohort characteristics, treatment variables, and outcomes of the validation set were compared with the original

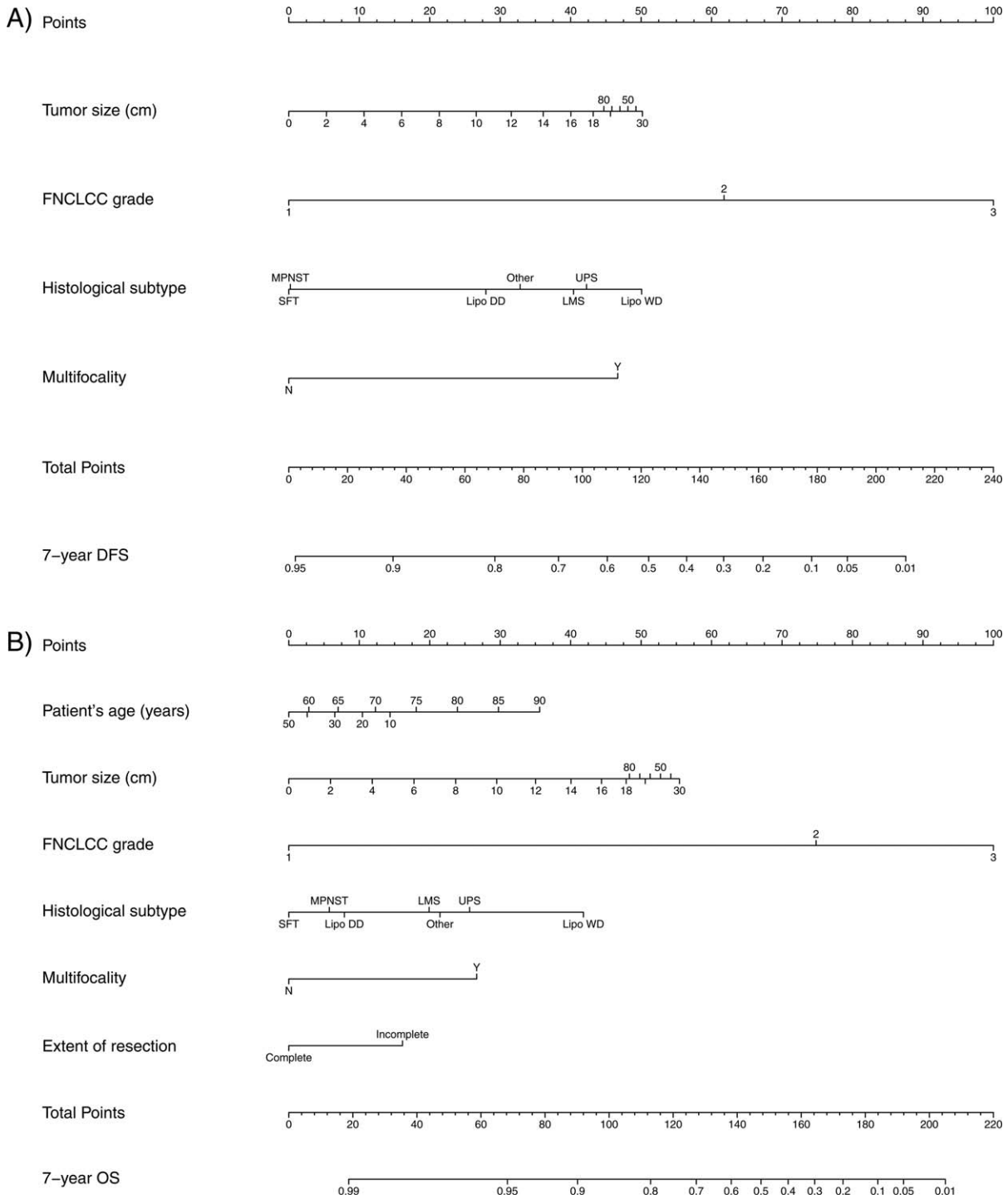

Figure 1. Nomogram for 7-year (A) disease-free survival (DFS) and (B) overall survival (OS) in patients with primary retroperitoneal sarcoma. FNCLCC indicates Federation Nationale des Centres de Lutte Contre le Cancer (National Federation of Centers for the Fight Against Cancer); Lipo DD, dedifferentiated liposarcoma; Lipo WD, well-differentiated liposarcoma; LMS, leiomyosarcoma; MPNST, malignant peripheral nerve sheath tumor; SFT, solitary fibrous tumor; UPS, unclassified/undifferentiated pleomorphic sarcoma. Reprinted from Gronchi A, Miceli R, Shurell E, et al. Outcome prediction in primary resected retroperitoneal soft tissue sarcoma: histology-specific overall survival and disease-free survival nomograms built on major sarcoma center data sets. *J Clin Oncol*. 2013;31:1649-1655 with permission from American Society of Clinical Oncology.[8]

