



Original Investigation

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# Quality of Life Assessment in Patients with Surgically Treated **Parasagittal Meningiomas**

Rodrigo Inácio PONGELUPPI<sup>1</sup>. Stephanie Naomi Funo de SOUZA<sup>1</sup>. Rodrigo Augusto Monteiro CARDOSO<sup>1</sup>. Davi Casale ARAGON<sup>2</sup>, Ricardo Santos de OLIVEIRA<sup>1</sup>, Benedicto Oscar COLLI<sup>1</sup>

<sup>1</sup>University of São Paulo, University Hospital of Ribeirão Preto Medical School, Division of Neurosurgery, Sao Paulo, Brazil <sup>2</sup>University of São Paulo, Ribeirão Preto Medical School, Department of Pediatrics, Sao Paulo, Brazil

Corresponding author: Rodrigo Inácio PONGELUPPI 🗵 rodrigopongeluppi@gmai.com

## ABSTRACT

AIM: To assess quality of life (QoL) in patients with parasagittal meningiomas (PSM), and to identify the risk factors for different levels of QoL.

MATERIAL and METHODS: Patients were contacted and interviewed via telephone. A total of 136 patients with PSM underwent surgery at our institution between 1984 and 2020. Among them, 45 had agreed to participate in the research. The scales utilized included the Functional Assessment of Cancer Therapy General (FACT-G), Brain (FACT-Br), and Meningioma (FACT-MNG). Medical records were also reviewed.

RESULTS: The mean KPS was 93.3 (70-100). Overall, the mean scores for the FACT-G, FACT-Br, and FACT-MNG scales were 98.4/108 (55–108; SD: 12.9), 179.3/200 (98–200; SD: 22.4), and 219.3 (119–248; SD: 29.7). Considerable variability in scales scores was observed among those with the same KPS score. Preoperative KPS score was significantly associated with both FACT-Br [-21.64; 95% Crl (-34.04, -9.59)] and FACT-MNG [-31.88; 95% Crl (-47.24, -15.25)]. Preoperative KPS was identified as a risk factor for QoL impairment.

CONCLUSION: Variability in the scale scores among those with the same KPS score highlights the importance of structured assessment. Moreover, KPS may overlook impairments in QoL. To date, this has been the first study to assess QoL in PSM patients.

KEYWORDS: Brain tumor, Meningioma, Quality of life

ABBREVIATIONS: 95% Crl: Credibility interval, Ant: Anterior third, FACIT: Functional Assessment of Chronic Illness Therapy, FACT-Br: Functional Assessment of Cancer Therapy - Brain, FACT-G: Functional Assessment of Cancer Therapy - General, FACT-MNG: Functional Assessment of Cancer Therapy - Meningiomas, JAGS: Just Another Gibbs Sampler (statistical software), KPS: Karnofsky Performance status, L: Large size, M: Middle size, Mid: Middle third of the superior sagittal sinus, Post: Posterior third of the superior sagittal sinus, PSM: Parasagittal meningiomas, QoL: Quality of life, S: Small size, SSS: Superior sagittal sinus, vs: Versus, WHO: World Health Organization

Rodrigo Inácio PONGELUPPI (D): 0000-0003-1769-5489 Stephanie Naomi Funo de SOUZA 0000-0001-5144-8743 Rodrigo Augusto Monteiro CARDOSO Di : 0000-0002-2016-9642

Davi Casale ARAGON Ricardo Santos de OLIVEIRA (0): 0000-0003-0390-5553 Benedicto Oscar COLLI

10000-0003-1019-3654 : 0000-0002-0222-6770

## INTRODUCTION

eningiomas, which arise from the arachnoid cap cells (8,17,26), are the most frequent primary brain tumors (24). Studies have shown that meningiomas can develop across several locations within the brain, with diverse clinical presentations (5,7,17,28).

Parasagittal meningiomas (PSM) are defined as those that fill the sinodural angle, with no brain parenchyma interposed between the lesion and the superior sagittal sinus (SSS) (10). This location is the second most common intracranial site for meningioma development (7,10,17,18,21,34).

Surgery remains the primary treatment for PSM, with the extent of resection, among other factors, predicting the likelihood of recurrence (7,11,18,31). Surgery for these lesions can be challenging, especially in cases with venous sinus infiltration (29).

