Oncological results of elderly patients undergoing surgery for retroperitoneal sarcomas

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Abstract

Introduction: The number of elderly patients diagnosed with cancer has increased. There are no studies that assess the oncological results in elderly patients with retroperitoneal sarcomas. The purpose of this study was to define the demographic characteristics and prognostic factors in elderly patients with retroperitoneal sarcomas. **Methods:** A retrospective study including 25 elderly patients (> 65 years) diagnosed with retroperitoneal sarcomas at the National Institute of Cancerology (Mexico). Demographic variables and prognostic factors were analyzed. **Results:** Twenty-five patients, 16 men (64%) and 9 women (36%) with a median age of 69.3 years (65-82 years). Tumor size average of 24.4 cm (8-61 cm); 19 patients (76%) had high-grade tumors, the most frequent histological type was liposarcoma. Overall-survival was 34.6 months (95% CI: 20.86-48.40) for patients with ECOG < 1 and 3.44 months (95% CI: 1.68-5.2) for those with ECOG > 1. In the multivariate analysis, the performance status measured by ECOG ($p < 0.001$), the presence of comorbidities ($p = 0.038$) and the presence of resections with macroscopic residual disease ($p < 0.001$) were associated with lower overall-survival. **Conclusion:** Age should not be a limitation to determine which group of patients are those who should not undergo an oncological treatment; performance status and the presence of comorbidities are prognostic factors that should be considered in elderly patients with retroperitoneal sarcomas.

Key words: Retroperitoneal sarcomas. Elderly. Prognostic factors. Performance status.

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Introduction

The number of elderly patients diagnosed with cancer has dramatically increased in recent years. This has allowed for the knowledge on cancer biological behavior in this particular population group to be gradually increased, thereby improving oncological outcomes¹.

Soft tissue sarcomas (STS) are relatively infrequent tumors, which account for 1% to 2% of total cancer cases in adults². In the USA, an incidence of 12,310 new cases has been estimated for 2016, which will involve 4,990 deaths³. Approximately 10-20% of cases occur in the retroperitoneum, with a prevalence of 0.3-0.4 cases/100,000 population⁴. The prognosis of patients with retroperitoneal sarcomas (RPS) is poor, with a 5-year overall survival (OS) of 30.5% and a natural history of disease recurrence⁵. Out of total STS cases, 30-43.5% are reported to occur in patients older than 60 years, with only 15% being located in the retroperitoneum⁶.

Owing to retroperitoneal anatomy, patients are often asymptomatic for prolonged periods. In addition, elderly patients' performance status and comorbidities favor late diagnoses, which lead to adverse oncological and functional outcomes. In general, average tumor size at diagnosis is 15-18 cm⁶⁻⁹. The cornerstone of treatment is based on the possibility of performing resections with negative margins (currently defined as R0-R1), with adjuvant treatment with radiotherapy added¹⁰. However, the proximity of some structures, such as large vessels, the kidneys, the liver, etc., limits the possibility of increasing the resection margins and the possibility of administering adjuvant treatment with radiotherapy owing to at-risk organs' tolerance^{8,9}. The use of systemic treatment is restricted to metastatic disease or to some types of histology, such as synovial sarcoma¹¹. One of the most important prognostic factors in RPS is tumor grade, and two thirds of the patients tend to have intermediate-high grade neoplasms, which increases the risk of local and distant recurrence¹². Low-grade tumors rarely cause distant metastasis, and when they recur, it tends to be locally^{13,14}.

Currently, there is little information on RPS prognostic factors in the elderly, with most conclusions being based on extrapolated results from other tumors and/or sarcomas of the extremities. The purpose of this review is to assess the prognostic factors in terms of disease-free interval (DFI) and overall survival (OS) in a series of cases treated at the National Institute of Cancerology of Mexico.

Material and Methods

Analytical, retrospective, observational study of elderly patients (> 65 years, according to the World Health Organization definition) diagnosed with RPS and treated at the National Institute of Cancerology of Mexico in the period comprised from January 1, 2005 to December 31, 2014. Patients diagnosed with retroperitoneal tumors of non-mesenchymal origin (lymphoma, germ cell tumors and adrenal tumors) were excluded from the study.