TABLE 1. Demographic, Clinical, and Histologic Characteristics of Patients in the Retroperitoneal Sarcoma Nomogram Development and Validation Sets

Variable		Development Set N = 523 (%)	Validation Set N = 631 (%)	*P*
Median age, y		57 (IQR, 48–67; range, 16–88)	59 (IQR, 49–68; range, 18–95)	.248
Median tumor size, cm		16 (IQR, 10–26; range, 2–75)	21 (IQR, 13–30; range, 1–65)	<.0001
FNCLCC grade	1	147 (28.1)	193 (32.7)	<.0001
	2	122 (23.3)	235 (39.8)	
	3	254 (48.6)	162 (27.5)	
	Missing data	0	41	
Histologic subtype	LMS	92 (17.8)	137 (21.7)	<.0001
	DDLPS	155 (30.0)	231 (36.6)	
	WDLPS	121 (23.4)	158 (25.0)	
	MPNST	16 (3.1)	17 (2.7)	
	UPS	70 (13.5)	18 (2.9)	
	SFT	26 (5.0)	33 (5.2)	
	Other	37 (7.2)	37 (5.9)	
	Missing data	6	0	
Multifocality	No	490 (93.7)	565 (89.5)	0.016
	Yes	33 (6.3)	66 (10.5)	

Abbreviations: DDLPS, dedifferentiated liposarcoma; FNCLCC, Federation Nationale des Centres de Lutte Contre le Cancer (National Federation of Centers for the Fight Against Cancer); IQR, interquartile range; LMS, leiomyosarcoma; MPNST, malignant peripheral nerve sheath tumor; SFT, solitary fibrous tumor; UPS, unclassified/undifferentiated pleomorphic sarcoma; WDLPS, well-differentiated liposarcoma.

"development set" from which the nomogram was constructed using the Mann-Whitney-Wilcoxon test or the chi-square test when continuous or categorical variables, respectively, were involved in the comparison.

OS and DFS curves were estimated using the Kaplan-Meier method. OS was computed as the interval between the date of surgery and the date of death from any cause. DFS was computed as the interval between the date of surgery and the date of first disease recurrence (regardless of whether it was local, distant, or both) or death from any cause, whichever occurred first.

External validation was performed by applying the nomogram to the patients in the validation set. Calibration plots were used to compare nomogram-predicted probabilities with observed outcomes; in a perfectly calibrated nomogram, the observed and predicted outcomes would align along the 45° line of the calibration plot. The discriminative ability of the nomogram was quantified by the Harrell C statistics.

The statistical analyses did not include patients with missing values among the nomogram variables and were conducted using SAS statistical software (SAS Institute Inc, Cary, NC) and R statistical software (R Foundation, Vienna, Austria; http://www.r-project.org/)

RESULTS

The validation set included 631 patients who underwent surgical resection with curative intent for primary RPS at 1 of 6 sarcoma centers: 1) Mount Sinai Hospital/Princess Margaret Cancer Centre at the University of Toronto (Toronto, Ontario, Canada); 2) Brigham and Women's Hospital, Dana-Farber Cancer Institute, Harvard Medical School (Boston, Mass); 3) Royal Marsden Hospital NHS Foundation Trust (London, UK); 4) Mannheim University Hospital (Mannheim, Germany); 5) Netherlands Cancer Institute (Amsterdam, the Netherlands); and 6) Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology (Warsaw, Poland). Cohort variables for the original development set and validation set are compared in Table 1. The validation set was characterized by a larger median tumor size (21 cm vs 16 cm; $P<.0001$), more patients with grade 2 tumors (40% vs 23%), and fewer patients with grade 3 tumors (27% vs 49%) (overall $P<.0001$). Treatment details are summarized in Table 2. Completeness of surgical resection and use of radiotherapy were similar between the 2 cohorts, but the validation set included fewer patients treated with chemotherapy (9% vs 40%; $P<.0001$).