These tumors can be classified into three groups based on their location: anterior third, between the crista galli and coronal suture; middle third, between the coronal and lambdoid sutures; and posterior third, posterior to the lambdoid suture (4). The most frequent location is the middle third of the SSS, which can present with a predominantly crural paresis and a higher risk of functional impairment (9-11,13-15). Headache, visual loss, and epilepsy have also been identified as frequent symptoms (33).

Most surgical series on PSM have assessed patients from a functional point of view using the Karnofsky Performance Scale (KPS). However, the quality of life (QoL) has been poorly assessed in these patients (30).

There are specific and validated scales designed to assess cancer patients in general, such as the Functional Assessment of Cancer Therapy—General (FACT-G) (22), and patients with brain malignant neoplasms, such as Functional Assessment of Cancer Therapy—Brain (FACT-Br) (36). For the evaluation of patients with meningiomas, Zlotnick et al. designed a scale with elements from the FACT-G and FACT-Br, as well as sitespecific assessment for meningiomas based on the Functional Assessment of Cancer Therapy—Meningioma (FACT-MNG). The latter, however, still lacks validation from studies. On all scales, scores are directly proportional to the estimated QoL.

Using the previously described scales, the present study therefore aimed to assess the QoL in patients with PSM who underwent surgical treatment and identify risk factors for different levels of QoL.

#### MATERIAL and METHODS

This study included patients with confirmed histological diagnosis of PSM who underwent surgery between 1984 and 2020. Medical records were reviewed for data collection.

After evaluating tumor size, the lesions were grouped into small, medium, and large for those with a linear diameter of <3 cm, between 3 and 6 cm, and >6 cm, respectively, for statistical analysis purposes (4,9,11,12).

Regarding location, the lesions were grouped into the middle third, which has greater functional impairment (4,9,11,12) and non-middle third lesions for statistical analysis purposes.

After also reviewing surgical records, the extent of resection was classified as described by Simpson: grade I, complete resection with excision of the dura attachment; grade II, resection of all visible tumor remnants and coagulation of the dura attachment; grade III, macroscopically complete resection without coagulation of the dura attachment and with the possibility of remaining tumor in the venous sinus or hyperostotic bone; grade IV, incomplete resection; and grade V, biopsy (28). For statistical analysis purposes, the extent of resection was categorized as either Simpson I or others.

After combining radiological and surgical information, the extent of SSS invasion was classified into six grades as described by Sindou: type I, fixation on the lateral wall of the sinus; type II, invasion of the lateral recess; type III, lateral wall invasion; type IV, invasion of the sidewall and roof; type V, completely occluded sinus; and type VI, occluded sinus and extending beyond its walls (Figure 1) (1,29). Sindou's types were grouped between low grade (I and II) and high grade (III, IV, V, and VI) for statistical analysis.

The scales applied included FACT-G, FACT-Br, and FACT-MNG (Figure 2). Licensing by the Functional Assessment of Chronic Illness Therapy System (FACIT System) was obtained. The patients' KPS score was also evaluated.

There was a tendency toward an increase in the mean KPS score, albeit not statistically significant perhaps due to the small number of patients in each group. Because of this, patients were grouped into those who had a KPS of 100 or <100.

KPS scores both before the surgery and at last assessment were used for analysis.

Patients were contacted to obtain permission for study participation. A trained interviewer described the study and administered the interview via telephone. Questionnaires took, on average, between 10 and 20 min to complete.

Only patients and physicians had access to the responses, thereby preserving confidentiality. Only collaborative patients who agreed to complete the scales were included, excluding those who were debilitated or unable to answer the questions.

A total of 136 patients with PSM underwent surgery at our institution between 1984 and 2020. Among them, 45 agreed to participate in the research. This study was approved by our institution's ethics committee. Consent was obtained for all participants via telephone.

To compare the means of the dependent variables according to the categories of each independent variable, simple and multiple linear regression models were utilized under a Bayesian approach. Differences between means and 95% credibility intervals (95% Crl) were determined. In each case, covariates were adjusted for in the multiple models. All statistical analyses were conducted using JAGS from R 4.1.1 software.



Figure 1: Illustration showing different aspects of parasagittal meningiomas according to the original description from Sindou Classification - adapted from Sindou (29).