All patients received follow-up after the last cancer treatment every 3-4 months during the first two years, then every 6 months until 5 years and then annually. Follow-up was carried out by physical examination at each control visit, in addition to a computed tomography or magnetic resonance imaging every six months or in case recurrence was suspected.

The decision on patients' treatment was made by a multidisciplinary team that included a surgical oncologist, a radiotherapist, a medical oncologist, an oncology pathologist and an imaging specialist. A group of expert pathologists carried out the review of the specimens, with tumor grade being determined according to the *Fédération Nationale des Centres de Lutte Contre le Cancer* (FNCLCC) criteria.

Demographic variables such as gender and age, comorbidities, performance status as assessed with the scale designed by the Eastern Cooperative Oncology Group (ECOG), symptomatology, histological type, tumor grade, clinical stage using the American Joint Committee on Cancer staging system (AJCC 8th edition), type of treatment, complications, DFI and OS were analyzed. OS was estimated using the Kaplan-Meier method, and tumor size, performance status, comorbidities, tumor grade and resection status were compared using the log-rank test. A p-value < 0.05 considered statistically significant. The statistical analysis was carried out using the statistical program SPSS® v.22.0.

Results

Twenty-five patients were obtained, 16 men (64%) and 9 women (36%), with a median age of 69.3 years (range: 65-82 years). The most common symptom was the presence of palpable abdominal mass in 11 cases (44%), followed by abdominal pain and nonspecific abdominal discomfort (20 and 24% respectively). The time from the onset of symptoms to treatment initiation was 6 months (range: 1-36 months). No patient had metastatic disease at diagnosis. ECOG-assessed performance status was

0 in 10 cases (46%), 1 in 6 (24%) and 2 in 9 (36%). All patients underwent exploratory laparotomy with curative intent; 10 (40%), simple resection, 9 (36%), wide resection and 6 (24%) were considered unresectable.

Complete resection (no macroscopic disease) was achieved in 19 cases (74%), with multi-visceral resection being performed in nine cases (36%). The organ that most frequently was resected was the kidney in six cases (24%), followed by the colon in five cases (20%) and the spleen in three cases (12%); in six cases, more than two organs were resected (Table 1). Four patients received adjuvant radiotherapy; two, chemotherapy and radiotherapy, and one, chemotherapy; the rest was left on surveillance. Median tumor size was 24.4 cm (8-61 cm). The most common histology was liposarcoma; 80% of cases were high-grade tumors and 76% of cases were at clinical stage III (AJCC 2010); nine cases had local recurrence and no patient had distant recurrence. Median follow-up was 18.7 months (1-74 months). OS at one year was 52%, at three years 19%, and at five years 12% (Fig. 1). OS was 34.6 months (20.86-48.40 months) for patients with ECOG < 1 and 3.44 months (1.68-5.2 months) for those with ECOG > 1. In the multivariate analysis, ECOG-measured performance status, the presence of comorbidities and resection status were associated with shorter OS, whereas tumor grade was not (Table 2).

Discussion

Aging has been associated with an increase in neoplastic diseases, which, together with a deterioration in performance status, entails a dismal prognosis. Currently, with the improvement in cancer diagnosis and treatment, we see more frequently a group of elderly patients with longer OS and DFI; however, they only represent a minority. Little has been explored on which are the prognostic factors that more strongly impact on this group of patients. In our case series, we found that the presence of low performance status, comorbidities and unresectable lesions were associated with a worse prognosis, whereas some factors that are common in younger populations, such as tumor grade, size and clinical stage were not.

Surgical resection remains the mainstay of RPS treatment, ensuring disease-free resection margins as long as the structures to be resected can be sacrificed with the lowest possible morbidity. This point is highly important in elderly patients, because the combination of age and comorbidities in them has already left functional sequelae such as decreased glomerular filtration and intestinal motility and absorption alterations, among