Outcomes are summarized in Table 3. The median follow-up in the validation set was 58 months (interquartile range, 36-87 months). Rates of local disease recurrence, distant disease recurrence, death, and death without disease recurrence were similar in the validation and development cohorts. Figure 2 shows the DFS and OS curves for both the development and validation sets. In the validation set, the 7-year DFS rate was 38.4% (95% confidence interval [95% CI], 33.9%-43.4%) and the 7-year OS rate was 58.0% (95% CI, 53.1%-63.4%); the corresponding estimates in the development set were 35.7% (95% CI, 30.3%-42.1%) and 50.5% (95% CI, 44.4%-57.4%), respectively.

TABLE 2. Treatments for Patients in the Development and Validation Sets

Variable		Development Set N = 523 (%)	Validation Set N = 631 (%)	*P*
Extent of resection	Complete (R0/R1)	475 (90.8)	598 (94.8)	.013
	Incomplete (R2)	48 (9.2)	33 (5.2)	
Chemotherapy	Yes	207 (39.6)	57 (9.0)	<.0001
	No	316 (60.4)	574 (91.0)	
Radiotherapy	Yes	193 (36.9)	200 (31.7)	.073
	No	330 (63.1)	431 (68.3)	

Abbreviations: R0 resection, macroscopically complete surgical resection with negative microscopic margins; R1 resection, macroscopically complete surgical resection with positive microscopic margins; R2, macroscopically incomplete surgical resection.

TABLE 3. Patient Outcomes in the Development and Validation Sets

		Development Set N = 523 (%)	Validation Set N = 631 (%)	*P*
Median follow-up, mo		45 (IQR, 22–72)	58 (IQR, 36–87)	<.001[a]
Recurrences	Local	130 (24.9)	161 (25.5)	.092[b]
	Distant	94 (18.0)	117 (18.5)	.377[b]
Deaths		171 (32.7)	205 (32.5)	.009[c]
Deaths without recurrence		34 (6.5)	52 (8.2)	.568[b]

Abbreviation: IQR, interquartile range.
[a] *P* value at log-rank test for the comparison of the "reverse Kaplan-Meier" curves.
[b] *P* value at Gray test for the comparison between the crude cumulative incidence curves of local recurrence, distant metastasis, and deaths without recurrence.
[c] *P* value at log-rank test for the comparison of the Kaplan-Meier curves.

In the validation set, the Harrell C statistic concordance index values were very similar to those obtained in the development set for both DFS and OS (DFS: 0.69 vs 0.71 [Fig. 3 A]; OS: 0.73 vs 0.74 [Fig. 3 B]).

DISCUSSION

Correlation between observed and nomogram-predicted DFS and OS rates suggests good calibration of the multi-institutional RPS nomogram in a larger, independent validation cohort.[8] The data presented here demonstrate that the nomogram applies well to patients undergoing surgery for primary RPS performed by specialized sarcoma surgeons at sarcoma centers. Because the data are based on outcomes after surgical resection of primary RPS, this nomogram is not applicable to patients who have undergone surgical resection for recurrent disease, unlike the single-institution nomogram from The University of Texas MD Anderson Cancer Center.[4] Furthermore, unlike the recently reported RPS nomogram from MSKCC, the multi-institutional RPS nomogram validated in the current study does not incorporate vascular resection or association with a prior radiation field as independent variables because these were very rare in the development set.[3] In addition, this international, multi-institution RPS nomogram includes age and tumor size as continuous rather than categorical variables; the latter is true of some of the single-institution nomograms.[3,4] Although the relevance or advantage of such detail may be debated, we have found that some of the largest tumors (>30 cm) may have a better prognosis than those measuring in the range of 20 to 30 cm, reflecting a more favorable tumor biology in tumors that have reached such a large size likely through prolonged indolent growth.

As a nomogram constructed based on data from multiple institutions and validated by other additional institutions, this nomogram has broad applicability. Nevertheless, it reflects predicted outcomes in patients undergoing such procedures by experienced sarcoma surgeons and multidisciplinary teams at high-volume sarcoma centers. Data used as part of the initial development set and the current validation set were pooled in a previously reported survival analysis.[6] OS outcomes from that combined data set were favorable when compared with OS reported in a Surveillance, Epidemiology, and End Results analysis, which included surgical resections performed in a percentage of regions in the United States, bearing in mind all the caveats of such a post hoc comparison. Nevertheless, the nomogram in the current study establishes a benchmark against which other institutional outcomes may be compared.