A) FACT-G					B) FACT-Br: FACT-G questionnaire + site specific questions (brain)								
		Not at all	A little bit	Some- what	Quite a bit	Very Much			Not at all	A little bit	Some- what	Quite a bit	Very Much
	Physical Well-Being							Additional Concerns					
GP1	I have a lack of energy	0	1	2	3	4	Br1	I am able to concentrate	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4	Br2	I have had seizures (convulsions)	0	1	2	3	4
GP3		0	-	2	2		Br3	I can remember new things	0	1	2	3	4
0.5	Because of my physical condition, I have trouble	0	1	2	3	4	Br4 Br5	I get frustrated that I cannot do things I used to	0	1	2	3	4
0.004	meeting the needs of my family					_	Br6	I have trouble with my every oft	0	1	2	3	4
Gr4	I have pain	0	1	2	3	4	Br7	I feel independent	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4	NTX6	I have trouble hearing	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4	BrS	I am able to find the right word(s) to say what I mean	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4	Br9	I have difficulty expressing my thoughts	0	1	2	3	4
-	Cosial/Equily Well Daing		-	_			Br10 Pe11	I am bothered by a change in my personality	0	1	2	3	4
0.01	Social/Faining wen-Being						Br12	I am able to make decisions and take responsibility	0	1	2	3	4
GSI	I feel close to my friends	0	1	2	3	4	Br13	I am able to put my thoughts together	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4	Br14	I need help in caring for myself (bathing, dressing, eating, etc.)	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4	Br15	I am able to put my thoughts into action	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4	Br16	I am able to read like I used to	0	1	2	3	4
GS5	I am satisfied with family communication about	0	1	2	3	4	Br17	I am able to write like I used to	0	1	2	3	4
	my illness			-			Br18 Br10	I am able to drive a vehicle (my car, truck, etc.)	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my	0	1	2	3	4	Br20	I have trouble reening sensations in my arms, hands, or legs	0	1	2	3	4
	main support)	Ŭ	1	-	5		Br21	I have trouble with coordination	0	1	2	3	4
GS7	I am satisfied with my sex life	0	1	2	3	4	An10	I get headaches	0	1	2	3	4
	Emotional Well-being			_		C) FACT-MNG: FACT-Br questionnaire + SF-36* (questions concerning pr				ng phy	sical		
GE1	I feel sad	0	1	2	3	4	capabilities) + Tumor-site specific questions						
GE2	I am satisfied with how I am coping with my	0	1	2	3	4		1					
	illness		1001						Not at all	A little	some- what	Quite	Very
GE3	I am losing hope in the fight against my illness	0	1	2	3	4			at an	bit	with	aon	without
GE4	I feel nervous	0	1	2	3	4		SF-36 questions					
GE5	I worry about dving	0	1	2	3	4		I am limited in performing vigorous activities, such as running,	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4		I am limited in performing moderate activities, such as moving	0	1	2	3	4
-	Functional Wall Daing		1	2	5			a table, pushing a vacuum cleaner, bowling, or playing golf					
GE1	гипсионат wen-венид							I have difficulty climbing several flights of stairs	0	1	2	3	4
GET	I am able to work (include work at home)	0	1	2	3	4		I have difficulty walking several blocks	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4		I have difficulty bathing or dressing myself Parassagital/Falx Maningiama	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4		i ai assagital/r aix ivieningioilla	0		2	2	
GF4	I have accepted my illness	0	1	2	3	4		IVIY SHORI IERIH MEMORY IS WORSE My leg is weak	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4		My leg is numb	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4		My arm is weak	0	1	2	3	4
GE7	T and enjoying the times I usually to for full	0	1	-	2	-		My arm is numb	0	1	2	3	4
Gr/	I am content with the quality of my life right now	0	1	2	3	4		I have a blind spot in my vision	0	1	2	3	4

Figure 2: Questionaires of the assessed scales in the study: A) FACT-G questionaire; B) FACT-Br site-specific questions C) FACT-MNG.

#### **Data Availability Statement**

All data generated or analyzed during this study area included in this article. Further enquiries can be directed to the corresponding author.

## RESULTS

The mean age was 49.11 years (4.4-74.1) at the time of surgery and 59.39 years (16.1-84.7) at the time of the last assessment. The mean follow-up duration was 9.98 years (0.68-37.34).

There was a predominance of women (84.4%) among the included patients. Only one patient had type 2 neurofibromatosis, with the others being non-syndromic.

Tumor volume ranged between 0.9 and 209.9 mL (mean 40.1 mL). Moreover, 42.2%, 35.5%, and 22.2% of the lesions were located in the middle third, anterior third, and posterior third of the SSS, respectively.

Most tumors were classified as Sindou type I (31.1%), followed by type II (24.4%), type IV (17.8%), type III (13.3%), and type VI (11.1%).