Table 1. Demographic and retroperitoneal sarcoma characteristics in the elderly

Characteristics	N (%)
Gender	
Male	16 (64)
Female	9 (36)
Stage	
IB	4 (16)
IIB	2 (8)
III	19 (76)
Grade (FNCLCC)	
Grade 1	4 (16)
Grade 2	2 (8)
Grade 3	19 (76)
Histology	
Liposarcoma	17 (68)
MPNST	3 (12)
Leiomyosarcoma	2 (8)
Undifferentiated pleomorphic sarcoma	2 (8)
Other	1 (4)
ECOG	
≤1	16 (64)
>1	9 (36)
Comorbidity	
HBP	8 (32)
DM2	6 (24)
HBP/DM2	6 (24)
Pneumopathy	1 (4)
None	4 (16)
Resection	
Marginal	10 (40)
Wide*	9 (36)
Irresectable	6 (24)
No. of resected organs	
1	3 (12)
2	4 (16)
3	1 (4)
4	1 (4)
Resected organ	
Kidney	6 (24)
Colon	5 (20)
Spleen	3 (12)
Pancreas	2 (8)
Ileum	1 (4)
Adjuvant treatment	
No	18 (72)
RT	4 (16)
CT	1 (4)
CT/RT	2 (8)
Recurrence	
Yes	9 (36)
No	16 (64)

*Multi-visceral resections and compartmentectomies are included.
 FNCLCC: Fédération Nationale des Centres de Lutte Contre le Cancer;
 MPNST: malignant peripheral nerve sheath tumor; HBP: high blood pressure;
 DM2: type 2 diabetes mellitus; RT: radiotherapy; CT: chemotherapy.

others. These factors are always important when making treatment decisions, since if the resection is going to

Figure 1. Kaplan-Meier curves for overall survival (A), ECOG (B), comorbidities (C) and resection status (D).

Table 2. Multivariate analysis of retroperitoneal sarcoma in the elderly

Variable	Median (months)	95% CI	P
Performance status			
ECOG <1	34.63	20.86-48.4	<0.001
ECOG >1	3.44	1.68-5.2	
Comorbidities			
None	63	44.3-81.6	0.038
HBP	17.4	12.7-22.01	
DM2	11	2.06-19.93	
HBP/DM2	13.66	0.0-34.19	
FNCLCC grade			
G1	8.6	0.0-17.7	NS
G2	26	0.0-53.7	
G3	23.86	12.08-35.6	
Resection			
Unresectable	3.5	1.42-5.57	<0.001
Complete	33.4	19.19-47.66	

FNCLCC: Fédération Nationale des Centres de Lutte Contre le Cancer; HBP: high blood pressure; DM2: type 2 diabetes mellitus.

worsen the performance status or be incompatible with life, even if the lesion is susceptible to surgical resection, the best medical support should be preferred. It is

important always taking into account that, due to all this, elderly patients tend to have longer hospital stays and, consequently, an increased risk for acquiring infectious diseases or developing neuropsychiatric disorders such as delirium, etc. All these factors should be taken into account for treatment assessment. Within the group of patients we evaluated, we can see that the presence of a low preoperative performance status and comorbidities are closely related to a poor prognosis^{7,15,16}.

Most studies in the literature have shown that patients who underwent complete resection (R0/R1) had better OS and DFI regardless of age, as demonstrated in our series, with complete resection being established as a prognostic factor when compared with resections where residual macroscopic disease was observed¹²⁻¹⁷.

The main variables that have been observed to be associated with OS decrease are age, male gender, grade, adjacent organ involvement and tumor grade, although, in our study, they showed no statistical significance. Another important point is adjuvant treatment, particularly radiotherapy, which has been shown to prolong DFI, although in our study, probably because of the small number of subjects that received it, adjuvant treatment had no impact¹⁷⁻²¹.

We emphasize that a low performance status and the presence of comorbidities are associated with a worse prognosis in elderly patients with RPS. The present study has several limitations, such as the small sample size (owing to the low incidence of the disease). It is a retrospective study, which should give cause for the conduction of prospective studies on the subject.

Conclusion

The increase in life expectancy of the world population and, consequently, the increase in the incidence of cancer in elderly populations, and in particular RPS, forces us to determine which group of patients benefit from multimodal treatment versus the best medical support. We suggest that patients with low performance status or uncontrolled comorbidities do not benefit from multimodal treatment. In addition, we consider that, in order to improve the results, oncogeriatric units should be added to the multimodal oncological treatment teams.

Conflict of interests

The authors declare not having any conflict of interest.

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