The multi-institutional RPS nomogram in the current study provides a more individualized and disease-relevant estimation of OS than the AJCC classification. The 7th edition of the AJCC classification essentially only risk stratifies RPS based on grade alone (which still remains the most important prognosticator) because approximately 95% of RPS are T2b tumors. The current multi-institutional RPS nomogram provides a more specific estimation of both DFS and OS and, based on the corroboration of the external validation set reported

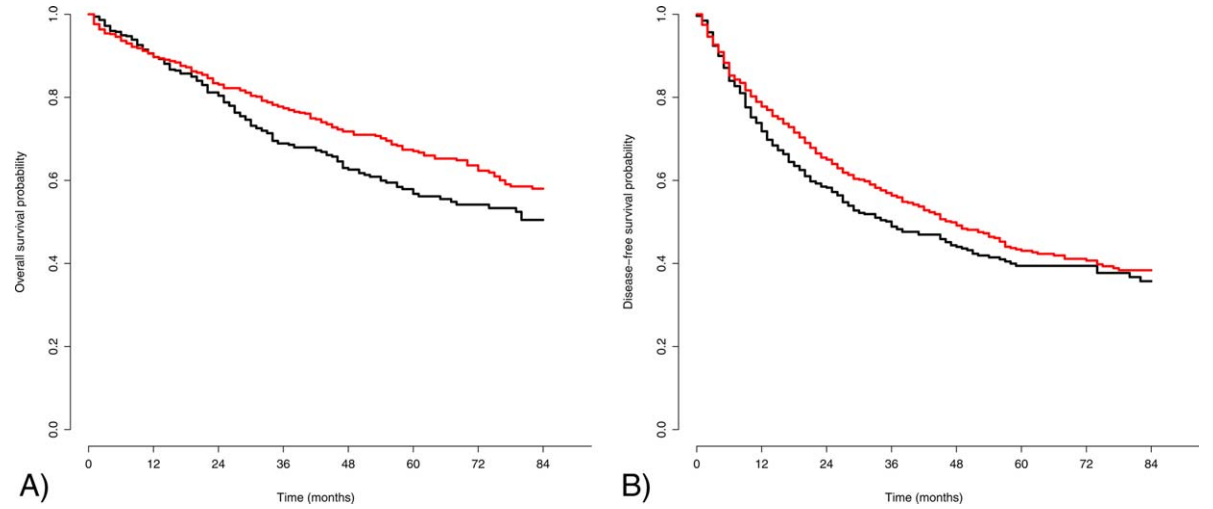

Figure 2. Kaplan-Meier curves for (A) disease-free survival and (B) overall survival for the development (black) and validation (red) sets.