Gross total resection was achieved in 82.2% of the patients (64.4%, 17.8%, and 17.8% of the resections were classified as Simpson I, II, and IV, respectively). Moreover, 41 patients

**Table I:** Evolution of KPS. Numbers of Individuals in Preoperative,Early Postoperative and Late Postoperative Periods wereSpecified

KPS value	Preoperative	Early postoperative	Late postoperative
100	31	30	28
90	5	4	8
80	2	2	6
70	4	8	3
60	2	1	0
50	1	0	0

Table II: Variability in Scale Scores According to KPS Range

(91.1%) had World Health Organization (WHO) grade 1 meningiomas, whereas 4 (8.9%) had grade 2 meningiomas.

The mean preoperative KPS score was 93.8 (60–100), with the majority being 100 (66.7%). There was a small reduction in the mean KPS score [to 92.5 (60–100)] during the immediate postoperative period, and recovery in the last KPS evaluated [to 93.3 (70–100)]. Evolution of KPS was summarized in Table I.

Overall, the mean FACT-G, FACT-Br, and FACT-MNG scales scores were 98.4/108 (55–108; SD: 12.9), 179.3/200 (98–200; SD: 22.4), and 219.3 (119–248; SD: 29.7), respectively.

We found considerable variability in the scare scores among those with the same KPS during the last assessment. These findings are summarized in Table II.

Preoperative KPS score was significantly associated with the scores of both FACT-Br [difference between means of -21.64; 95% CrI (-34.04, -9.59)] and FACT-MNG [difference between means of -31.88; 95% CrI (-47.24, -15.25)]. However, after adjusting for tumor volume and location as covariates, no significant association had been observed.

Conversely, the KPS score at the time the scales were completed was not significantly associated with the values obtained from the scales.

No significant association was found between tumor size and QoL. Similarly, no significant association was observed between lesion location and scale scores, between greater sinus invasion and worse QoL, and between the extent of resection and QoL scores.

The results of the statistical analysis are summarized in Table III.

## DISCUSSION

Meningiomas are common benign intracranial tumors that are characteristically slow-growing and, eventually, asymptomatic (20). PSM accounts for 21%–31% of intracranial meningiomas (9).