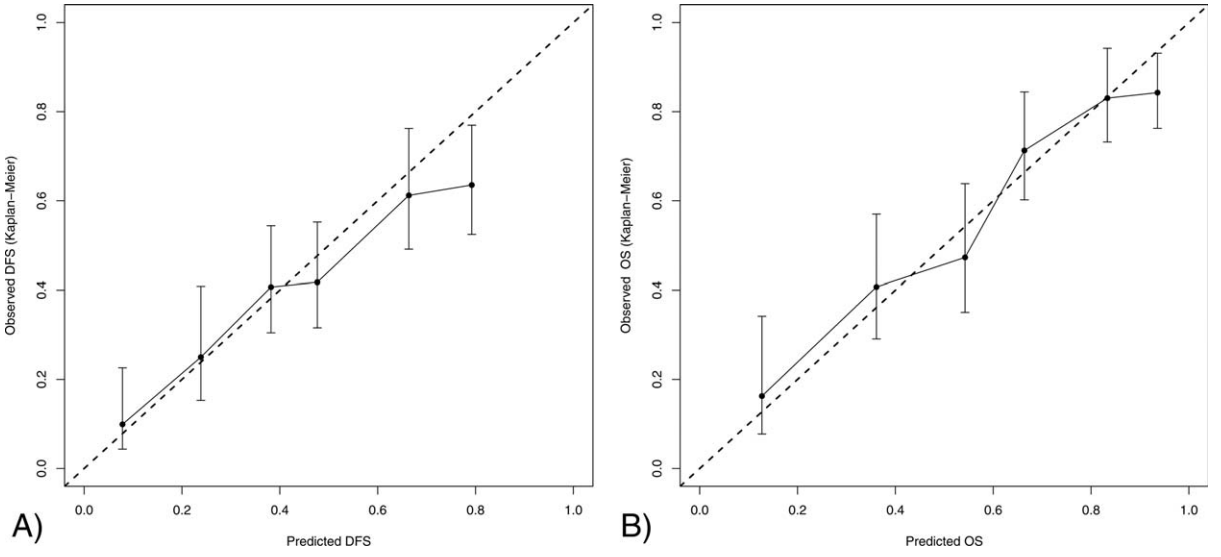

Figure 3. Calibration plot for external validation of the (A) disease-free survival (DFS) and (B) overall survival (OS) nomograms. Nomogram-predicted probabilities were stratified into 6 equally sized subgroups. For each subgroup, the mean predicted probability (x-axis) was plotted against the Kaplan-Meier probability observed in the validation cohort (y-axis). Vertical lines indicate the 95% confidence intervals of the Kaplan-Meier estimates. The dashed line in each panel indicates the reference line along which an ideal nomogram would lie.

herein, will be proposed for inclusion in the 8th edition of the AJCC classification.

Nomograms have the flexibility to incorporate additional independent prognostic factors. The use of chemotherapy did not appear to impact outcome in the nomogram used herein. There was a significantly lower percentage of patients undergoing chemotherapy in the validation set compared with the development set (9% vs 40%; $P<.0001$) (Table 2), reflecting institutional bias in default therapy for RPS. However, this did not appear to affect the predictive value of the multi-institutional RPS nomogram. The percentage of patients undergoing radiotherapy was similar in the 2 data sets. The ongoing phase 3 randomized study of preoperative radiotherapy plus surgery versus surgery alone for patients with retroperitoneal sarcoma (STRASS) trial will define the standard of care with respect to the potential benefit of preoperative radiotherapy for RPS. If found to be independently predictive

of outcome, preoperative radiotherapy could be added as a separate prognostic factor in the future.

There has been much debate recently concerning the optimal extent of surgical resection.[10-15] In the recent single-institution nomogram reported by Tan et al, the number of organs resected was incorporated.[3] However, in the multi-institutional RPS nomogram validated in the current study, organ resection was not included because we noted institutional variation in the number of organs resected. This may well reflect not only different institutional practices, but also the broad variability of presentation of these tumors, which may be represented differently in the various institutional case mixes. In the series reporting combined outcomes from the majority of the institutions in the development and validation sets, the number of organs resected was not found to be an independent prognosticator.[6] Thus, the number of organs resected is not as predictive of the extent of surgical resection as in single-institution nomograms, which reflect a more uniform treatment strategy.[3] The number of organs resected remains a prognosticator only as long as it reflects a uniform approach to the removal of the disease, which then still has to be tailored to the single patient.

Eventually, the DFS nomogram could be replaced with separate nomograms for local and distant recurrence-free survival. Whether OS or disease-specific survival is a more optimal measure of long-term outcome is a matter of debate. A small percentage of patients in each of the development and validation cohorts died without developing disease recurrence (7% and 8%, respectively). Future editions may include a disease-specific survival nomogram, as the recent study from MSKCC study reported.[3]

Conclusions

External validation of the multi-institutional RPS nomogram established its broad applicability in predicting outcomes in patients with primary RPS who were treated at experienced centers, and supports its inclusion in the 8th edition of the AJCC classification.

FUNDING SUPPORT

No specific funding was disclosed.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Chandrajit P. Raut: Conceptualization, methodology, validation, formal analysis, investigation, resources, data curation, writing–original draft, writing–review and editing, visualization, supervision, and project administration. **Rosalba Miceli:** Methodology, software, validation, formal analysis, investigation, resources, and writing–review and editing. **Dirk C. Strauss:** Conceptualization, methodology, formal analysis, investigation, resources, data curation, and writing–review and editing. **Carol J. Swallow:** Conceptualization, methodology, formal analysis, investigation, resources, data curation, and writing–review and editing. **Peter Hohenberger:** Conceptualization, methodology, formal analysis, investigation, resources, data curation, and writing–review and editing. **Frits van Coevorden:** Conceptualization, methodology, formal analysis, investigation, resources, data curation, and writing–review and editing. **Piotr Rutkowski:** Conceptualization, methodology, formal analysis, investigation, resources, data curation, and writing–review and editing. **Marco Fiore:** Conceptualization, methodology, validation, formal analysis, investigation, data curation, and writing–review and editing. **Dario Callegaro:** Conceptualization, methodology, validation, formal analysis, investigation, data curation, and writing–review and editing. **Paolo G. Casali:** Data curation and writing–review and editing. **Rick L. Haas:** Resources, data curation, and writing–review and editing. **Andrew J. Hayes:** Resources, data curation, and writing–review and editing. **Charles Honore:** Resources and writing–review and editing. **Amanda J. Cannell:** Data curation and writing–review and editing. **Jens Jakob:** Resources and writing–review and editing. **Milena Szacht:** Data curation and writing–review and editing. **Mark Fairweather:** Resources, data curation, and writing–review and editing. **Raphael E. Pollock:** Conceptualization, methodology, investigation, data curation, and writing–review and editing. **Sylvie Bonvalot:** Conceptualization, methodology, formal analysis, investigation, resources, data curation, and writing–review and editing. **Alessandro Gronchi:** Conceptualization, methodology, validation, formal analysis, investigation, resources, data curation, writing–review and editing, visualization, supervision, and project administration.

REFERENCES

1. Crago AM, Singer S. Soft tissue sarcoma. In: Ashley S, Cance W, Chen H, Jurkovich G, Napolitano L, Pemberton J, Riall T, Swanson S, Valentine J, eds. ACS Surgery: Principles and Practice. 7th ed. New York: Decker Intellectual Properties Inc; 2011.
2. Ardoino I, Miceli R, Berselli M, et al. Histology-specific nomogram for primary retroperitoneal soft tissue sarcoma. *Cancer*. 2010;116:2429-2436.
3. Tan MC, Brennan MF, Kuk D, et al. Histology-based classification predicts pattern of recurrence and improves risk stratification in primary retroperitoneal sarcoma [published online ahead of print April 24, 2015]. *Ann Surg*.
4. Anaya DA, Lahat G, Wang X, et al. Postoperative nomogram for survival of patients with retroperitoneal sarcoma treated with curative intent. *Ann Oncol*. 2010;21:397-402.
5. Kattan MW, Leung DH, Brennan MF. Postoperative nomogram for 12-year sarcoma-specific death. *J Clin Oncol*. 2002;20:791-796.
6. Gronchi A, Strauss DC, Miceli R, et al. Variability in patterns of recurrence after resection of primary retroperitoneal sarcoma (RPS): a report on 1007 patients from the Multi-Institutional Collaborative Transatlantic RPS Working Group [published online ahead of print December 31, 2015]. *Ann Surg*.
7. Nathan H, Raut CP, Thornton K, et al. Predictors of survival after resection of retroperitoneal sarcoma: a population-based analysis and critical appraisal of the AJCC staging system. *Ann Surg*. 2009;250:970-976.
8. Gronchi A, Miceli R, Shurell E, et al. Outcome prediction in primary resected retroperitoneal soft tissue sarcoma: histology-specific overall survival and disease-free survival nomograms built

on major sarcoma center data sets. *J Clin Oncol.* 2013;31:1649-1655.
9. Coindre JM. Grading of soft tissue sarcomas: review and update. *Arch Pathol Lab Med.* 2006;130:1448-1453.
10. Gronchi A, Lo Vullo S, Fiore M, et al. Aggressive surgical policies in a retrospectively reviewed single-institution case series of retroperitoneal soft tissue sarcoma patients. *J Clin Oncol.* 2009;27:24-30.
11. Bonvalot S, Miceli R, Berselli M, et al. Aggressive surgery in retroperitoneal soft tissue sarcoma carried out at high-volume centers is safe and is associated with improved local control. *Ann Surg Oncol.* 2010;17:1507-1514.
12. Bonvalot S, Rivoire M, Castaing M, et al. Primary retroperitoneal sarcomas: a multivariate analysis of surgical factors associated with local control. *J Clin Oncol.* 2009;27:31-37.
13. Raut CP, Swallow CJ. Are radical compartmental resections for retroperitoneal sarcomas justified? *Ann Surg Oncol.* 2010;17:1481-1484.
14. Pisters PW. Resection of some-but not all-clinically uninvolved adjacent viscera as part of surgery for retroperitoneal soft tissue sarcomas. *J Clin Oncol.* 2009;27:6-8.
15. Gronchi A, Pollock R. Surgery in retroperitoneal soft tissue sarcoma: a call for a consensus between Europe and North America. *Ann Surg Oncol.* 2011;18:2107-2110.