KPS	Number of patients	Scale	Minimum	Maximum	Average (SD)
70		FACT-Br	119/200	145/200	129.7 (11.1)
70	3 (6.7%)	FACT-MNG	133/248	164/248	153.0 (14.2)
	6 (13.3%) —	FACT-Br	153/200	183/200	168.7 (10.4)
80		FACT-MNG	189/248	224/248	201.1 (12.7)
~~~	8 (17.8%) —	FACT-Br	156/200	191/200	177.2 (12.2)
90		FACT-MNG	189/248	227/248	216.0 (14.9)
100	28 (62.2%) —	FACT-Br	98/200	200/200	187.4 (19.3)
100		FACT-MNG	119/248	248/248	231.2 (24.7)

Table III: Statistical Analysis of Associations between the Scores on FACT-Br and FACT-MNG Scales and the Following Variable	s: KPS
Size, Location, Simpson Grade and Sindou Type. Associations with Statistical Significance were Highlighted in Bold	

Variable	Model	Average difference	Crl 95%	
FACT-Br	Circala	-21.64	-34.04, -9.59	
FACT-MNG	Simple	-31.88	-47.24, -15.25	
FACT-Br	Covariates: localization	-9.26	-25.73, 4.84	
FACT-MNG	and volume	-16.21	-36.16, 3.48	
FACT-Br	Circula	-9.78	-24.95, 5.55	
FACT-MNG	Simple	-15.35	-33.25, 3.48	
FACT-Br	Coverietore Cimeroon	-10.12	-23.98, 4.88	
FACT-MNG	Covariates: Simpson	-16.21	-34.51, 2.34	
FACT-Br		7.95	-6.35, 23.26	
FACT-MNG	I VS II-IV	12.63	-5.91, 32.42	
FACT-Br		-3.36	-17.03, 9.93	
FACT-MNG	1-11 VS 111-V1	-3.1	-21.53, 14.63	
FACT-Br		4.07	-9.81, 17.13	
FACT-MNG	Ivid VS Ant and Post	6.73	-9.98, 24.43	
	S vs M	-2.24	-20.09, 15.44	
FACT-Br	S vs L	-1.01	-20.83, 17.52	
	M vs L	1.24	-15.27, 17.46	
	S vs M	-6.33	-26.73, 15.43	
FACT-MNG	S vs L	-2.18	-25.05, 21.88	
	M vs L	4.16	-17.85, 26.88	
	VariableFACT-BrFACT-MNGFACT-BrFACT-MNGFACT-MNGFACT-BrFACT-MNGFACT-BrFACT-MNGFACT-BrFACT-BrFACT-MNGFACT-BrFACT-BrFACT-BrFACT-BrFACT-BrFACT-BrFACT-BrFACT-BrFACT-BrFACT-MNGFACT-MNGFACT-MNGFACT-MNGFACT-MNGFACT-MNG	VariableModelFACT-BrSimpleFACT-MNGCovariates: localization and volumeFACT-BrCovariates: localization and volumeFACT-BrSimpleFACT-BrCovariates: SimpsonFACT-BrCovariates: SimpsonFACT-BrI vs II-IVFACT-BrI vs II-IVFACT-BrI vs II-IVFACT-BrI vs II-IVFACT-BrI vs II-IVFACT-BrMid vs Ant and PostFACT-MNGS vs MFACT-BrMid vs Ant and PostFACT-BrS vs MFACT-BrS vs MFACT-BrS vs LM vs LS vs MFACT-MNGS vs L	VariableModelAverage differenceFACT-BrSimple-21.64FACT-MNGSimple-31.88FACT-BrCovariates: localization and volume-9.26FACT-MNGand volume-16.21FACT-BrSimple-9.78FACT-BrOvariates: Simple-15.35FACT-BrCovariates: Simpson-10.12FACT-BrCovariates: Simpson-16.21FACT-BrCovariates: Simpson-16.21FACT-BrI vs II-IV12.63FACT-BrI vs II-IV12.63FACT-BrI vs II-IV12.63FACT-Br-3.36-10.12FACT-BrI vs III-VI-3.1FACT-BrMid vs Ant and Post6.73FACT-BrS vs M-2.24FACT-BrS vs M-2.24FACT-BrS vs M-6.33FACT-MNGS vs M-6.33FACT-MNGS vs M-6.33	

Ant: Anterior third, Crl: Credibility interval, L: Large size, M: Middle size, Mid: Middle third, Post: Posterior third, S: Small size; vs: versus.

While surgery offers the potential for cure, the prospect of surgical excision raises concerns regarding eventual functional deficits and possible deleterious effects on QoL (20,30). However, only a few studies have assessed QoL using standardized and validated scales (20). Most of the available research had used Short-Form 36 (SF-36) or EuroQol-5D scales that, though validated, are crude instruments for specifically evaluating central nervous system diseases (30).

Although the brain module of the FACT scale (FACT-Br) can overcome these drawbacks, this scale is designed to assess malignant diseases and side effects of adjuvant therapy (20,30).

One study that used an adapted FACT-Br questionnaire in 165 meningioma patients found that 77% of the patients self-reported satisfaction with QoL. The authors defined satisfaction with QoL based on answers of "quite a bit" or "very much" to question GF7 ("are you satisfied with your quality of life"). Using this criterion, 86.7% [39] of our patients can be considered satisfied with their QoL. Nonetheless, given that different sites of meningiomas had been grouped, comparisons between the

present and previous studies was not possible (20). Meningiomas have heterogeneous clinical presentations depending on location, and different QoL impairments are expected (35). Therefore, we opted to evaluate only patients with PSM in our study.

Differences in meningioma locations along the SSS influences both clinical presentation and surgical difficulty. Lesions located in the anterior third of the SSS have been described as the most favorable, with the SSS being generally resectable *en bloc* without clinical impairment in this location. Moreover, a lower mortality rate has been reported in this subset of patients (9). Lesions located in the posterior third of the SSS are the least frequent and least studied, although visual impairment and seizures have been described (3,9). However, Biroli et al. had described favorable outcomes for PSMs located in the posterior third of the SSS, which were comparable to those located in other SSS areas (3). PSMs located in the middle third of the SSS were associated with a higher incidence of transient or permanent motor function deterioration as either a presenting symptom or during the postoperative period. Thus, some authors have correlated this location to worse functional outcomes (12) and higher mortality rates (9).

Therefore, for comparative analysis, patients were grouped according to the location of the PSM, namely middle third and non-middle third. However, no significant association was found [mean differences: FACT-Br 4.07, 95% Crl (9.81, 17.13); FACT-MNG 6.73, 95% Crl (9.98, 24.43)]. Similarly, other studies showed no association between location and postoperative complications (19), functional status (9), or discharge disposition (19).

The extent of SSS invasion has been suggested to increase surgical complexity (4,29), risk for complications (14), and higher recurrence rates (2). Similarly, lesion size has been associated with increased SSS invasion, higher reoperation rates (16), WHO histological grades 2 and 3 (23), need for irradiation (16), and greater peritumoral brain edema (27). Lesions <3 cm have also been associated with better functional status (33).

In contrast, the current study did not demonstrate worse QoL results in patients with greater Sindou type [I–II vs. III–VI mean difference for FACT-Br –3.36, 95% CrI (–17.93, 9.93) and FACT-MNG –3.1, 95% CrI (–21.53, 14.63)] or larger tumors [S vs L mean difference for FACT-Br –1.01, 95% CrI (–20.83, 17.52) and FACT-MNG –2.18, 95% CrI (–25.05, 21.88)]. Accordingly, other studies found no correlation between functional outcomes and tumor size (9,19) or extent of SSS invasion (19). Moreover, our findings for long-term survivors showed that these factors may not be critical for this subset of patients.

The extent of resection has been identified as an independent factor for tumor recurrence (7,11,18,25), with studies showing higher KPS scores for those with Simpson grade I–II disease (33). However, our findings did not demonstrate better QoL scores for Simpson I patients [mean difference for FACT-Br 7.95, 95% CrI (–6.35, 23.26) and FACT-MNG 12.63, 95% CrI (–5.91, 32.42)].

Given that FACT-MNG scales have not been evaluated in the published series, no comparison could be made with our results. However, we believe that the mean score of 219.3/248 (SD 29.7), though heterogeneous and associated with high KPS scores, represented favorable outcomes for most patients.

FACT-Br was quantitatively analyzed in meningioma patients, with mean scores of 146.1 and 131.7 for non-epileptic and epileptic patients, respectively (32). Similarly, another study showed that baseline scores for brain metastasis patients ranged from 143.6–144.4 (6). Therefore, our patients demonstrated better results compared to those included in the previous study (mean: 179.3; SD 22.4).

The variability of the scores among those with the same KPS score highlights the importance of a structured QoL assessment. KPS functional assessment may overlook impairments in QoL, for which good outcomes must be sought (30). A dif-

ference of  $\geq$ 10 points in the total QoL scales score was considered clinically relevant (6), and a SD of 11.1, 10.4, 12.2, and 19.3 were found for KPS scores of 70, 80, 90, and 100, respectively, which suggested the heterogeneity of these groups of patients. Moreover, no significant association was found between the KPS at the time of the assessment and overall scores. However, preoperative KPS scores appear to be a risk factor for long-term QoL impairment both in FACT-Br [difference between means of -21.64; 95% Crl (-34.04, -9.59)] and FACT-MNG [difference between means of -31.88; 95% Crl (-47.24, -15.25)].

#### Limitations

The number of questions and time spent answering them may be a noteworthy drawback and limiting factor for routine clinical use of the scales.

Another limitation of this study was that we assessed longterm survivors, among whom surgical complexity may not be an important factor.

Moreover, selection bias is noteworthy: only 45 of the 136 could be contacted and consented to participate.

# CONCLUSION

Given that PSMs are complex diseases, QoL assessments help physicians understand the impact of surgical treatment on the patients. Our series demonstrated favorable longterm QoL results and that factors associated with greater surgical complexity were not associated with worse QoL or functional status. Despite the importance of QoL assessments in surgical planning and follow-up, this has been the first study to assess QoL specifically in PSM patients. Considering the heterogeneity and complexity of this disease, the decision for surgical treatment should include not only functional status but also expected QoL.

#### **AUTHORSHIP CONTRIBUTION**

Study conception and design: RIP, SNFS, RAMC, DCA, RSO, BOC

Data collection: RIP, SNFS, RAMC

Analysis and interpretation of results: RIP, SNFS, RAMC, DCA, RSO, BOC

Draft manuscript preparation: RIP, SNFS, RAMC

Critical revision of the article: RIP, SNFS, RAMC, DCA, RSO, BOC Other (study supervision, fundings, materials, etc...): RSO, BOC All authors (RIP, SNFS, RAMC, DCA, RSO, BOC) reviewed the results and approved the final version of the manuscript.

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